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Impact of early growth on blood pressure from childhood to adulthood: birth-twenty cohort

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Original Article

Association Between Early Life Growth and Blood Pressure Trajectories in Black South African Children

Juliana Kagura, Linda S. Adair, Richard J. Munthali, John M. Pettifor, Shane A. Norris

Abstract—Early growth is associated with blood pressure measured on one occasion, but whether early life growth patterns are associated with longitudinal blood pressure trajectories is under-researched. Therefore, we sought to examine the association between early growth and blood pressure trajectories from childhood to adulthood. Blood pressure was measured on 7 occasions between ages 5 and 18 years in the Birth to Twenty cohort study, and conditional variables for growth in infancy and mid-childhood were computed from anthropometric measures (n=1937, 52% girls). We used a group-based trajectory modeling approach to identify distinct height-adjusted blood pressure trajectories and then tested their association with growth between birth and mid-childhood adjusting for several covariates. Three trajectory groups were identified for systolic and diastolic blood pressure: lower, middle, and upper in boys and girls, separately. In boys, predictors of the middle or upper systolic blood pressure trajectories versus the lower trajectory were in birth weight (odds ratio 0.75 [95% confidence interval 0.58–0.96] per SD) and relative weight gain in infancy (4.11 [1.25–13.51] per SD). In girls, greater relative weight gain and linear growth in both infancy and mid-childhood were consistently associated with an almost 2-fold higher likelihood of being in the upper versus lower systolic blood pressure trajectory. The associations for the diastolic blood pressure trajectories were inconsistent. These findings emphasize the importance of identifying children at risk of progression to high blood pressure. Accelerated growth in infancy and mid-childhood may be a key target for early life intervention in prevention of elevated blood pressure progression. **(*Hypertension*. 2016;68:00-00. DOI: 10.1161/HYPERTENSIONAHA.116.08046.)** • **Online Data Supplement**

Key Words: adolescence ■ blood pressure ■ childhood ■ growth ■ trajectories

Hypertension

Hypertension remains a major cause of morbidity and premature mortality and a leading risk factor for the global burden disease worldwide.[1] High blood pressure (BP) in adulthood will affect 3 quarters of the population in low- and middle-income countries by 2025.[2] Of great concern is the emergence of hypertension in pediatric populations concomitant with the rising epidemic of obesity.[3] We recently showed BP tracks from early childhood to late adolescence in a black South African population; 1 in 3 children with elevated BP at age 5 years (>90th percentile for age, height, and sex) remains so at age 18 years.[4] Because children with elevated BP may show early signs of cardiovascular damage and renal injury and are likely to have high BP in adulthood,[5,6] identifying children with atypical BP patterns and risk factors may be crucial for early life intervention to modify progression to hypertension in adulthood.

Substantial evidence suggests that early life growth predicts elevated BP, particularly in children who are small at birth but experience accelerated growth in childhood.[7–9] Conventional growth modeling techniques have been used to explore how early life growth relates to mean levels or changes in BP in children and adolescents. Those studies use a single mean growth curve to describe BP trajectories in a given population and assume that covariates influence the growth curve in a similar way.[10] Yet, BP is a highly variable physiological characteristic; hence describing a population using a single estimated trajectory oversimplifies the complexity of BP tracking patterns that characterize children and adolescents. In addition, height is a known marker of early life environment and a major correlate of BP in childhood and adolescence[11] and, thus, should be incorporated in longitudinal modeling of BP.

Recently, investigators have begun to use finite mixture models to identify distinct clusters of individuals following similar patterns of BP change over time.[12,13] One recent study identified 4 systolic BP (SBP) trajectory groups between ages 7 and 38 years using group-based trajectory modeling (GBTM) on data from the Dunedin longitudinal birth cohort. That study reported that low birth weight was associated with higher odds of being in the hypertensive trajectory group.[14] In support of those findings, a UK birth cohort reported 2 to 3 BP trajectory groups in midlife (36–53 years) and confirmed that individuals with higher birth weight were likely to be in the normative BP group than in the BP increaser groups.[15] Trajectories of BP in black children and adolescents in South Africa have not been identified and are complicated by more ambiguous

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definitions of elevated BP in children than in adults. GBTM may be useful in identifying children with atypical patterns of SBP and diastolic BP (DBP) and their associated risk factors.

To our knowledge, no study in Africa within a low- and middle-income country scenario has explored the association between early life growth and trajectories of BP in children and adolescents, which is likely to be important because of the increasing burden of hypertension on this continent. We hypothesized that early growth, in particular lower birth weight and rapid postnatal weight gain, is associated with a higher height-adjusted BP trajectory in a Black South African pediatric population. The aim of this study was to use Bt20 (Birth to Twenty) longitudinal birth cohort data to (1) identify distinct trajectory groups for BP between 5 and 18 years of birth, (2) examine the association between early growth and BP trajectories, and (3) assess the influence of height on the association between early growth and BP trajectories.

Methods

Study Population

The data analyzed here are from the Bt20 cohort study of singleton children born within a 7-week period in Soweto, Johannesburg, in 1990 (n=3273). Details of recruitment and selection criteria for the cohort study are described elsewhere.[16] All parents and caregivers of the children provided written informed consent, and the University of Witwatersrand Committee granted ethical approval for Research on Human Subjects (certificate number: M130556). The study sample was restricted to black participants (≈78% of the cohort) who had not been pregnant during adolescence and had anthropometric measurements and SBP and DBP measurements at ≥2 of the following mean ages: 5 years (n=1046; 49.0% boys), 8 years (1175; 48.8%), 10 years (n=695; 48.6%), 13 years (n=1355; 47.5%), 14 years (n=1392; 47.4%), 16 years (n=1657; 48.1%), and 18 years (n=1592; 48.2%). The overall sample size was n=1937 (1005 girls and 932 boys).

Assessment of Blood Pressure

BP was measured in a seated position in triplicate: after a 5-minute rest and a 2-minute interval between measurements, using Dinamap Signs monitor 1846SX (Critikon) at 5 years and an Omron M6 (Omron, Kyoto, Japan) at 8 to 18 years. All the measurements were taken by a trained research assistant using an appropriate cuff size. Hypertension status at age 5 years was classified as greater than 95th percentile for age, sex, and height using the Fourth report on National High Blood Pressure program in children and adolescence.[17]

Assessment of Growth

Birth weight and gestational age were obtained from birth notification records entered at birth. Subsequently, weight was measured using a digital scale to the nearest 0.1 kg, and height was measured using a calibrated stadiometer. Birth weight and weight-for-age and height-for-age *z* scores were computed using WHO growth standards.[18] To deal with high correlation of repeated weight and height measures in longitudinal data, conditional weight independent of height (relative weight gain) and relative height gain independent of weight (relative linear growth) were computed as standardized residuals derived from sex-specific linear regressions of a current growth measure on a prior one in infancy (0–2 years) and mid-childhood (2–5 years).[19,20]

Assessment of Covariates

Maternal and infant characteristics at birth were identified using standard questionnaires. Socioeconomic status (SES) in infancy was represented as a count of household assets reported by the mother or caregiver.

Statistical Analysis

GBTM was performed using a STATA plug-in program of SAS Proc Traj to estimate model parameters using maximum likelihood estimation in STATA 11.[21] We used a censored normal model for continuous variables, first without covariates, then including height as a time-varying covariate (preliminary analyses). To identify the groups, 2 class models were specified for SBP and DBP for each sex and then classes were added sequentially until parsimony was attained for linear, quadratic, and cubic terms (Table S1 in the online-only Data Supplement). To test the model with the best fit, we used the following criteria: low Bayesian Information Criterion, high posterior probabilities (>0.7), not <1% of total sample in a trajectory group, and prior knowledge from the literature.[22] Thereafter, the groups defined from the best-fitting models were used as categorical outcome variables in multinomial logistic regression models with covariates (time-varying and time-invariant), yielding the log-odds estimates, standard errors, and *P* values, from which odd ratios and 95% confidence intervals were computed.

Not all participants had measures at all occasions; hence, we compared those who were included in the sample and those with missing BP measures with respect to key variables to inform whether missingness was random (Table S2). Descriptive statistics were conducted to characterize average BP per occasion by BP class membership. ANOVA was used to describe continuous study sample characteristics for each BP trajectory and to validate the trajectory groups using BP status at age 5 years, and χ^2 test was used for categorical study variables. Multinomial logistic regressions were conducted in Traj, and the estimates and standard errors were converted to odds ratios and 95% confidence intervals.

Results

One thousand and five girls and 932 boys had BP measurements on at least 2 occasions. There were no significant differences between the analyzed sample and those not included (n=631) with regards to birth weight, weight in infancy and mid-childhood, and height in infancy and childhood, but the 2 samples differed with regards to SES in infancy. Those in the included sample had lower number of household assets compared with those excluded (*P*<0.0001).

In each sex, the best-fitting models included three distinct trajectories for SBP and DBP with cubic terms (Table S1). For descriptive purposes, the BP trajectories were labeled as lower, middle, or upper. The lower trajectory was considered as the reference group in all regression analyses (Figures 1 and 2). The BP trajectories represent mean BP based on the posterior probabilities of being assigned to a particular class. In boys (Figure 1A–1D), the upper SBP trajectory group (16.4%) started at 125.0 mm Hg at age 5 years and increased to 132.4 mm Hg by age 18 years. The middle SBP trajectory group (55.3%) started at 107.3 mm Hg and increased to 122.9 mm Hg. The lower SBP trajectory group (28.2%) started at 101.9 mm Hg and increased to 115.2 mm Hg. In girls (Figure 2A–2D), the upper SBP trajectory group (13.6%) started at 120.5 mm Hg and increased to 125.7 mm Hg; the middle SBP group (53.2%) started at 110.4 mm Hg and increased to 116.9 mm Hg; and the lower SBP group (33.2%) started at 99.0 mm Hg and increased to 107.5 mm Hg (Table 1).

Adding child's height between 5 and 18 years as a time-varying covariate reduced by half the proportion of individuals in the upper SBP trajectory in both boys (7.1%) and girls (7.5%; Figures 1B and 2B) but made no major differences for DBP (Figures 1D and 2D). Table S3 describes the association of age terms and height and BP trajectories for the time-varying models. Height between ages 5 and 18 years was positively associated with all BP trajectories in boys and girls, except an apparent protective effect on the upper SBP trajectory in girls (estimate

Hypertension

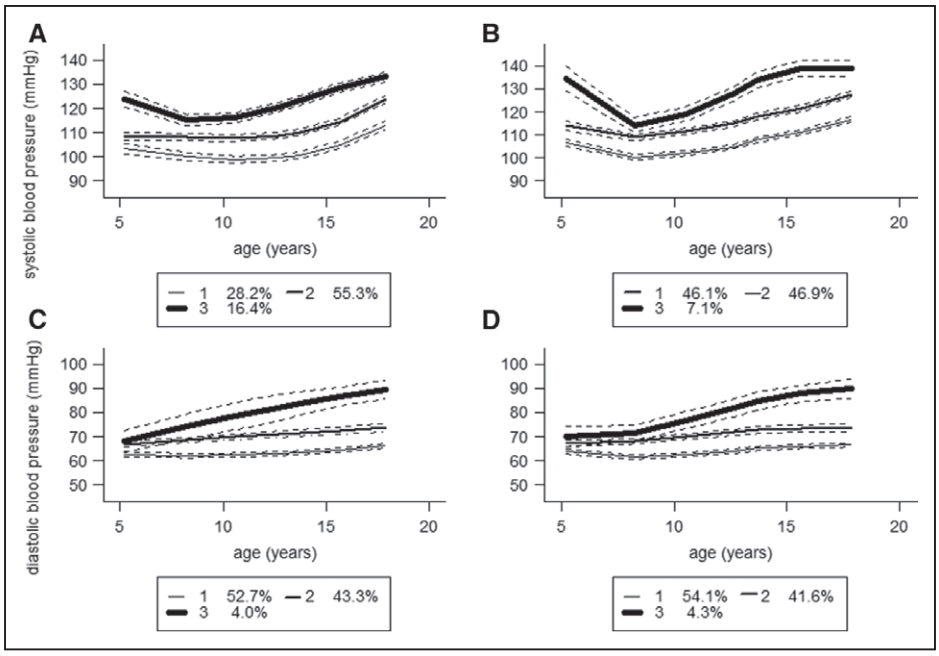


Figure 1. Trajectories of blood pressure for boys between 5 and 18 years of age from group-based trajectory models. **A**, Systolic blood pressure over time. **B**, Systolic blood pressure over time adjusted for height as a time-varying covariate. **C**, Diastolic blood pressure over time. **D**, Diastolic blood pressure over time accounting for height per time point.

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–0.25, SE 0.10; *P*=0.0125). The DBP trajectory for girls was not associated with height between ages 5 and 18 years.

Hypertension status at age 5 years was highly predictive of height-adjusted BP trajectory (Table S4). The relative risk of being in the upper and middle SBP trajectory given a BP status above the 95th percentile for age, sex, and height was 3.85 and 21.80 times higher compared with that in the lower trajectory in boys. In girls, the relative risk ratios were almost 6- and 7-fold greater for the middle and upper relative to the lower SBP trajectory for a BP measure above the 95th percentile for age, height, and sex. With respect to DBP trajectories, BP status at age 5 years was highly predictive of the BP trajectory groups, with higher risk for the upper and middle trajectory groups compared with the lower one in both sexes.

Hypertension

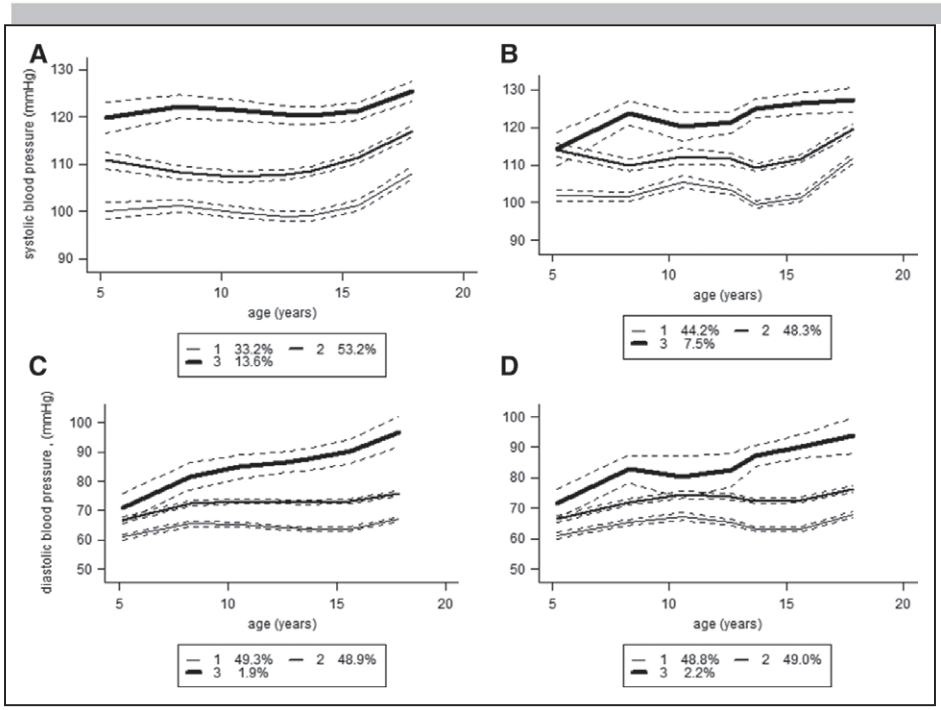


Figure 2. Girls' trajectories of blood pressure for between 5 and 18 years of age from group-based trajectory models. **A**, Systolic blood pressure changes with age. **B**, Systolic blood pressure over time adjusted for height at each time point. **C**, Diastolic blood pressure over time. **D**, Diastolic blood pressure over time accounting for height per time point.

Table 1. Sex-Specific Mean BP by Trajectory Group Membership

Mean Age, y	SBP Trajectory Group Membership						DBP Trajectory Group Membership					
	Boys			Girls			Boys			Girls		
	Low	Middle	Upper	Low	Middle	Upper	Low	Middle	Upper	Low	Middle	Upper
5	101.9 (10.8)	107.3 (10.4)	125.0 (12.0)	99.0 (8.6)	110.4 (9.9)	120.5 (13.3)	60.5 (7.5)	65.8 (7.8)	69.9 (8.3)	60.5 (6.9)	67.2 (8.7)	70.0(8.6)
8	101.7 (7.5)	110.8 (8.6)	119.0 (10.9)	101.7 (7.0)	110.3 (8.4)	125.5 (10.0)	65.9 (7.0)	73.1 (7.5)	75.1 (6.8)	66.1 (7.0)	73.8 (7.5)	85.6 (12.0)
10	98.5 (9.1)	106.8 (9.4)	117.9 (14.7)	99.1 (8.5)	107.0 (9.6)	119.2 (13.2)	63.8 (7.4)	69.7 (7.8)	76.4 (12.0)	64.2 (7.5)	71.0 (7.5)	80.3 (12.8)
13	96.9 (6.7)	107.2 (6.6)	119.1 (9.2)	98.0 (6.6)	107.5 (6.9)	119.3 (8.8)	61.0 (5.9)	69.7 (6.4)	80.6 (11.5)	62.8 (5.7)	72.3 (6.6)	83.3 (7.4)
14	98.6 (6.9)	109.1 (7.3)	122.6 (9.9)	99.0 (6.8)	108.5 (7.5)	120.3 (9.7)	63.0 (5.9)	72.7 (6.7)	86.7 (8.5)	65.1 (5.9)	75.1 (6.9)	91.0 (7.2)
16	105.3 (8.0)	117.3 (9.0)	132.3 (11.3)	100.0 (8.3)	112.7 (9.1)	124.1 (10.6)	62.8 (6.4)	72.3 (1.1)	90.9 (13.1)	62.9 (6.7)	73.2 (7.3)	93.4 (12.6)
18	111.4 (7.6)	122.9 (8.2)	132.4 (10.4)	107.5 (7.0)	116.9 (8.1)	125.7 (9.2)	66.8 (6.4)	75.3 (7.2)	88.1 (7.8)	67.2 (6.2)	76.6 (6.9)	97.5 (12.2)
Height adjusted												
5	103.7 (10.4)	110.7 (12.0)	130.9 (10.4)	100.6 (9.1)	113.6 (10.9)	113.1 (13.6)	61.4 (7.8)	64.9 (8.1)	76.7 (9.8)	60.4 (7.0)	70.0 (8.2)	70.0 (8.2)
8	104.7 (8.3)	113.7 (9.5)	118.0 (10.3)	102.9 (7.4)	113.2 (9.2)	126.9 (11.0)	66.7 (7.2)	73.6 (7.8)	73.9 (5.1)	66.1 (6.9)	85.3 (11.0)	85.3 (11.0)
10	101.4 (9.8)	109.6 (10.9)	117.8 (15.3)	100.0 (8.4)	110.0 (10.2)	118.9 (17.3)	64.2 (7.5)	70.3 (8.1)	76.1 (10.6)	63.8 (7.4)	80.4 (11.3)	80.4 (11.3)
13	100.6 (7.8)	110.0 (7.9)	121.0 (10.9)	100.0 (7.0)	109.1 (7.4)	122.8 (9.9)	61.6 (6.0)	70.6 (6.9)	80.8 (13.4)	62.7 (5.7)	84.0 (7.1)	84.0 (7.1)
14	102.2 (7.9)	112.2 (8.5)	128.2 (10.4)	100.3 (7.2)	110.3 (7.3)	124.9 (9.9)	63.6 (6.2)	73.5 (7.0)	86.8 (9.7)	65.0 (5.9)	89.5 (7.4)	89.5 (7.4)
16	109.1 (9.1)	121.2 (9.9)	137.2 (12.5)	102.0 (8.8)	114.7 (9.1)	128.0 (11.6)	63.5 (6.7)	72.9 (7.9)	96.3 (11.9)	62.6 (6.5)	91.2 (12.2)	91.2 (12.2)
18	115.2 (8.9)	125.7 (8.3)	134.0 (13.5)	109.2 (7.4)	118.3 (7.7)	130.4 (11.9)	67.2 (6.4)	76.5 (7.7)	87.4 (7.9)	67.0 (6.1)	96.0 (11.8)	96.0 (11.8)

Summary statistics showing mean blood pressure and standard deviations across the trajectory group memberships of blood pressure between ages 5 and 18 on 7 time points depicted by mean ages.

Hypertension

SBP trajectory group membership in boys was associated with relative linear growth in infancy and childhood and SES in infancy, whereas in girls, it was associated with relative weight and relative height gain in infancy and childhood, parity, maternal age and household assets in infancy, and SBP at age 5 years. With respect to DBP, rapid relative weight gain in infancy, rapid linear growth in mid-childhood, DBP at age 5 years, and SES in infancy were significantly associated with the girls' trajectory group membership (Table 2). For the height-adjusted BP trajectories, weight gain in infancy and childhood, parity, BP at 5 years of age, and SES between 0 and 2 years of age remained as determinants of class membership for the girls, whereas in boys, relative linear growth in mid-childhood and BP at age 5 years were associated with BP trajectory groups.

Relative weight gain in infancy and rapid linear growth between birth and mid-childhood was associated with SBP trajectory group membership in boys after adjusting for time-invariant covariates (Table 3). However, in height-adjusted models, a unit increase in birth weight reduced the risk of being in the middle trajectory by 25% (odds ratio [OR] 0.75, 95% confidence interval 0.58–0.96; *P*=0.0223), whereas rapid weight gain in infancy was associated with almost a 4-fold higher risk (OR 4.11, 95% CI 1.25–13.51; *P*=0.0202) of being in the upper trajectory. In girls, relative weight gain and linear growth in infancy were associated with higher odds of being in the middle and upper relative to the lower SBP trajectory in height-adjusted models.

Rapid weight gain in infancy and mid-childhood and linear growth were associated with higher odds of being in the middle versus lower DBP trajectory (Table 4). However, in height-adjusted models, an association only remained for relative weight gain in infancy (OR 1.43, 95% CI 1.06–1.95; *P*=0.0214). The upper versus lower DBP trajectory group in boys was positively associated with relative weight gain in infancy and linear growth in mid-childhood, but these associations were diminished or reversed in height-adjusted models, leaving linear growth in infancy as the only significant predictor of upper versus lower DBP trajectory (OR 0.47, 95% CI 0.29–0.76; *P*=0.0021). In girls, relative weight gain and linear growth in mid-childhood were positively associated with being in the middle versus lower DBP trajectory, whereas weight gain in infancy was a predictor of upper versus lower DBP trajectory (OR 2.53, 95% CI 1.14–5.57; *P*=0.0219).

Discussion

Using GBTM, we identified 3 sex-specific trajectories for SBP and DBP; each showing gradual increases in BP with age in Black South African children. In boys, upper and middle BP height-adjusted trajectory membership was inversely associated with birth weight and positively associated with relative weight gain and linear growth in infancy. Girls who experienced accelerated growth (both in weight and height) in infancy and childhood tended to be in the upper versus lower SBP trajectory, whereas rapid growth in infancy positively predicted being in the middle versus lower class. With regard to DBP in girls, rapid relative weight gain in infancy and mid-childhood was predictors for the upper and middle trajectories (in comparison to the lower trajectory). These findings support the hypothesis that accelerated relative weight gain in early life may program higher long-term disease risks.[23]

A major feature of our study is that we confirmed heterogeneity in BP over time in children and adolescents by

Table 2. Study Sample Characteristics by Sex and BP Trajectory Groups

	SBP Trajectory Group						DBP Trajectory Group					
	Boys			Girls			Boys			Girls		
Study Characteristics	Lower	Middle	Upper	Lower	Middle	Upper	Lower	Middle	Upper	Lower	Middle	Upper
Gestational age, wk	38.0 (1.5)	37.9 (1.9)	38.0 (2.0)	37.9 (1.8)	38.0 (1.8)	37.8 (1.9)	37.9 (1.9)	38.0 (1.6)	37.8 (2.9)	37.9 (1.9)	37.9 (1.6)	38.1 (2.2)
Birth weight, g	3110.4 (0.5)	3132.2 (0.5)	3116.1 (0.5)	3023.8 (0.5)	3027.7 (0.5)	3061.3 (0.4)	3125.2 (0.5)	3132.4 (0.5)	3078.6 (0.6)	3025.4 (0.5)	3034.7 (0.5)	3121.4 (0.4)
Relative weight gain: infancy	−0.05 (0.9)	0.14 (1.0)	0.17 (1.0)	−02 (1.0)	0.20 (1.0)	0.30 (1.0)*	0.05 (1.0)	0.17 (1.0)	0.01 (1.1)	0.07 (1.0)	0.20 (0.9)	0.78 (0.8)†
Relative weight gain: mid-childhood	−0.14 (1.0)	0.02 (1.0)	0.07 (1.2)	−0.16 (1.0)	−0.08 (1.0)	0.32 (1.0)*	−0.06 (1.0)	0.04 (1.1)	0–0.13 (1.5)	−0.14 (1.1)	0.001 (1.0)	0.44 (1.0)
Relative linear growth: infancy	−0.31 (0.8)	−0.05 (1.0)	0.19 (0.9)‡	−0.31 (0.9)	0.01 (1.0)	0.14 (1.0)‡	−0.13 (1.0)	−0.03 (1.0)	0.16 (1.0)	−0.12 (1.0)	−0.01 (1.0)	−0.31 (1.2)
Relative linear growth: mid-childhood	−0.20 (1.1)	0.04 (1.0)	0.04 (0.9)†	−0.19 (1.0)	0.03 (1.0)	0.40 (0.9)‡	−0.13 (1.0)	0.11 (1.0)	0.30 (1.1)†	−0.07 (1.0)	0.07 (1.0)	0.64 (1.0)†
SBP at 5 y of age/ mm Hg	103.1 (11.9)	108.4 (11.1)	124.7 (14.0)‡	104.0 (1.4)	115.6 (11.4)	118.7 (16.0)‡	…			…		
DBP at 5 y of age/ mm Hg	…			…			60.2 (7.7)	63.8 (7.9)	71.7 (7.9)‡	60.4 (6.8)	66.7 (8.7)	69.4 (10.7)‡
Parity: ≤2	92 (41.4)	298 (33.8)	51 (35.7)	149 (48.5)	301 (33.6)	40 (33.6)	278 (33.8)	156 (39.5)	7 (25.0)	304 (36.7)	182 (38.0)	4 (28.6)
Parity: >2	130 (58.6)	583 (66.1)	92 (64.3)	158 (51.5)	595 (66.4)	79 (66.4)‡	545 (66.2)	239 (60.5)	21 (75.0)	525 (63.3)	297 (62.0)	10 (71.4)
SES in infancy (household assets)	4 (2)	3 (2)	3 (2)*	4 (2)	3 (2)	3 (2)†	3 (2)	3 (2)	3 (1)	3 (2)	3 (2)	3 (1)*
Height adjusted												
Gestational age	38.0 (1.7)	37.9 (2.0)	37.9 (2.0)	37.9 (1.8)	37.9 (1.9)	37.9 (1.5)	37.9 (1.8)	38.0 (1.7)	37.6 (3.1)	37.8 (2.0)	38.0 (1.7)	38.0 (2.1)
Birth weight	3160.0 (0.5)	3077.2 (0.5)	3070.0 (0.5)	3031.1 (0.5)	3026.1 (0.5)	3074.1 (0.4)	3140.0 (0.5)	3090.7 (0.5)	3133.3 (0.5)	3009.6 (0.5)	3040.0 (0.5)	3111.8 (0.4)
Relative weight gain: infancy	0.11 (1.0)	0.10 (1.0)	0–0.02 (1.1)	−02 (0.9)	0.25 (1.0)	0.26 (0.9)*	0.08 (1.0)	0.15 (1.0)	0–0.19 (1.0)	0.02 (1.0)	0.23 (1.0)	0.81 (0.8)‡
Relative weight gain: mid-childhood	0.01 (1.1)	0–0.07 (1.0)	0.03 (1.2)	−0.19 (1.0)	−0.02 (1.0)	0.19 (1.0)†	−0.06 (1.0)	0.07 (1.1)	0–0.03 (1.0)	−0.17 (1.1)	0.02 (1.0)	0.44 (1.0)†
Relative linear growth: infancy	−0.09 (0.9)	−0.06 (1.0)	0–0.33 (0.9)	−0.15 (1.0)	0.01 (1.0)	0–0.09 (1.0)	−0.04 (1.0)	−0.18 (0.9)	0–0.04 (1.0)	−0.06 (1.0)	0–0.06 (1.0)	−0.51 (1.2)
Relative linear growth: mid-childhood	−0.09 (1.0)	0.05 (1.1)	0.24 (0.8)†	−0.07 (1.0)	0.04 (1.0)	0.24 (0.8)	−0.04 (1.0)	0.005 (1.0)	0.12 (0.9)†	−0.06 (1.0)	0.05 (1.0)	0.40 (0.9)
SBP at 5 y of age/ mm Hg	110 (12.0)	103.7 (8.1)	130.9 (10.4)‡	100.6 (9.1)	113.6 (10.9)	113.1 (13.7)‡	…			…		
DBP at 5 y of age/ mm Hg	…			…			61.4 (7.8)	64.9 (8.1)	76.7 (9.8)‡	60.4 (7.0)	67.0 (8.6)	69.6 (8.2)‡
Parity: ≤2	162 (36.8)	262 (35.1)	17 (28.3)	206 (47.8)	265 (31.8)	19 (32.8)‡	305 (34.2)	130 (38.8)	6 (28.6)	207 (43.1)	278 (33.7)	5 (29.4)*
Parity: >2	278 (63.2)	484 (64.9)	43 (71.7)	225 (52.2)	568 (68.2)	39 (67.2)	585 (65.7)	205 (61.2)	15 (71.4)	273 (56.9)	547 (66.3)	12 (70.6)
SES in infancy	3 (2)	3 (2)	3 (2)	3 (2)	3 (2)	3 (2)	3 (2)	3 (2)	3 (1)	3 (2)	3 (2)	3 (1)†

Model showing the summary statistics of factors associated with the BP trajectories with level of significance: *P<0.01, †P<0.05, ‡P<0.001. Analysis of variance for continuous exposures (gestational age, birth weight, weight and linear growth between 0 and 2 y, 2 and 5y, BP at 5 y, and asset-based SES score) and χ^2 test for categorical variable, parity, associated with the BP trajectories.

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reporting 3 latent classes for SBP and DBP for each sex. Previous longitudinal cohort data analyses of BP trajectories focused on adult populations[24,25] or growth curve modeling using one BP trajectory.[26] Consistent with the findings from the Framingham Heart study of 1060 males aged 25+ with longitudinal BP measurements at 4 time points, we identified 3 trajectory classes for SBP and DBP.[12] However, other studies found different numbers of classes, including a UK study that reported 2 classes each for SBP and DBP in midlife in men.[15] The CARDIA cohort (Coronary Artery Risk Development in Young Adults) in the United States examined adults aged 18 to 30 years at baseline and reported 5 distinct trajectories of mid-BP (mean of SBP and DBP). However, this study did not disentangle the age-related changes in SBP and DBP, which are physiologically distinct measures.[27]

In the present study, height between 5 and 18 years of age was found to be closely associated with trajectory groups, except for the girls' upper SBP and DBP trajectories. These findings might imply that stature may have a greater impact on BP in boys than in girls. With regards to sex differences, a study of BP trajectories in a Caribbean adolescent population aged 11 to 18 years reported that rate of change of both SBP and DBP was

Table 3. Association of Birth Weight, Relative Weight Gain, and Linear Growth in Infancy and Mid-Childhood and SBP Trajectory Groups Between 5 and 18 Years

	Model 1			Model 2			Model 3			Model 4		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Boys												
Middle vs lower trajectory group												
Birth weight (*z* score)	1.02	0.76–1.38	0.8736	0.99	0.73–1.35	0.9738	0.77	0.6–0.98	0.0307	0.75	0.58–0.96	0.0223
Relative weight gain in infancy	1.54	1.14–2.09	0.0050	1.65	1.2–2.26	0.0021	1.21	0.95–1.55	0.1237	1.23	0.96–1.59	0.1046
Relative weight gain in mid-childhood	1.20	0.94–1.54	0.1522	1.28	0.96–1.7	0.0918	1.25	0.99–1.57	0.0653	1.26	0.98–1.62	0.0712
Relative linear growth in infancy	1.76	1.28–2.43	0.0005	1.72	1.26–2.35	0.0007	0.84	0.64–1.11	0.2157	0.84	0.64–1.11	0.2299
Relative linear growth in mid-childhood	1.65	1.24–2.18	0.0005	1.58	1.19–2.11	0.0018	0.85	0.67–1.09	0.2021	0.89	0.7–1.15	0.3774
Upper vs lower trajectory group												
Birth weight(*z* score)	1.03	0.7–1.51	0.8705	1.02	0.66–1.56	0.9453	0.69	0.31–1.55	0.3652	0.67	0.28–1.61	0.3685
Relative weight gain in infancy	1.58	1.08–2.33	0.0190	1.67	1.09–2.56	0.0196	3.74	1.43–9.83	0.0074	4.11	1.25–13.51	0.0202
Relative weight gain in mid-childhood	1.34	0.95–1.89	0.0950	1.36	0.92–2.02	0.1221	1.21	0.59–2.48	0.6088	1.20	0.54–2.65	0.6604
Relative linear growth in infancy	2.15	1.41–3.28	0.0004	2.18	1.39–3.43	0.0007	1.62	0.67–3.93	0.2847	1.98	0.71–5.48	0.1912
Relative linear growth in mid-childhood	1.44	1–2.09	0.0513	1.53	1.02–2.3	0.0400	1.02	0.44–2.34	0.9645	1.12	0.39–3.2	0.8392
Girls												
Middle vs lower trajectory group												
Birth weight (*z* score)	1.23	0.93–1.63	0.1490	1.12	0.85–1.48	0.4309	1.09	0.84–1.42	0.5190	0.97	0.73–1.28	0.8223
Relative weight gain in infancy	1.39	1.04–1.86	0.0276	1.37	1.02–1.85	0.0350	1.33	1.02–1.75	0.0378	1.33	1–1.76	0.0492
Relative weight gain in mid-childhood	1.00	0.75–1.32	0.9802	1.09	0.81–1.46	0.5669	1.11	0.85–1.44	0.4507	1.22	0.93–1.59	0.1546
Relative linear growth in infancy	2.11	1.51–2.94	0.0000	2.07	1.48–2.91	0.0000	1.60	1.15–2.21	0.0053	1.58	1.15–2.17	0.0046
Relative linear growth in mid-childhood	1.14	0.87–1.49	0.3394	1.12	0.85–1.48	0.4209	1.03	0.79–1.36	0.8098	1.01	0.75–1.35	0.9578
Upper vs lower trajectory group												
Birth weight (*z* score)	1.34	0.93–1.94	0.1123	1.31	0.89–1.92	0.1682	1.35	0.94–1.94	0.1043	1.27	0.86–1.88	0.2246
Relative weight gain in infancy	1.67	1.14–2.44	0.0085	1.59	1.06–2.37	0.0236	1.69	1.14–2.5	0.0084	1.63	1.08–2.46	0.0211
Relative weight gain in mid-childhood	1.65	1.18–2.31	0.0038	1.76	1.22–2.55	0.0026	1.69	1.2–2.38	0.0026	1.77	1.22–2.56	0.0025
Relative linear growth in infancy	2.35	1.59–3.48	0.0000	2.23	1.48–3.35	0.0001	1.98	1.33–2.96	0.0008	1.90	1.27–2.86	0.0019
Relative linear growth in mid-childhood	1.95	1.37–2.78	0.0002	1.99	1.36–2.91	0.0004	2.03	1.38–2.99	0.0003	2.12	1.39–3.23	0.0005

The multinomial logistic regression showing odds ratios, 95% confidence intervals, and the *P* values from GBTM showing the following: Model 1: multinomial logistic regression of growth variables and SBP trajectory classes adjusted for gestational age (time-invariant covariate—a proxy for intrauterine environment). Model 2: multinomial logistic regression of growth variables and SBP trajectory classes adjusted for gestational age, parity, SES in infancy, maternal age (time-invariant covariates—intrauterine environment and maternal factors). Model 3: multinomial logistic regression of growth variables and SBP trajectory classes with height as time-varying covariate (a marker of childhood environment) and gestational age as a time-invariant covariate. Model 4: multinomial logistic regression of growth variables and SBP trajectory classes with height as time-varying covariate and gestational age, parity, SES in infancy, and maternal age as a time-invariant covariates. CI indicates confidence interval; GBTM, group-based trajectory modeling; OR, odds ratio; SBP, systolic blood pressure; and SES, socioeconomic status.

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Table 4. Association of Birth Weight, Relative Weight Gain, and Linear Growth in Infancy and Mid-Childhood and DBP Trajectory Groups Between 5 and 18 Years

	Model 1			Model 2			Model 3			Model 4		
	OR	95%CI	*P* Value	OR	95%CI	*P* Value	OR	95%CI	*P* Value	OR	95%CI	*P* Value
Boys												
Middle vs lower trajectory group												
Birth weight (*z* score)	0.97	0.72–1.33	0.8688	0.99	0.71–1.38	0.9371	0.82	0.64–1.06	0.1359	0.83	0.63–1.10	0.2019
Relative weight gain in infancy	1.73	1.23–2.42	0.0015	1.76	1.22–2.56	0.0028	1.37	1.04–1.8	0.0251	1.43	1.06–1.95	0.0214
Relative weight gain in mid-childhood	1.37	1.01–1.85	0.0447	1.44	1.03–2.01	0.0351	1.22	0.96–1.56	0.1029	1.26	0.96–1.64	0.0926
Relative linear growth in infancy	1.02	0.71–1.46	0.9100	1.13	0.76–1.67	0.5598	0.72	0.55–0.94	0.0171	0.78	0.58–1.05	0.1001
Relative linear growth in mid-childhood	1.51	1.06–2.15	0.0228	1.68	1.19–2.38	0.0034	0.97	0.75–1.24	0.8032	1.14	0.86–1.52	0.3633
Upper vs lower trajectory group												
Birth weight (*z* score)	0.93	0.65–1.34	0.7133	0.93	0.63–1.36	0.7017	0.81	0.46–1.42	0.4609	0.68	0.45–1.03	0.0658
Relative weight gain in infancy	1.57	0.98–2.52	0.0614	1.77	1.16–2.72	0.0087	1.03	0.55–1.90	0.9359	1.38	0.89–2.15	0.1519
Relative weight gain in mid-childhood	1.12	0.72–1.72	0.6190	1.40	0.94–2.08	0.0976	0.93	0.56–1.54	0.7739	1.37	0.88–2.13	0.1627
Relative linear growth in infancy	1.21	0.81–1.81	0.3535	1.17	0.76–1.78	0.4787	0.75	0.36–1.56	0.4392	0.47	0.29–0.76	0.0021
Relative linear growth in mid-childhood	1.75	1.20–2.54	0.0036	1.83	1.23–2.71	0.0028	1.05	0.63–1.76	0.8473	0.80	0.53–1.21	0.2848
Girls												
Middle vs lower trajectory group												
Birth weight (*z* score)	1.07	0.86–1.35	0.5310	1.02	0.80–1.30	0.8553	1.03	0.82–1.30	0.7790	0.99	0.78–1.26	0.9339
Relative weight gain in infancy	1.36	1.07–1.73	0.0108	1.27	0.99–1.63	0.0611	1.31	1.03–1.67	0.0265	1.27	0.98–1.63	0.0677
Relative weight gain in mid-childhood	1.23	1.00–1.51	0.0511	1.30	1.04–1.63	0.0234	1.20	0.97–1.47	0.0956	1.28	1.02–1.61	0.0317
Relative linear growth in infancy	1.27	1.01–1.59	0.0392	1.24	0.97–1.58	0.0809	1.15	0.89–1.47	0.2858	1.08	0.83–1.42	0.5544
Relative linear growth in mid-childhood	1.28	1.03–1.58	0.0234	1.27	1.00–1.60	0.0460	1.18	0.94–1.48	0.1502	1.17	0.91–1.49	0.2205
Upper vs lower trajectory group												
Birth weight (*z* score)	1.16	0.44–3.06	0.7615	1.47	0.73–2.97	0.2830	1.46	0.72–2.95	0.2944	1.44	0.68–3.03	0.3379
Relative weight gain in infancy	4.25	1.51–11.94	0.0061	2.90	1.36–6.18	0.0057	2.65	1.25–5.58	0.0106	2.53	1.14–5.57	0.0219
Relative weight gain in mid-childhood	1.08	0.47–2.48	0.8640	1.58	0.81–3.10	0.1835	1.47	0.77–2.82	0.2468	1.52	0.80–2.90	0.2047
Relative linear growth in infancy	0.88	0.37–2.14	0.7856	1.07	0.55–2.10	0.8396	0.88	0.44–1.74	0.7039	1.00	0.49–2.02	0.9942
Relative linear growth in mid-childhood	2.20	0.90–5.36	0.0840	1.56	0.80–3.04	0.1950	1.52	0.80–2.90	0.1996	1.48	0.74–2.96	0.2715

Multinomial logistic regression models showing the odds ratios, 95% confidence intervals, and *P* values of the association between growth and BP trajectories: Model 1: multinomial logistic regression of growth variables and DBP trajectory classes adjusted for gestational age (time-invariant covariate). Model 2: multinomial logistic regression of growth variables and DBP trajectory classes adjusted for gestational age, parity, SES in infancy, maternal age (time-invariant covariates). Model 3: multinomial logistic regression of growth variables and DBP trajectory classes with height as time-varying covariate and gestational age as a time-invariant covariate. Model 4: multinomial logistic regression of growth variables and DBP trajectory classes with height as time-varying covariate and gestational age, parity, SES in infancy, and maternal age as a time-invariant covariates. CI indicates confidence interval; DBP, diastolic blood pressure; GBTM, group-based trajectory modeling; OR, odds ratio; and SES, socioeconomic status.

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greater in boys than in girls.[28] Sex discrepancies in BP trajectories and their associations with early growth might be attributed to influence of androgens on the regulation of long-term BP in response to early environmental factors.[29] Although the specific mechanisms underpinning sex differences in the programming of life course BP are not fully known, testosterone is reportedly positively associated with renin angiotensin activation and oxidative stress, which in turn contribute to elevated BP differently in males[30] and in females.[31]

This study confirms that BP increases with age and height between ages 5 and 18 years, except in the upper BP trajectories for girls. Unlike in adults, height is a recognized major determinant of childhood BP and is routinely considered to evaluate childhood BP centiles and hypertension status.[32] Childhood height is an indicator of growth of the arterial tree, which influences hemodynamic BP control mechanisms, especially vasculature structure and function.[33] These findings are consistent with several cross sectional studies[34] and confirm the importance of inclusion of age and height in the definition of elevated BP in children and adolescents. Because there are physiological increases in childhood BP with height, it is important to consider the effect of height as a covariate when identifying trajectory groups, so as to avoid simply categorizing tall children with normal BP for their height.

For height-adjusted BP trajectories, the association between infant and mid-childhood linear growth and BP, especially for boys and for DBP, implies that change in BP may be more susceptible to later stature in boys than in girls. In support of the fetal origins hypothesis, we reported that higher birth weight was associated with lower odds of being in the middle versus the lower boys' SBP trajectory in the final models. This finding may indicate that children who are born low weight but who go on to increase their stature after mid-childhood may be at risk of having moderately increasing BP.

In support of the growing evidence on BP tracking in childhood,[35] we have shown that hypertensive status at age 5 years was highly predictive of BP trajectory between 5 and 18 years. This finding validates the importance of early detection through routine BP screening in childhood to identify children who are most likely to follow elevated BP trajectories over their life course. Early onset of elevated BP may indicate that physiological mechanisms influencing variation in BP and risk of elevated BP might start in early life and may amplify with age in response to genetic and environmental factors.

A major strength of this study is its prospective nature. In addition, there were no major differences between those children excluded from the study and the analytic sample with regards to key study characteristics, and any differences were adjusted in the multivariate models. We used GBTM to identify sex-specific BP trajectories. This is an extension of traditional growth modeling, which takes into account time-varying and time-invariant covariates in characterizing the change in BP over time and heterogeneity within BP data. GBTM is suitable for examining physiological traits like BP, which are highly variable in children and adolescents and provides better model fit and parsimony compared with linear mixed models.[22] However, inferences regarding latent class membership and their association with relative weight gain in early life might not extend to the entire South African population because the analyses were confined to the black ethnic sample. Use of ambulatory BP monitoring measure may provide more insight into BP trajectories compared with an average BP measurement on one occasion. Future research studies need to replicate GBTM in other cohort studies using other time-varying covariates like physical activity and dietary patterns.

In the context of an emerging epidemic of hypertension in black low- and middle-income country populations, this study suggests that BP trajectories may be set early in childhood, with BP in early childhood highly predictive of BP trajectories. Early life growth, in particular high relative weight gain, may be a crucial target for interventions to interrupt elevated BP trajectories and to prevent the early onset of raised BP. Further research is needed to identify individuals in the middle and upper trajectories, to assess other cardiovascular disease indicators, such as left ventricular hypertrophy, arterial stiffness, and to consider appropriate interventions in early life to interrupt the trajectories and benefit long-term health.

Perspectives

In summary, this study highlights that the potential for early interventions aimed at optimizing growth in early life may play an important role in prevention of elevated BP progression in children and adolescents. This calls for a concerted effort among global healthcare practitioners, researchers, and other related organizations to prioritize pediatric hypertension on the global health agenda, especially in low- to middle-income countries where the burden of disease attributed to hypertension is already high in midlife and exerting pressure on the healthcare system. Future research needs to explore the clinical relevance of the elevated BP trajectories, the key risk factors, and progression to hypertension and cardiovascular disease in adulthood.

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Disclosures

None.

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Novelty and Significance

What Is New?

- This is the first study to show distinct blood pressure (BP) trajectories from early childhood to late adolescence in African children.
- Rapid early growth predicts higher longitudinal BP trajectories in childhood.

What Is Relevant?

- Age-related changes in systolic BP in children and adolescents are height-dependent; hence, longitudinal profiles of pediatric BP should account for stature.

Summary

Distinct trajectories of age-, sex-, and height-dependent BP are detectable in children from 5 years of age. Rapid growth (both in weight and linear) in infancy and mid-childhood predict the progression of BP between mid-childhood and late adolescence.