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Secular trends in blood pressure trajectories in Chinese children and adolescents: the impact of changing physical growth

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Abstract:	Background: Globally, 80% of cardiovascular disease (CVD) occur in low-/middle-income countries. High blood pressure (BP), a major risk factor for CVD, has its origins in early-life. We investigated how age trajectories of BP (childhood to late-adolescence) have changed recently in China and the mediating roles of physical growth. Methods: Using the longitudinal data on 3,785 children from the China Health and Nutrition Survey 1991-2015, we estimated mean BP trajectories (7 to 18y) for cohorts born in 1981-85, 1986-90, 1991-95, and 1996-2000 using random effect models. Models were adjusted for BMI and/or height growth to assess their impact on BP trends. Results: BP trajectories shifted upwards across cohorts. Compared to the earliest cohort, mean BP was higher in the latest cohort throughout childhood to late adolescence. For example, the increment in systolic BP was 4.4mmHg[95% CI: 2.9-5.8] in boys and 4.0mmHg[2.6-5.5] in girls at 9y, narrowed slightly during adolescence, and was 3.0mmHg[0.7-5.4] and 2.6mmHg[0.4-4.8] respectively at 17y. BMI and height trajectories also shifted upwards. The overall increment was greater for height than BMI. When adjusting for physical growth, the increment in BP trajectories reduced (more for height than BMI), but remained in childhood (p<0.05). Conclusions: The upward shift of BP trajectories among Chinese youths was largely explained by trends in physical growth, especially increasing height. Other early-life factors might have also contributed to the BP trends. Substantial increases in mean BP in children within a short time frame is a public health concern and will affect future CVD, especially in the developing world.

Abbreviations definition list

Abbreviations

CVD: cardiovascular disease

BP: blood pressure

SBP: systolic blood pressure

DBP: diastolic blood pressure

CHNS: China Health and Nutrition Survey

BMI: body mass index

CI: confidence interval

Condensed Abstract

Using longitudinal data on 5,118 children/adolescents from the China Health and Nutrition Survey 1991-2015, we demonstrated that age trajectories (7-18y) of blood pressure (BP) shifted upwards across cohorts born in 1981-85, 1986-90, 1991-95, and 1996-2000. Mean systolic BP was greater in the latest than earliest cohort by ≥4mmHg at 9y, narrowed to ≤3mmHg at 17y. The upward-shift of BP trajectories was largely explained by increasing height and BMI growth. Other early-life factors might also play a role. Increases in mean BP in children within a short time frame is a public health concern and will affect future CVD.

Title page

Secular trends in blood pressure trajectories in Chinese children and adolescents: the impact of changing physical growth

Short title: Trends in blood pressure in Chinese children

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Abstract

Background: Globally, 80% of cardiovascular disease (CVD) occur in low-/middle-income countries. High blood pressure (BP), a major risk factor for CVD, has its origins in early-life. We investigated how age trajectories of BP (childhood to late-adolescence) have changed recently in China and the mediating roles of physical growth.

Methods: Using the longitudinal data on ~~5,118~~3,785 children ~~with repeated follow-up measures~~ from the China Health and Nutrition Survey 1991-2015, we estimated mean BP trajectories (7 to 18y) for cohorts born in 1981-85, 1986-90, 1991-95, and 1996-2000 using random effect models. Models were adjusted for BMI and/or height growth to assess their impact on BP trends.

Results: BP trajectories shifted upwards across cohorts. Compared to the earliest cohort, mean BP was higher in the latest cohort throughout childhood to late adolescence. For example, the increment in systolic BP was 4.4~~3.9~~mmHg[95% CI: 2.9~~6~~-5.8~~3~~] in boys and 4.0mmHg[2.6-5.~~3~~5] in girls at 9y, narrowed slightly during adolescence, and was 3.0~~2.7~~mmHg[0.7~~5~~-5.4~~4.9~~] and 2.~~3~~6mmHg[0.4~~3~~-4.8~~3~~] respectively at 17y. BMI and height trajectories also shifted upwards. The overall increment was greater for height than BMI. When adjusting for physical growth, the increment in BP trajectories reduced (more for height than BMI), but remained in childhood (p<0.05).

Conclusions: The upward shift of BP trajectories among Chinese youths was largely explained by trends in physical growth, especially increasing height. Other early-life factors might have also contributed to the BP trends. Substantial increases in mean BP in children within a short time frame is a public health concern and will affect future CVD, especially in the developing world.

Keywords: Blood pressure trajectories, physical growth, BMI trajectories, height trajectories, Chinese children and adolescents

Introduction

High blood pressure (BP) is a major modifiable risk factor for adult cardiovascular disease (CVD), one of the leading causes of premature mortality globally[1]. Over three quarters of CVD-related deaths occur in low-/middle-income countries[2,3]. A recent analysis of data from 1479 population-based studies in 200 countries/territories showed that mean BP for adults has decreased in many high-income countries, but increased among East/Southeast Asian countries in recent decades[4]. Increases in BP in some low-/middle-income countries have been attributed to increasing urbanization, poor provision of antihypertensive management, unhealthy lifestyle, and population ageing[4].

BP tracks from childhood into adulthood[5]. Elevated BP in children or adolescents is associated with surrogate markers for future CVD[6,7], thus increasing the risk of CVD and mortality in adulthood[8]. In addition, risk factors for high BP in childhood tend to persist into adulthood. Therefore, secular trends in childhood BP, which is little affected by antihypertensive treatment (unlike in adults), and its risk factors can provide crucial evidence for the early prevention of adult CVD. Yet, trends in childhood BP are not well described, especially from developing countries. A recent systematic review has found little change in mean BP in children and adolescents in high-income countries (1963-2012), but inconsistent trends in middle-income countries based on five studies[9]. Discrepancies in BP trends for children may be partly due to the heterogeneity in methods of BP measurement (e.g. device, number of readings) and adjustments (e.g. for age, height) over time and across studies. As limited data are available from low-/middle-income countries, there is a need to supplement current evidence on BP trends in children with recent studies from developing countries, like China. China has experienced rapid economic growth, which has brought changes in health behaviours such as increases in the intake of high-calorie foods and sedentary lifestyle. These changes have contributed to increases in obesity among all ages[10] and adult hypertension in the Chinese population[11].

Obesity, an important risk factor for raised BP[12], has increased among all ages in recent decades in China[10], and it is reasonable to assume that this could have contributed to increasing BP in Chinese children. However, the limited studies of BP trends in Chinese children have shown conflicting findings. A fluctuated trend in mean BP has been found in Chinese students (1995-2014)[13], whereas increases in mean BP levels and elevated BP (or hypertension) have been reported in children and adolescents in the China Health and Nutrition Survey (CHNS) (1995-2011)[14-16]. It is known that BP levels increase with age, especially during childhood. These studies did not examine how age trajectories of BP have changed over time. Childhood development of BP, which is closely related to physical growth[17,18], provides important information about the development of CVD risk[19].

There is a lack of evidence on the impact of changing nutritional status on age trajectories of BP in children of low-/mid-income countries. Using the CHNS from 1991 to the most recent sweep in 2015, we aimed to examine (1) whether child-to-late adolescent trajectories of BP have changed in recent decades among Chinese children; (2) how growth trajectories of BMI and height (indicators of nutritional status) have changed during the same period; and (3) whether changes in growth trajectories explain changes in BP trajectories.

Methods

Study population

We used data from the China Health and Nutrition Survey (CHNS), an ongoing mixed longitudinal household survey with sweeps in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, and 2015[20]. Nine provinces (Guangxi, Guizhou, Henan, Hubei, Hunan, Jiangsu, Shandong, Heilongjiang, and Liaoning) were included in all sweeps. Three autonomous cities (Beijing, Chongqing and Shanghai) added from 2011 were not included in this study. A multistage random clustering sampling design was adopted to ensure adequate representation. Within each province, the capital city, a low-income city and four (one high-, two middle- and one low-income) counties were selected. Two urban and two suburban communities (from each city) or one township and three rural villages (from each county) were selected. Twenty households were chosen from each community, town or village. Since 1991, all members of the selected households have been included (1989-survey included only pre-school children and adults aged 20-45y). Physical examination was conducted in each sweep.

All participants provided written informed consent. The University of North Carolina and the Chinese Centre for Disease Control and Prevention reviewed and approved the data collection procedures. Details about CHNS[20] can be found at https://www.cpc.unc.edu/projects/china.

Measurements

Blood pressure: BP of children aged ≥7y was measured three times from the right arm in sitting position at 1-2 minute intervals after 10 minutes rest by trained health workers using a standard mercury sphygmomanometer. Systolic and diastolic BP (SBP and DBP) were identified by Korotkoff phase I and phase V (phase IV for those without phase V). The means of three SBP and DBP[16] were calculated.

Body sizes: Height (to the nearest 0.1cm) and weight (0.1kg) were measured with lightweight clothes and no shoes using a calibrated beam scale and a portable stadiometer respectively. Body mass index (BMI, kg/m^2) was calculated.

Study sample

Our analyses included 3,785~~5,118~~ children born between 1981-2000, who were 7-18y in surveys from 1991 to 2015 and had ~~who~~ two or more ~~ad~~ BP and/or body size measures. From the study sample, we derived four cohorts who were born in 5y intervals (1981-85, 1986-90, 1991-95 and 1996-2000).

Statistical analysis

We first derived internal z-scores for BP (gender-, age- and height-specific), BMI and height (gender- and age-specific) from the earliest (1981-85) cohort to allow comparisons of trends for different measures. We applied two-level (or random-effects) linear models to repeated measures of BP, BMI and height z-scores (measurements as level-1 units, clustered within level-2 units individuals) to estimate differences in mean values between the earliest and latest cohorts. We tested their trends across cohorts (i.e. changes in mean BP, BMI and height z-scores with each succeeding cohort).

Second, to assess how the age trajectories of BP have changed across cohorts, we explored fractional polynomial functions (first- to third-degree) to capture the non-linear curves for age-related BP trajectories. For SBP and DBP, the best-fitting fractional polynomials were cubic functions (age, age^2 and age^3 for boys; age and age^3 for girls) based on the mean square errors, Akaike information criterion and Bayesian information criterion, and the consistency of age terms across cohorts. As repeated BP measures (level-1) are correlated within individuals (level-2), we adopted the random intercept (α_{0j}) and random age term (β_{1j}) in the cubic model as follows:

$$BP_{ij} = \alpha_{0j} + \beta_{1j} age_{ij} + \beta_2 age_{ij}^2 + \beta_3 age_{ij}^3 + \sum_{k=2}^{4} \gamma_{ko} C_k + \sum_{k=2}^{4} \gamma_{k1} C_k \, age_{ij} + \sum_{k=1}^{4} \gamma_{k2} C_k \, Y_{jk} + \varepsilon_{ij},$$

where BP_{ij} is the measurement for individual j at time i, ε_{ij} is the residual error term, C_k (K=2, 3, 4) are dummy variables representing cohorts born in 1986-90, 1991-95 and 1996-2000 (baseline: cohort born in 1981-85), and Y_{jk} is the birth year for individual j in cohort K.

We also applied random-effects fractional polynomial models to estimate the age trajectories of BMI and height for each cohort and gender, and to assess whether they have changed across cohorts. The best-fitting fractional polynomials were age^2 and age^3 for BMI, and age^2, age^2·ln(age) and age^3 for height in both genders. The mean age trajectories of BP, BMI and height were plotted by cohort and gender to visualize their development throughout childhood to late-adolescence.

To assess the impact of trends in body sizes on changes in BP trajectories over time, models for SBP and DBP were adjusted in sequence for BMI only, height only, and BMI and height simultaneously (BMI and height z-scores were used). We estimated mean BP trajectories for the earliest (1981-85) and latest (1996-2000) cohorts and their differences across ages from unadjusted and adjusted models. To illustrate our findings, we provided estimates for differences in mean BP, BMI and height at specific ages (e.g. 7, 9, 13, and 17y).

To assess whether using different BP outcomes would affect the patterns of BP trajectories over time, we repeated the analyses using the average of the last two BP readings or the lowest two readings and found similar results as those using the average of three readings (data not shown). Thus we presented the latter here. As the distribution of BMI was slightly skewed, we repeated the analyses using log-transformed BMI. The trends in trajectories of geometric mean BMI (data not shown) were similar to those of the arithmetic mean (thus we showed the later here).

Due to the multi-stage sampling design of the CHNS, we explored the impact of community- and household-level clustering of BP measures on the estimated trends. We applied (1) four-level linear models to estimate differences in mean z-scores for BP and growth measures between the earliest and latest cohorts and tested their trends across cohorts and (2) four-level fractional polynomial models to examine how age trajectories of BP have changed across cohorts, with and without adjustment for physical growth. These analyses showed similar results as those estimated from two-level models. In addition, the proportion of the total variance in BP that was attributable to households (level-3) and communities (level-4) was modest (15-17% for SBP and DBP). Therefore, we presented results from two-level models.

As a sensitivity analysis, we repeated all the ~~primary analysis~~analyses including all (~~3785~~ n=5,118) children with one or more ~~who had two or more (≥2) repeated~~ BP and/or growth measurements to assess the impact of sample attrition.

All analyses were conducted in R 3.6.1. Packages *mfp*, *lme4* and *ggplot2* were used for fractional polynomial, mixed-effects modelling and figure acquisition respectively.

Results

The number of children in each cohort ranged from ~~835~~ 600 to ~~1767~~ 1276 (**Table 1**). Among 3,785~~5,118~~ children included in the analyses, ~~1743 (34.1%) had two and~~ 2042 (~~39.9~~53.9%) had three or more repeated outcome measures (**Supplementary Table S1**).

Age trajectories of blood pressure across cohorts

Mean SBP and DBP z-scores increased across cohorts, by 0.0~~6~~7 (95% CI: 0.04 to 0.09~~8~~) and 0.08~~7~~ (0.0~~.~~6~~5~~ to 0.~~09~~10) respectively for each successive cohort (**Table 1**). Mean trajectories of SBP and DBP shifted upwards, with later-born children having higher mean BP than their earlier-born counterparts (**Figure 1**). Compared to the earliest cohort, the latest cohort had greater mean SBP throughout childhood until late-adolescence (**Figure 3.1**). For example, the estimated increment was 4.4~~3.9~~mmHg (2.9~~6~~ to 5.~~3~~8) in boys and 4.0mmHg (2.6 to 5.~~3~~5) in girls at 9y. The slope of the curve for the difference in mean BP (corresponding to the y-axis to the right), which is <0, indicates that the slope of BP trajectories was greater in the earliest than latest cohort, i.e. the rate of increase in SBP with age was faster in the earliest cohort. Thus, the increment in mean SBP between cohorts narrowed slightly during adolescence, but remained at 3.0~~2.7~~mmHg (0.7~~5~~ to 5.4~~4.9~~) and 2.6~~3~~mmHg (0.4~~3~~ to 4.8~~3~~) respectively at 17y (**Table 2; Figure 3.1**). Mean trajectories of DBP also showed an upward trend and the increment (similar to that for SBP) was 4.0~~3.8~~mmHg (2.9~~8~~ to 5.1~~4.8~~) in boys and 3.9mmHg (2.8 to 5.1~~0~~) in girls at 9y, reduced to 2.7~~3~~mmHg (1.0~~0.7~~ to 4.4~~3.9~~) in boys and had no increment in girls at 17y (**Table 2; Figures 4.1**).

Age trajectories of body sizes

Mean BMI and height z-scores increased across cohorts, by 0.11 (0.08 to 0.13~~4~~) and 0.~~19~~20 (0.17 to 0.2~~1~~3) respectively for each successive cohort (**Table 1**). Mean trajectories for BMI and height also shifted upwards across cohorts (**Figures 2**). For example, between the earliest and latest cohorts, an increment of 0.8kg/m^2 in mean BMI in boys persisted throughout childhood to late-adolescence: 0.8kg/m^2 (0.5 to 1.1) at 9y, 0.8kg/m^2 (0.5 to 1.1) at 13y and 0.7~~8~~kg/m^2 (0.2~~3~~ to 1.2~~3~~) at 17y. In girls, the increment persisted in childhood: ~0.9kg/m^2 (0.6 to 1.2), narrowed during adolescence, and was 0.2kg/m^2 (-0.3 to 0.~~6~~7) at 17y, which was non-significant (**Figure 2.1**). The increment in mean height in boys widened in childhood: from 3.7~~8~~cm (2.5~~7~~ to 4.8) at 7y to 5.~~6~~8cm (4.7~~7~~ to 6.8~~6~~) at 13y and in girls, changed little in childhood: 3.8~~4.0~~cm (2.5~~9~~ to 5.~~2~~1) at 7y and 4.4~~5~~cm (3.4~~5~~ to 5.54) at 13y. The increment narrowed thereafter and was 4.3~~0~~cm (2.9~~7~~ to 5.7~~3~~) in boys and 2.~~2~~0cm (~~1.~~0.7 to 3.4) in girls at 17y (**Figure 2.2**). The overall trend was greater in height than in BMI: the average increment in height z-score was 0.58 (0.~~5~~49~~0~~ to 0.6~~6~~7), compared to 0.35~~7~~ (0.26~~8~~ to 0.4~~6~~5) in BMI z-score (**Table 1**).

Impact of changing body sizes on blood pressure trajectories across cohorts

When adjusting for measures of physical growth, the upward shift of mean BP trajectories reduced. The reduction was greater with adjustment for height than for BMI and the pattern was more evident in boys

(**Figures 3.2-3.3 & 4.2-4.3**). For example, in boys, the increment in mean SBP at 9y was 4.4~~3.9~~mmHg (2.9~~6~~ to 5.8~~3~~) between the earliest and latest cohorts, reduced to 3.~~3~~7mmHg (2.3~~0~~ to 5.2~~4.7~~) after adjusting for BMI only and to 2.7~~4~~mmHg (1.~~0~~3 to 4.2~~3.7~~) after adjusting for height only. In girls the increment reduced from 4.0mmHg (2.6 to 5.5~~3~~) to 3.~~3~~4mmHg (2.0~~1.9~~ to 4.~~7~~9) and 3.0mmHg (1.~~7~~6 to 4.4) respectively (**Table 2**).

When adjusting for both BMI and height, the increment in mean SBP reduced further and was non-significant from adolescence (i.e. 13.6~~5~~y in boys and 15.6y in girls) (**Figure 3.4**). For example, the adjusted increment was 2.3~~0~~mmHg (0.9~~7~~ to 3.7~~3~~) at 9y and 0.6mmHg (-1.7~~5~~ to 2.~~8~~9) at 17y in boys and correspondingly 2.5~~4~~mmHg (1.1 to 3.9~~8~~) and 1.6~~5~~mmHg (-0.5 to 3.~~4~~7) in girls (**Table 2**). Thus, the increment during childhood remained after the adjustments(*P*<0.05). For DBP trajectories, the impact of BMI and height showed similar patterns to SBP, except that the increment in mean DBP at 17 in girls reversed. This is likely due to the random error as the 95% CI contains the value zero (**Table 2, Figures 4.2-4.4**).

Sensitivity analysis

Trends in BP and body size (z-scores) across cohorts and the impact of changing body sizes on trends in BP trajectories for 5118 children (with ≥ ~~two~~one ~~repeated BP~~ measure~~s (n=3785~~) (**supplemental Table S3-S4, Figures S1-S4**) had similar patterns to those found in the study sample (n=~~5118~~3785 with ≥ two measures) (**Table1-2, Figures 1-4**).

Discussion

Using the longitudinal data on BP and physical growth of Chinese children spanning from 1991 to 2015, we found that the age trajectories of BP (7-18y) have shifted upwards. Between the earliest and latest cohorts, the increments in mean SBP and DBP were ~4mmHg in childhood and 2-3mmHg in late-adolescence (no increment in DBP in late-adolescence in girls). In addition, the trajectories of physical growth have shifted upwards, with greater increases in height than in BMI. The upward shift of BP trajectories was largely explained by physical growth, with a greater impact of increasing height than BMI, and in boys than in girls. Although the increments in BP narrowed slightly during adolescence, they remained in childhood after both height and BMI were accounted for.

Trends in blood pressure trajectories

Mean BP levels in children have changed little in high-income countries[15,21-24]. In low-/middle-income countries, however, the findings from limited studies are mixed[9,25]. An increasing trend in mean SBP has been found in children and adolescents (10-18y) from the Seychelles during 2006-2012[15], after a decrease during 1998-2006[15,25]. A fluctuating trend was also reported in the Chinese National Survey on Students'

Constitution and Health, where BP levels decreased from 1995 to 2005 and increased more recently from 2005 to 2014[13]. In the CHNS, previous studies showed increasing trends in BP in children during sub-periods, e.g. SBP and DBP increased by 4.7mmHg and 4mmHg respectively between 1991 and 2004[16] and by 6mmHg between 1991 and 2011[14]. Most existing studies on BP trends for children at different ages applied traditional regression models, adjusting for[15,16,24,25], or using z-scores standardized by[14,24,26] age, gender and/or height. In adults, a comparison of mean BP according to age by 10-year birth cohorts in the population-based Tromsø Study showed that adult BP trajectories have shifted downward[27,28]. However, few studies have explored how developmental trajectories of childhood BP have changed over time due to a lack of longitudinal data on BP from children born in different periods. In our study, we applied random-effect growth models to repeated BP measures in the CHNS and found large increments in mean SBP and DBP (~4-5mmHg) in childhood for those born up to 20y apart. The increments were smaller by late-adolescence due to a slower increase in BP with age in the latest cohort. An upward trend in BP trajectories in Chinese children has not been previously reported, and therefore our study adds important evidence concerning secular trends in the childhood development of BP.

Trends in growth trajectories

Our study shows upward shifts of BMI and height trajectories towards high BMI and taller stature across successive cohorts. The trend of increasing childhood BMI in many high-income countries has flattened in recent years, but continues in parts of Asia[29]. Studies of recent trends in childhood height, especially height trajectories, are sparse. One study compared four longitudinal British birth cohorts and showed substantial increases in child-to-adolescent trajectories of BMI and height between cohorts born in 1970 or earlier and the cohort born in 2000-01[30]. We found greater trends in height trajectories than in BMI trajectories. A large increase in childhood height (~4cm) over a short period reflects recent economic development and improving living standards in China[31].

In our study, height increments between the earliest and latest cohorts widened in childhood and were greater around puberty (more evident in girls). For BMI, the increment was similar across ages in boys and narrowed in late-adolescence in girls. A similar pattern was reported in a cross-sectional study where the increase per decade in mean height (1975-2010) was 3.8cm in 12y Chinese boys and 3.0cm in 11y Chinese girls, compared to 1.3cm and 0.8cm respectively at 18y[31]. In our study, the respective increase per decade was 3.7cm at 12y in boys and 3.0~~1~~cm at 11y in girls, and 2.2~~0~~cm and 0.6~~8~~cm at 18y in boys and girls respectively (data not shown). The smaller increment post puberty may suggest earlier maturation in Chinese children born more recently, as found in other studies[31,32]. In the CHNS there was no information on pubertal development for boys and only <30% of girls reported age of menarche, thus we are unable to verify in this study.

Impact of changing physical growth on BP trajectories

In our study, trends of BP trajectories were largely explained by changes in physical growth, especially the increasing height and possibly, tempo of growth. The contribution of childhood growth to BP trends varied across populations[24]. In the UK, a study showed that BMI explained ~15% of increase in childhood SBP between 1980-2004[33]. In the US National Health and Nutrition Examination Surveys (NHANES), BMI explained 29% of the increment in mean SBP between 1988/94 and 1999/2000[34]. Another study using ~~Using~~ the serial of cross-sectional samples from the NHANES (1976-2008) ~~, Zachariah et al~~ found that 32% of the increasing trend for mean pulse pressure was explained by the increase in BMI in children aged 8-17y[35]. However, in some countries, there was little increase in childhood BP despite the rise in obesity during recent decades [15,21,22,26]. A study of Chinese students found that the prevalence of high BP remained relatively stable during 1995-2014 while overweight prevalence increased dramatically[13]. Mean height has increased substantially among Chinese children in recent years. Yet, no study has investigated the effect of increasing height on BP trends, especially in comparison to the effect of rising BMI. In our study, the impact of height growth (accounting for 48% and 24% of SBP increment in boys and girls) was greater than that of BMI growth (20% and 16% respectively), possibly due to greater trends for height trajectories than BMI trajectories.

The increments in BP between the earliest and latest cohorts were greater in childhood than in late-adolescence (i.e. narrowed during adolescence). This pattern was also seen for BMI and height trajectories in girls (not boys), as later born boys had greater increments in BMI and height during adolescence. When BMI and/or height were adjusted for, the increment in BP at 17y was no longer significant (for DBP it reversed in girls, possibly due to the random error).

Nevertheless, changes in other early-life factors may have also contributed to the BP trends, given the increments in mean BP being evident by age 7 years even when BMI and height were accounted for. In China, undernutrition has become less common, whereas overnutrition has become more ~~common~~prevalent, with rapid urbanization and changes in lifestyles[36]. For example, decreases in physical activity[37], increases in sedentary behaviours (e.g. screen time)[38], daily fat intake[39] and unhealthy snacking behaviour[40] may have played a role in the rising BP trend in Chinese children, independent of their impact on trends in physical growth. Low birthweight, non-breastfeeding and maternal hypertension may be associated with elevated childhood BP[41,42]. High sodium intake, a putative risk factor for hypertension and stroke in adults[43,44], is high among the Chinese population~~ (e.g. from salt and soy sauce)~~. A recent meta-analysis[45] showed that sodium intake among Chinese children was double and potassium was less than half of WHO recommendations. In the CHNS, children were not followed from birth. There was limited information on peri~~re~~natal or early-life factors, and thus we are unable to examine their impacts.

Strengths and limitations

Our study has several strengths: **First**, CHNS is the first large longitudinal survey in China. Nine provinces included in the study representing 41% of the Chinese population and regions at different stages of economic development. **Second**, participants were followed-up in 10 sweeps over 26 years, with 74% children having ≥2 repeated measures, allowing us to investigate age trajectories of BP, BMI and height over time. **Third**, height, weight and BP were measured consistently across sweeps, thus the bias due to differences in measurements methods across cohorts was minimized. **Fourth**, random-effects models applied here account for ~~correlations~~ within individuals~~,~~ correlations and ~~and~~ allow the inclusion of individuals with different number and timing of measurements~~, or with incomplete data (e.g. children with a single measure). The models provide efficient parameter estimates when data is missing at random~~[46]. ~~In our study, mean BP, BMI and height of children i.e. with ≥2 measures were close to the respective mean values for children in the study sample. Thus, there is little evidence to suggest that missingness is not at random regarding BP and growth measures. Further sensitivity analysis of all children showed similar findings as those presented here.~~

However, there are also limitations. Despite the large sample size, there is a relatively small number of older adolescents in the latest cohort, which might explain the wider 95% CIs for the predicted BP trajectories for this age range. However, this limitation can be addressed using future CHNS sweeps.

Conclusions

The age-related BP trajectories have shifted upwards in Chinese children during 1991-2015. While improved nutrition, indicated by increasing height, and to a lesser extent increasing BMI, accounted for part of the BP trends, the increment in BP remained in childhood to early-adolescence. Further research is warranted to investigate changes in early-life factors beyond increases in BMI and height that have contributed to the BP trends in Chinese children. Increases in mean BP in children within a short time frame is a public health concern as it will impact future CVD risk in the long term, particularly in the developing world.

Affiliations

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Tables and Figures

Table 1. Mean (95% CI) z-scores for BP and body size measures for each cohort and trends across cohorts estimated from 2-level models* (N=3785 children with repeated measures)

Cohort	N†	z-SBP‡	z-DBP‡	z-BMI‡	z-height‡
	3785	0.08 (0.06, 0.10)	0.09 (0.07, 0.11)	0.12 (0.09, 0.14)	0.22 (0.20, 0.24)
1981-85	1253	-0.01 (-0.05, 0.03)	-0.01 (-0.05, 0.03)	0 (-0.04, 0.05)	0.01 (-0.04, 0.06)
1986-90	1276	0.1 (0.06, 0.15)	0.1 (0.06, 0.14)	0.11 (0.06, 0.17)	0.2 (0.15, 0.25)
1991-95	656	0.08 (0.02, 0.14)	0.13 (0.08, 0.19)	0.14 (0.07, 0.22)	0.43 (0.36, 0.5)
1996-2000	600	0.21 (0.15, 0.28)	0.25 (0.19, 0.31)	0.36 (0.26, 0.46)	0.59 (0.52, 0.67)
Difference ~		0.22 (0.15, 0.3)	0.26 (0.19, 0.33)	0.35 (0.26, 0.45)	0.58 (0.49, 0.67)
Trends #		0.07 (0.04, 0.09)	0.08 (0.06, 0.1)	0.11 (0.08, 0.13)	0.2 (0.17, 0.23)

Abbreviations: CI: confidence interval; SBP: systolic BP; DBP: diastolic BP; BMI: body mass index

* All values were estimated from 2-level models (level-1: measurement; level-2: individual)

† Sample size for children with BP, and/or growth measures, children with ≥2 repeated measures (N=3785)

‡ z-scores of BP, BMI and height were derived from the earliest (1981-85) cohort

~ Difference (in mean z-score) between the earliest and latest (1996-2000) cohorts

Trends in mean BP, BMI and height z-scores across cohorts, i.e. changes in mean values with each successive cohort

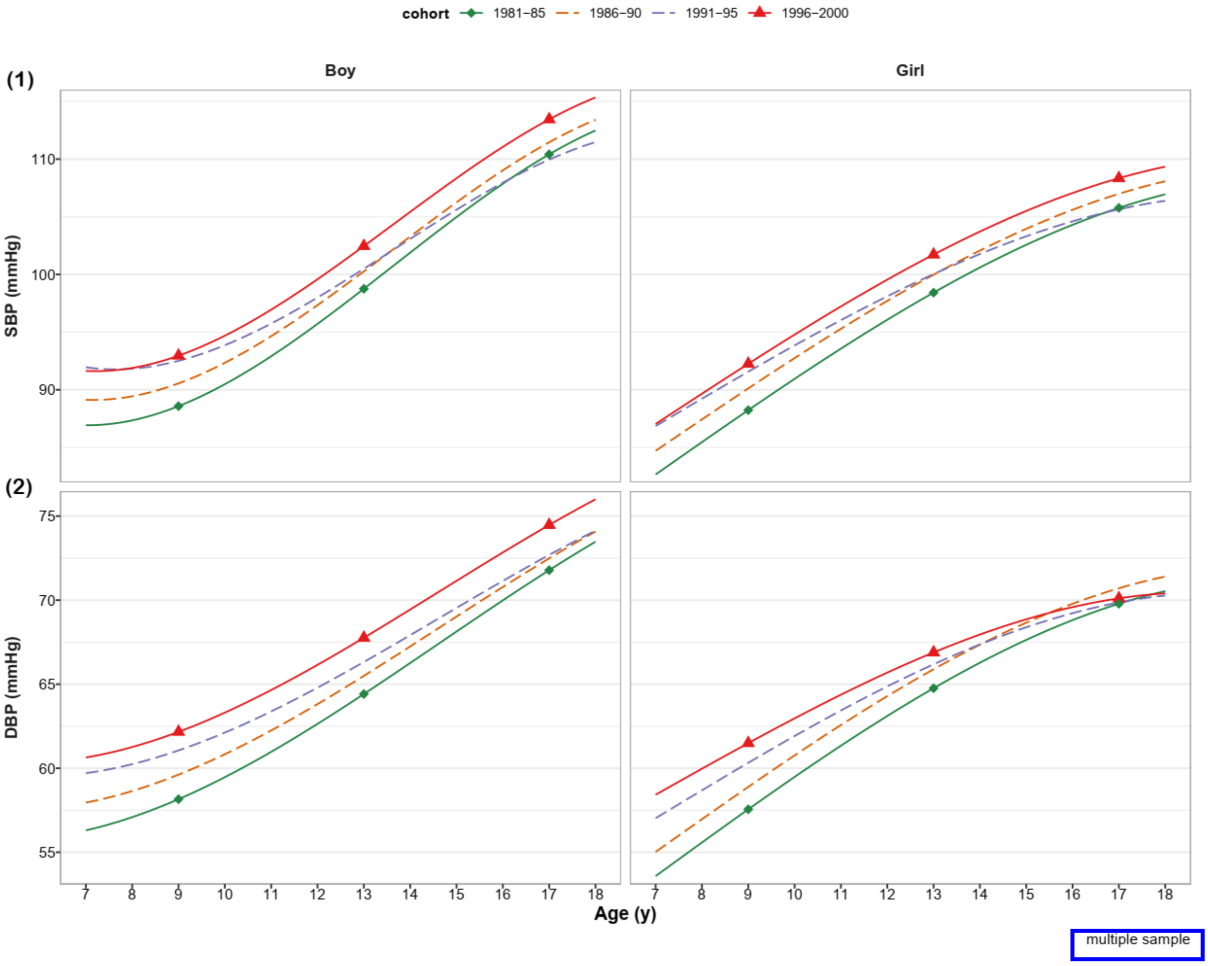
Table 2. Differences in mean SBP and DBP (95% CI) at ages 7, 9, 13, and 17y between the earliest and latest cohorts in boys & girls with adjustment for (1) none, (2) BMI, (3) height, (4) BMI and height * (N=3785)

		SBP (mmHg)		
Boys-adjusted for	**7y**	**9y**	**13y**	**17y**
(1) none	4.7(2.7,6.7)	4.4(2.9,5.8)	3.7(2.4,5)	3(0.7,5.4)
(2) BMI	4.1(2.1,6.1)	3.7(2.3,5.2)	3(1.8,4.2)	2.2(-0.1,4.6)
(3) height	3.1(1.1,5.1)	2.7(1.3,4.2)	2(0.7,3.2)	1.2(-1.1,3.6)
(4) BMI and height	2.7(0.7,4.7)	2.3(0.9,3.7)	1.5(0.2,2.7)	0.6(-1.7,2.9)
Girls-adjusted for				
(1) none	4.4(2.4,6.3)	4(2.6,5.5)	3.3(2.1,4.5)	2.6(0.4,4.8)
(2) BMI	3.7(1.8,5.7)	3.4(2,4.9)	2.8(1.6,4)	2.1(0,4.3)
(3) height	3.3(1.3,5.2)	3(1.6,4.4)	2.5(1.3,3.7)	2(-0.2,4.2)
(4) BMI and height	2.7(0.8,4.7)	2.5(1.1,3.9)	2.1(0.9,3.2)	1.6(-0.5,3.7)
Boys-adjusted for		**DBP (mmHg)**		
(1) none	4.3(2.9,5.8)	4(2.9,5.1)	3.3(2.4,4.3)	2.7(1,4.4)
(2) BMI	3.9(2.4,5.4)	3.6(2.5,4.6)	2.8(1.9,3.8)	2.1(0.4,3.8)
(3) height	3.4(1.9,4.9)	3(1.9,4.1)	2.3(1.3,3.2)	1.6(-0.2,3.3)
(4) BMI and height	3(1.6,4.5)	2.7(1.6,3.7)	1.9(1,2.8)	1.1(-0.6,2.8)
Girls-adjusted for				
(1) none	4.8(3.2,6.4)	3.9(2.8,5.1)	2.1(1.2,3.1)	0.3(-1.4,2.1)
(2) BMI	4.3(2.7,5.9)	3.5(2.3,4.6)	1.7(0.8,2.7)	0(-1.7,1.7)
(3) height	4(2.4,5.7)	3.2(2,4.4)	1.6(0.6,2.5)	-0.1(-1.8,1.6)
(4) BMI and height	3.7(2.1,5.3)	2.9(1.7,4)	1.2(0.3,2.2)	-0.4(-2.1,1.3)

Abbreviations: CI: confidence interval; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index

* Differences were estimated using random-effects fractional polynomial models, adjustments were made for BMI and height z-scores using first cohort.

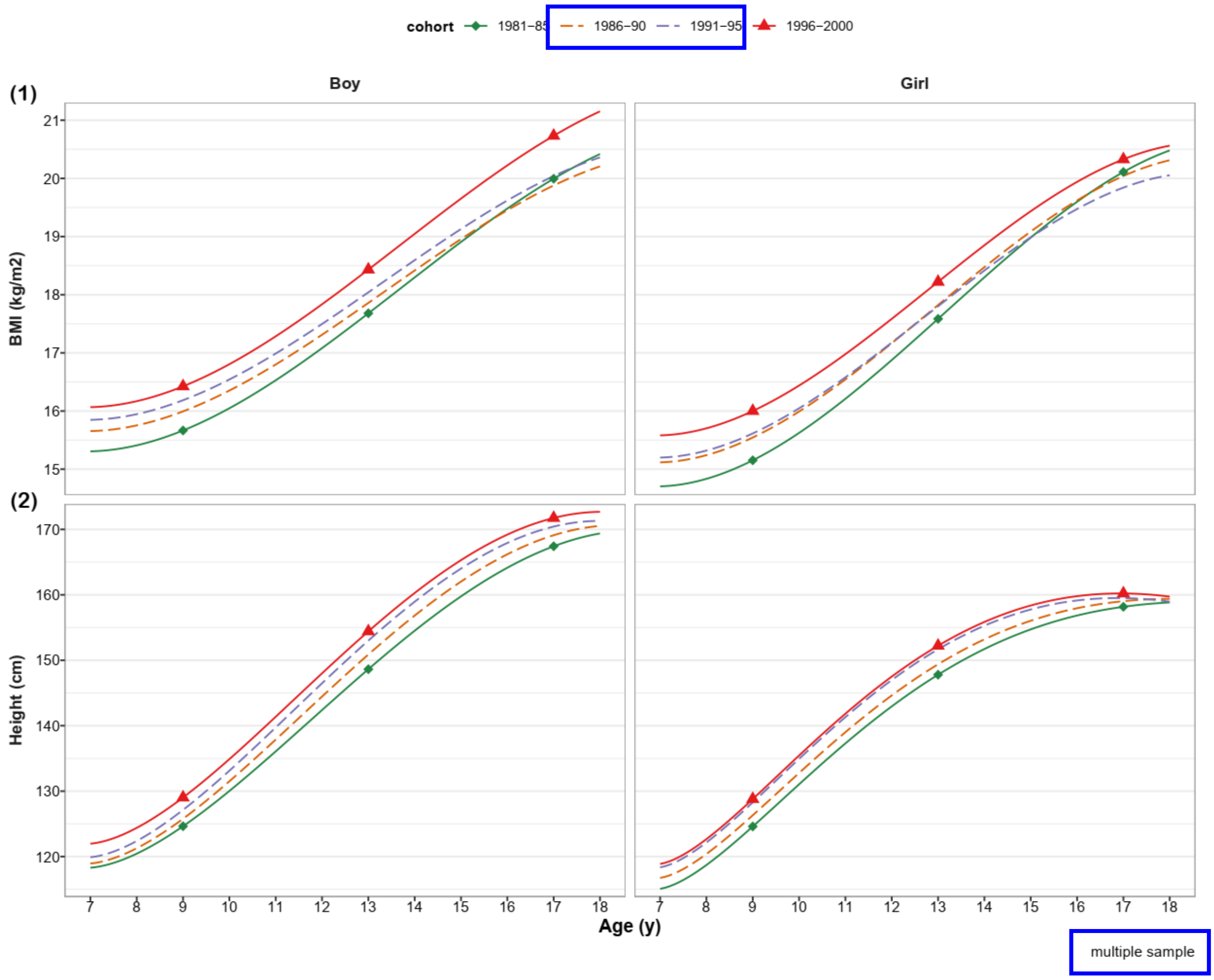
Figure 1. Mean trajectories of SBP and DBP for each cohort in boys & girls* (N=3785)



Abbreviations: SBP: systolic blood pressure; DBP: diastolic blood pressure.

* Mean age trajectories for four cohorts were estimated using random-effects fractional polynomial models.

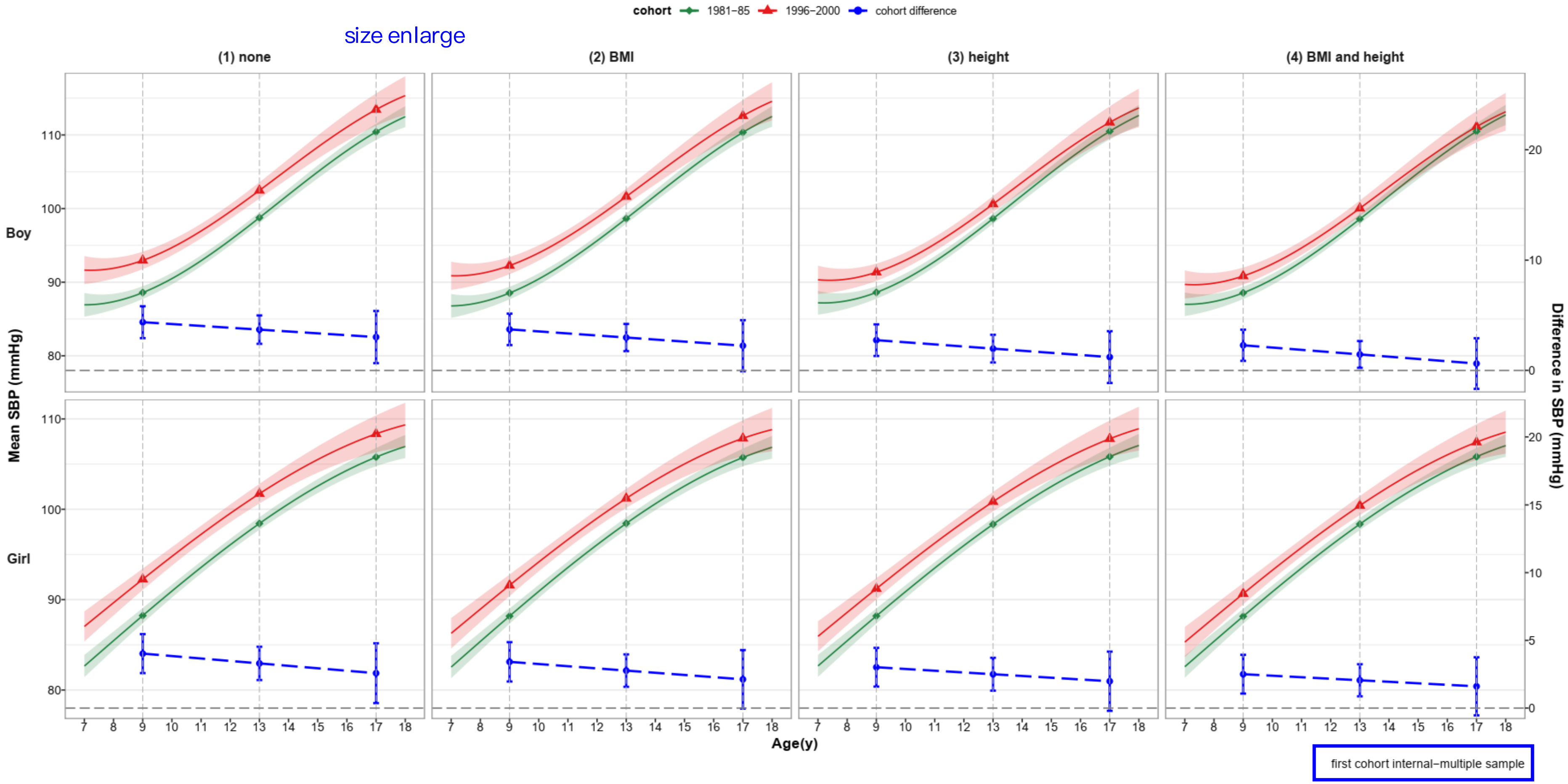
Figure 2. Mean trajectories of BMI and height for each cohort in boys & girls* (N=3785)



Abbreviations: BMI: body mass index.

* Mean age trajectories for four cohorts were estimated using random-effects fractional polynomial models.

Figure 3. Mean trajectories of SBP and differences (95% CI) between earliest and latest cohorts in boys & girls with adjustment for (1) none, (2) BMI, (3) height, (4) BMI and height *



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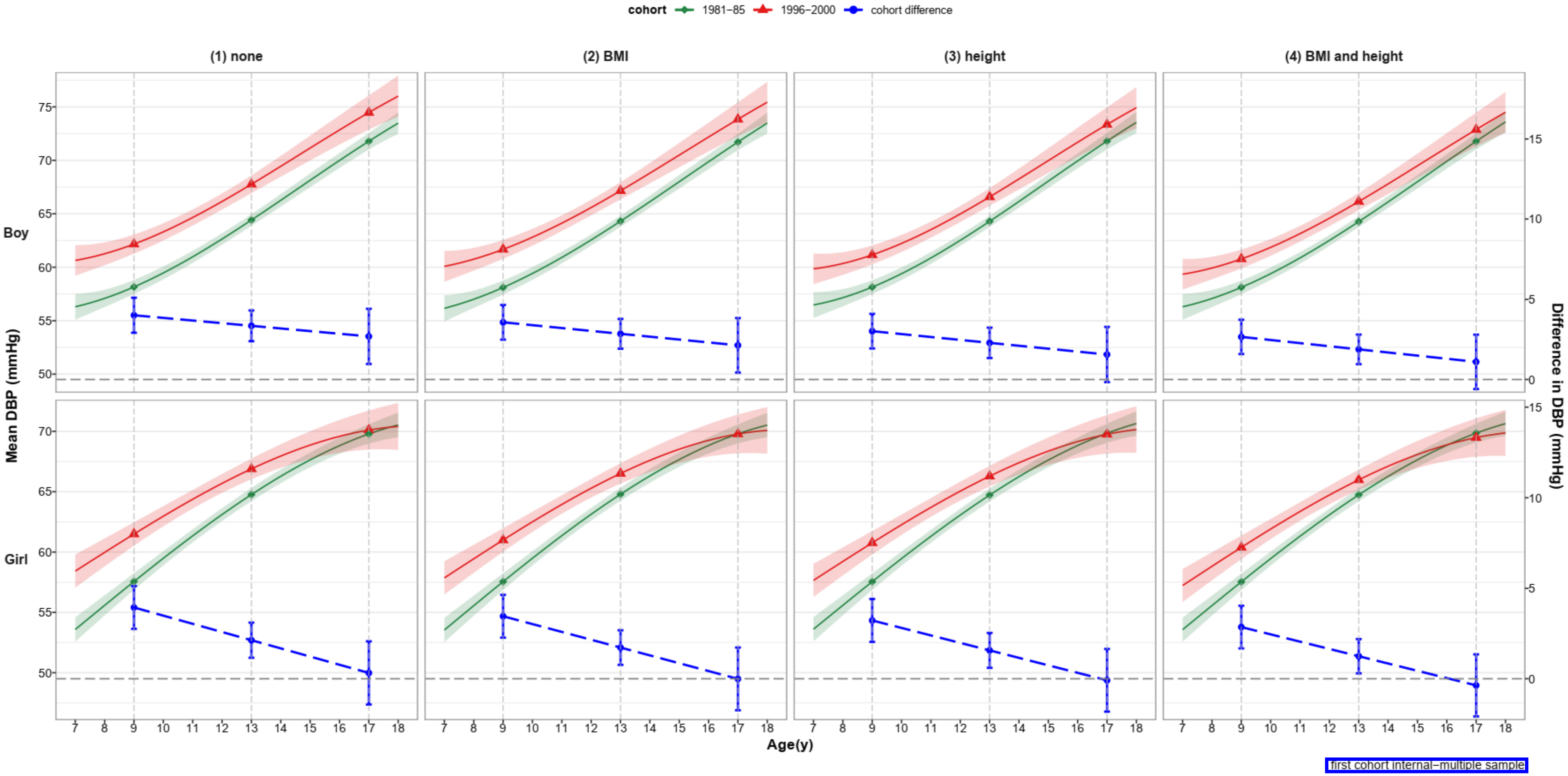
first cohort internal–multiple sample

Abbreviations: CI: confidence interval; SBP: systolic blood pressure; BMI: body mass index.

* Mean trajectories for the earliest and latest cohorts were estimated using random-effects fractional polynomial models, adjustments were made for BMI and height z-scores using first cohort.

Figure 4. Mean trajectories of DBP and differences (95% CI) between earliest and latest cohorts in boys & girls with adjustment for (1) none, (2) BMI, (3) height, (4) BMI and height *



Abbreviations: CI: confidence interval; DBP: diastolic blood pressure; BMI: body mass index.

* Mean trajectories for the earliest and latest cohorts were estimated using random-effects fractional polynomial models, adjustments were made for BMI and height z-scores using first cohort.