



The population-based prevalence of hypertension and correlates of blood pressure among Australian children

Nicholas G. Larkins^{1,2,3} · Armando Teixeira-Pinto^{2,3} · Siah Kim^{4,5} · David P. Burgner^{6,7,8} · Jonathan C. Craig^{2,3}

Received: 15 October 2018 / Revised: 10 December 2018 / Accepted: 23 January 2019 / Published online: 18 February 2019
© IPNA 2019

Abstract

Objective Hypertension is increasingly recognized as a disease spanning the entire life course. Continued efforts to refine the diagnosis and management of hypertension in children are highlighted by the recent American Academy of Pediatrics (AAP) guidelines, which include lower threshold values than the previous reference standard (Fourth Report). We aimed to determine the population-based prevalence of children exceeding thresholds for hypertension using these two guidelines. We also sought to identify the correlates of blood pressure (BP) among Australian children.

Methods Cross-sectional data from the Growing Up in Australia: Longitudinal Survey of Australian Children were analyzed. Blood pressure was measured in 7139 Australian children aged 10–12 years and sampled using population-based methodology. The association between BP and explanatory variables linked to BP in other populations was examined using multiple linear regression with fractional polynomial terms for continuous, non-linear relationships.

Results The threshold for hypertension was exceeded in 3.1% and 5.4%, and prehypertension in 3.0% and 3.7% of children, using the Fourth Report and AAP guidelines respectively. Children at the threshold for obesity had a 9.1 mmHg higher adjusted BP than those on the 50th centile for body mass index (BMI) (95% CI 8.4 to 9.9). BMI had a non-linear relationship with BP, and the magnitude of association between BMI and BP increased with BMI. Socioeconomic status, hypertension during pregnancy, birth weight, and sports participation were also independently associated with BP.

Conclusions Using the AAP guidelines is likely to substantially increase the population prevalence of hypertension. The association between BMI and BP was strongest and non-linear for obese children, who should be the focus of interventional trials.

Keywords Hypertension · Pediatrics · Child · Australia · Health surveys

Background

Hypertension is a key risk factor for cardiovascular disease with origins in early life, and best approached using a life course

model of health and disease [1]. Those who develop hypertension early in life will have greater cumulative risk exposure than those developing hypertension later [2]. The earlier identification of risk also offers an opportunity to alter adverse trajectories

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00467-019-04206-w>) contains supplementary material, which is available to authorized users.

✉ Nicholas G. Larkins
nicholas.larkins@uwa.edu.au

¹ Department of Nephrology, Perth Children's Hospital, 15 Hospital Ave, Nedlands, Western Australia 6009, Australia

² School of Public Health, University of Sydney, Sydney, New South Wales, Australia

³ Centre for Kidney Research, Kids Research Institute, Westmead, New South Wales, Australia

⁴ Department of Nephrology, Sydney Children's Hospital, Randwick, New South Wales, Australia

⁵ School of Women's and Children's Health, University of New South Wales, Sydney, New South Wales, Australia

⁶ Murdoch Children's Research Institute, Royal Children's Hospital, Parkville, Victoria, Australia

⁷ Department of Paediatrics, University of Melbourne, Melbourne, Victoria, Australia

⁸ Department of Paediatrics, Monash University, Melbourne, Victoria, Australia

at a younger age with greater benefit [1]. Despite this and the importance of hypertension on the global burden of non-communicable disease, there are limited population-based data on the prevalence of hypertension among children [3, 4]. Birth weight, socioeconomic status, ethnicity, breast feeding, maternal hypertension, diet, exercise, anxiety, and environmental factors have all been associated with blood pressure (BP) in different cohorts [1]. Repeated surveys such as the National Health and Nutrition Examination Survey provide population prevalence, but often lack information about early life determinants of hypertension [5]. Prospective cohort studies have more granularity and less missing data, but are more resource-intensive and may not allow population-based prevalence estimates.

The American Academy of Pediatrics (AAP) recently published updated BP guidelines that included revised reference values defining hypertension in childhood, which are lower than previous reference standard published by the National High Blood Pressure Education Working Group on High Blood Pressure in Children and Adolescents in 2004 (Fourth Report) [6, 7]. The AAP guidelines were derived from a reference population that excludes overweight and obese children; an approach designed to allow for the inclusion of additional population-based data despite an increasing prevalence of obesity [8]. The AAP guidelines also recommend a diagnosis of hypertension be confirmed by ambulatory blood pressure monitoring, which in combination with lowered thresholds may substantially increase demand on pediatric hypertension services.

Here, we present BP data from children aged 10 to 12 years from a large, national, population-derived study. We aimed to determine the prevalence of children exceeding thresholds for hypertension in mid-childhood according the AAP and Fourth Report guidelines, and investigate the correlates of BP in this population.

Methods

Population and participants

Growing Up in Australia: The Longitudinal Study of Australian Children (LSAC) is a large, prospective, cohort study involving children from all regions of Australia. Briefly, LSAC used a stratified, multi-stage cluster survey design to allow for the derivation of accurate population level estimates [9]. The study design was based on the bioecological model of health, which considers individuals' health and development to be determined by a wide range of factors beginning in early life [10].

The Longitudinal Study of Australian Children enrolled two cohorts in 2004; a baby cohort following children from birth and a kindergarten cohort following children from 4 years of age. Both cohorts have been followed biannually. Data

were collected by trained interviewers, mailed questionnaires, and linked administrative and government data. Written informed consent was provided by families and the study was approved by the Australian Institute of Family Studies Ethics Committee.

Sample recruitment and retention

Australia has a universal healthcare system, Medicare, making this the most complete database of the population [9]. Children were selected at random from the Medicare enrollment registry. Selected families were initially mailed with the information on the study and how to opt-out, prior to further contact to confirm participation. The total samples approached for the kindergarten and baby cohorts at baseline were 9893 and 8921 respectively. Of those approached, 4983 (50%) and 5107 (57%) agreed to participate, in the kindergarten and baby cohorts, with retention at 10 to 12 years of age of 4169 (84%) and 3764 (74%), respectively.

Measurement of BP

Blood Pressure was first measured in 2014 for the baby and 2010 for the kindergarten cohort (mean age 10.9 years) by research staff from the Australian Bureau of Statistics who received a 2-day, study-specific, training module. One further measurement has been taken for the kindergarten cohort at 12 to 14 years of age, but we opted to use the first timepoint only in this study, presenting a cross-section of the entire cohort at the same age. Measurements were taken with the child sitting quietly, using an automated sphygmomanometer (A&D Digital Blood Pressure Monitor, Model UA767). While the use of an oscillometric device to measure BP may produce discrepancies in diagnosis at an individual level, there is little difference in the average BP for populations determined by using oscillometric or aneroid devices [11]. Study assistants measured the mid-upper arm circumference to guide cuff selection (18 to 22 cm or 22 to 33 cm). The cuff was placed 2 to 3 cm above the elbow measured from the olecranon. The participant's arm was rested on a table at approximately heart level. Two measurements were taken with at least 1 min of rest between each reading. We used the mean value in analyses, provided that the difference between the two BP measurements was not more than 30 mmHg, in which case, the final value was recorded as missing.

BP threshold values

Elevated BP and hypertension were defined using the 90th and 95th age-, sex-, and height-specific centiles from the AAP guidelines [7]. Some additional changes in the AAP guidelines compared to the Fourth Report include using the term "elevated BP" in place of prehypertension; introducing a floor threshold

value of $\geq 130/80$ mmHg for stage 1 hypertension; and modifying the threshold for stage 2 hypertension to a BP of ≥ 95 th centile + 12 mmHg or $\geq 140/90$, whichever is lower (previously 99th centile + 5 mmHg). For linear regression analyses, we examined the systolic BP because this is more strongly related to cardiovascular events and has less variability than diastolic BP among children [2, 12].

Measurement of covariates

Weight was measured using electronic scales (Tanita UM-050; nearest 0.1 kg). Height was measured using a laser stadiometer, twice if the measurements were within 0.5 cm and otherwise three times, averaging the two closest measurements to produce the final value. Body mass index (BMI) was calculated as the weight in kilograms divided by the height in meter squared, then converted to *z* scores using Centre for Disease Control and Prevention (CDC) reference data because normal values vary by age and sex [13]. Obesity was defined by a BMI ≥ 95 th centile, and overweight ≥ 85 th centile and < 95 th centile, relative to the CDC reference population [14]. Socioeconomic status was measured using a composite index that included family income, parental occupation, and education [15]. Dietary variables were measured by 24-h recall. Emotional stress and psychological development were measured using the Strengths and Difficulties Questionnaire, with internalizing and externalizing variables grouped because of the low-risk nature of the population [16]. Neighborhood characteristics were measured by self-report and used to calculate a livability index value, as the mean of the response to two questions scored on a 4-point agreement scale. The first question was “this is a safe neighborhood” and the second was “there are good parks, playgrounds and play spaces in this neighborhood.” All remaining variables were from self or parent report. Premature birth was defined as < 37 completed weeks gestation, and low birth weight was defined at < 2500 g.

Statistical analysis

All estimates were weighted to account for survey design [17]. The Rao-Scott χ^2 value was used to compare categories. Otherwise, all associations were examined using linear regression, with covariates retained as continuous variables where applicable and the null hypotheses tested using the Wald test, adjusted for survey design. Blood pressure is known to vary by age, sex, and height [6]. Hence, all regression analyses were adjusted for age, sex, and height. Up to two fractional polynomial terms were used to transform covariates that were not linearly related to BP as determined by the likelihood ratio test at a selection threshold of 0.05 [18]. Fractional polynomial terms allow for a more accurate description of the relationship between variables than categorization, avoid the use of

arbitrarily defined thresholds, and respect the principle of parsimony in model selection (a linear term is used where there is no significant improvement by transformation). Beyond linearity, models were checked for normal and homoscedastic residuals, and collinearity using variance inflation factors. Outliers and influential points were examined. A backward stepwise selection process was used to determine the final multivariable model at a selection threshold of $p < 0.05$. The impact of missing data was checked in sensitivity analyses using multiple imputation by fully conditional specification. Here, BMI was categorized by quintile because the reliability of methods to impute polynomial terms is unclear [19]. Ten imputations were performed and then combined using Rubin’s rule [20]. The prediction of missing variables was performed using linear regression for normally distributed variables, predictive mean matching ($k = 5$) where the distribution was skewed, and discriminate function analysis for categorical variables. All variables presented, including the outcome were used in the prediction model, along with BMI as an auxiliary variable. Model diagnostics included inspection of the trace plots, the relative efficiency of imputation and fraction of missing information. Statistically significant results were defined as those with a two-sided *p* value of < 0.05 . Analyses were performed using SAS 9.4 (Sas Institute, Cary, NC) and R 3.4 (R Core Team, Vienna, Austria).

Results

Participant characteristics

Of the 7933 participants, 7139 (90.0%) had a valid systolic or diastolic BP and height recorded. The sample was reflective of the Australian childhood population at 10 to 12 years of age, consistent with the study design [21]. 1217 (17.2%) children were overweight and 859 (12.1%) were obese (Table 1). Overweight and obesity were more common in boys (1139 of 3681; 30.9%, 95% confidence interval [CI] 29.1 to 32.7%) than girls (937 of 3405; 27.5%, 95% CI 25.9 to 29.1%). The prevalence of prematurity and low birth weight were 6.8% and 7.1% respectively. The proportion of participants identifying as Aboriginal and/or Torres Strait Islander people was 3.7%.

Impact of the 2017 AAP guidelines

Using the AAP thresholds, 5.4% of children exceed the threshold for hypertension (95% CI 4.5 to 6.4), and 3.7% the threshold for elevated BP (95% CI 3.1 to 4.3). There was no difference in the proportion exceeding these thresholds by sex (Table 1). Hypertension was most common in obese children (146 of 859; 17.0%, 95% CI 13.9 to 20.1%). The threshold for hypertension, per the Fourth Report guideline, was exceeded in 224 children (3.1%, 95% CI 2.6 to 3.7%) and

Table 1 Characteristics of the LSAC cohort

Characteristic	Blood pressure category (n, row %) ^a			All (population %)
	Normal	Elevated	Hypertension	
Sex				
Male	3350 (90.5)	141 (3.8)	210 (5.7)	3700 (51.9)
Female	3122 (91.2)	124 (3.6)	178 (5.2)	3424 (48.1)
BMI				
Normal	4746 (94.7)	103 (2.1)	161 (3.2)	5010 (70.7)
Overweight	1071 (88.0)	69 (5.7)	76 (6.3)	1217 (17.2)
Obese	624 (72.7)	88.4 (10.3)	146 (17.0)	859 (12.1)
Socioeconomic status				
Quartile 1 (most disadvantaged)	2061 (87.3)	124 (5.2)	175 (7.4)	2360 (33.6)
Quartile 2	1709 (92.1)	55 (3.0)	93 (5.0)	1856 (26.4)
Quartile 3	1212 (92.4)	42 (3.2)	58 (4.4)	1312 (18.7)
Quartile 4 (most advantaged)	1413 (93.8)	40 (2.7)	53 (3.5)	1506 (21.4)
Aboriginal and/or Torres Strait Islander	225 (85.7)	7 (2.8)	30 (11.4)	263 (3.7)
Premature birth (< 37 weeks)	414 (86.3)	29 (6.1)	37 (7.7)	480 (6.9)
Low birth weight (< 2500 g)	376 (85.9)	26 (6.0)	35 (8.1)	438 (6.2)
Breast fed at 3 months of age	4548 (91.5)	186 (3.7)	236 (4.8)	4970 (70.0)
Maternal hypertension during pregnancy	416 (87.4)	30 (6.4)	30 (6.3)	476 (8.1)
Consumes ≥ 5 serves of vegetables per day	496 (88.8)	19 (3.5)	43 (7.7)	558 (7.9)
Consumes ≥ 2 serves of fruit per day	3577 (90.4)	149 (3.8)	229 (5.8)	3955 (55.9)
Consumes ≥ 3 serves of high fat food per day	2760 (90.9)	111 (3.6)	165 (5.4)	3035 (42.9)
Lives in a safe neighborhood with good parks	5237 (91.2)	213 (3.7)	291 (5.1)	5741 (81.9)
Participates in extra-curricular sports	5019 (91.9)	182 (3.3)	258 (4.7)	5459 (77.0)
Watches ≥ 14 h of TV per week	3417 (89.7)	160 (4.2)	234 (6.1)	3811 (53.8)
Strengths and Difficulties Questionnaire ^b				
Internalizing score ≥ 8	1331 (90.4)	60 (4.1)	82 (5.5)	1472 (20.9)
Externalizing score ≥ 8	1834 (90.9)	71 (3.5)	114 (5.7)	2019 (28.6)
Prosocial score ≤ 7	1218 (89.8)	55 (4.1)	83 (6.1)	1356 (19.2)

LSAC, Longitudinal Survey of Australian Children; IQR, inter-quartile range. All estimates adjusted for survey design. ^a Using the American Academy of Pediatrics 2017 guideline thresholds; ^b a higher internalizing or externalizing score is more abnormal, a lower prosocial score is more abnormal

prehypertension in 211 (3.0%, 95% CI 2.4 to 3.5%). The relative impact of the AAP guidelines on children differed according to their Fourth Report BP category (Table 2).

Among children exceeding the threshold for prehypertension, 70.3% were re-classified as hypertensive under the AAP guidelines. Proportionally, fewer children moved from the

Table 2 Comparison of Fourth Report and AAP 2017 blood pressure thresholds

AAP 2017	Fourth Report (n, column %)			
	Normal	Prehypertension	Stage 1 hypertension	Stage 2 hypertension
Normal	6472 (96.8)	0	0	0
Elevated BP	202 (3.0)	63 (29.7)	0	0
Stage 1 hypertension	15 (0.2)	149 (70.3)	149 (82.6)	0
Stage 2 hypertension	0	0	31 (17.4)	43 (100)

AAP, American Academy of Pediatrics [7]. Fourth Report—the Fourth Report from the National High Blood Pressure Education Program Working Group [6]

normal BP to the elevated BP or stage 1 hypertension categories, but a similar number of children were impacted because most children were initially normotensive. All of the children who moved from the normal BP category had a systolic or diastolic BP between the 85th and 90th centile using the Fourth Report.

Univariate associations

The results of linear regression for single variables of interest against BP after adjustment for age, sex, and height are displayed in Fig. 1. The strongest predictor of BP was BMI. This relationship was not linear and best expressed by a fractional polynomial term (Fig. 2). The rate of increase in BP with BMI z score was greater as BMI increased above the reference mean. The association between BP and BMI z score was less marked for children around or below the reference mean.

Multivariable model

The final multivariable model after backward stepwise selection is displayed in Fig. 3. The final model accounted for approximately a quarter ($R^2 = 26\%$) of the variability observed in BP. Children at the threshold for obesity had a BP that was on average 9.14 mmHg higher than children on the 50th CDC centile for BMI (95% CI 8.41 to 9.88). Children at the threshold for overweight had a BP that was on average 5.01 mmHg higher than children on the 50th CDC centile for BMI (95% CI 4.64 to 5.39). Many predictors that were statistically

significant in the single variable phase were no longer significant in the multivariable model, mostly because of confounding as opposed to a loss of statistical power. Socioeconomic status, maternal hypertension during pregnancy, and birth weight remained statistically significant after adjustment for each other and BMI. The observed effect sizes were smaller in magnitude compared to that for BMI, but were still clinically significant (Fig. 3). In addition to BMI, socioeconomic status was an important confounder in the relationship between the discarded covariates and BP (supplementary material, Table S1).

Sensitivity analyses

The proportion of missing data was < 5% for most variables. However, consistent with an arbitrary pattern of missingness, 25.9% of participants were missing one or more of the 17 variables of interest (supplementary material, Tables S2–3). The mean imputed and observed BP values displayed the same distribution (mean 98 mmHg, SD 11 mmHg). The estimates obtained following multiple imputation were consistent with those obtained using pairwise deletion, with the only notable difference being that extra-curricular sports participation retained statistical significance in the multivariable model after imputation (1.18 mmHg reduction in blood pressure, 95% CI 0.50 to 1.86, Table S4). This observation is consistent with sports participation being the last variable removed in the backward stepwise model selection process prior to multiple imputation ($p = 0.1$ for sports participation added to the multivariable model presented without imputation).

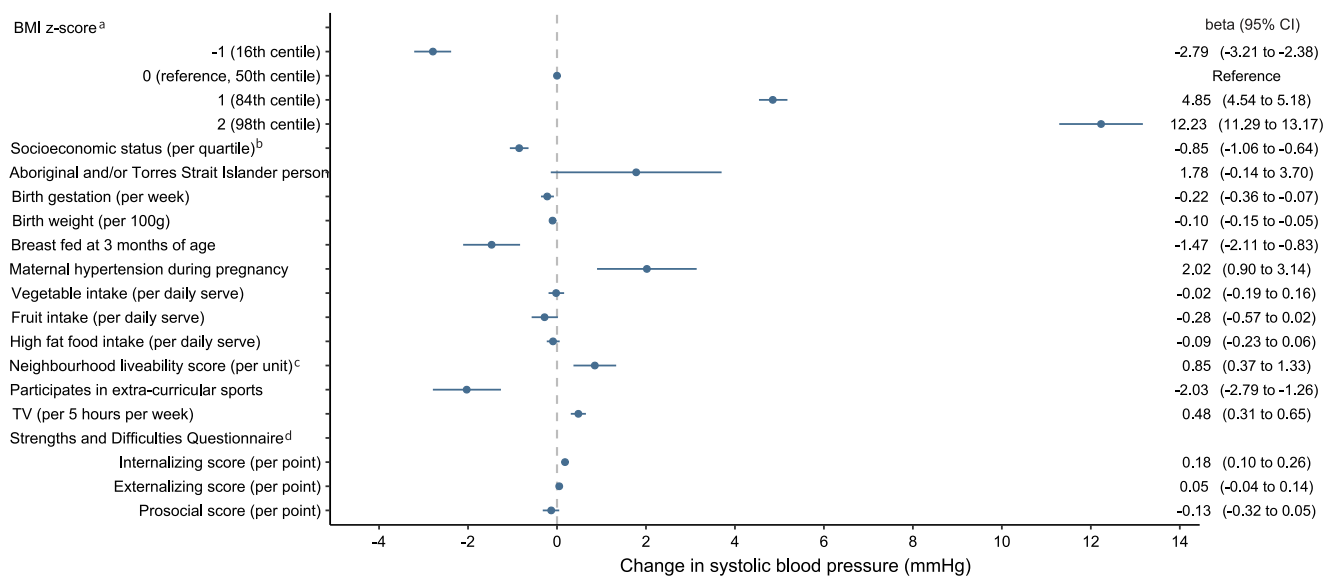


Fig. 1 Univariate associations with age, sex, and height adjusted systolic BP. beta increase in systolic BP (mmHg) per unit increase in the covariate, CI confidence interval, BMI body mass index, BP blood pressure. ^aModeled as fractional polynomial terms $((BMI + 10.8)/10)^3$ and $((BMI + 10.8)/10)^3 * \ln((BMI + 10.8)/10)$. ^bModeled as continuous covariate

(standardized) and expressed as a 0.67 unit increase in the z score. ^cScore from 0 to 4 with a higher value indicating better access to parks, green space, etc. ^dA higher internalizing or externalizing score is more abnormal, a lower prosocial score is more abnormal

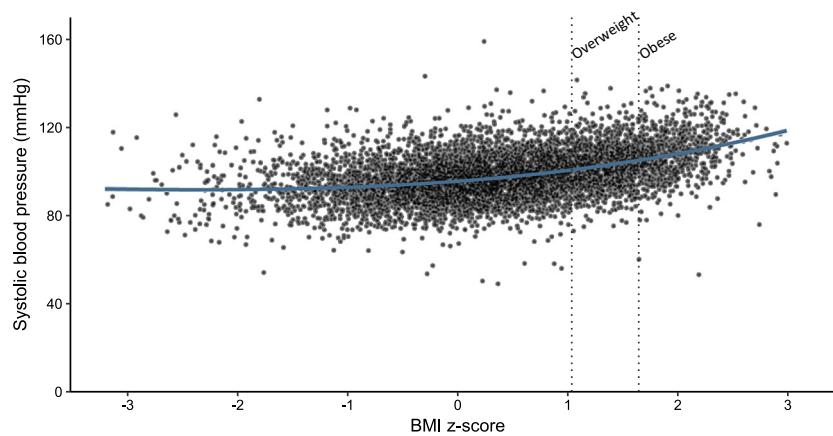


Fig. 2 The relationship between body mass index and BP. BMI body mass index, BP blood pressure. Adjusted for age, sex, and height. Modeled as fractional polynomial terms $((\text{BMI} + 10.8)/10)^3$ and $((\text{BMI} + 10.8)/10)^3 \cdot \ln((\text{BMI} + 10.8)/10)$. Blue line represents predicted value,

and gray band represents 95% confidence interval. Dotted lines are the threshold for overweight and obese as defined by the 85th and 95th Centre for Disease Control and Prevention percentiles respectively

Discussion

In this large, population-based study of Australian children, we found that 5.4% and 3.7% of participants exceeded the AAP thresholds for elevated BP and hypertension respectively, compared to 3.1% and 3.0% when using the Fourth Report. The strongest predictor of BP was BMI and this relationship was non-linear, with an increasing gradient as children entered the obese and overweight range. Socioeconomic status, maternal hypertension during pregnancy, and birth weight were predictive of BP in adjusted multivariable models. Participation in extracurricular sports was also associated with a reduced blood pressure after adjustment for these variables once missing data were accounted for by multiple imputation.

The prevalence of children exceeding the threshold for hypertension in this study was lower than in the Australian Health Survey (AHS), the only other comparable Australian, population-based survey (reported prevalence 5.8% using Fourth Report thresholds, 95% CI 4.4 to 7.2) [22]. The most notable differences between these studies are that the AHS included children from 5 to 17 years of age and the AHS sample size was smaller ($n = 2071$) with more missing data.

In the USA, data from NHANES have demonstrated an increasing prevalence of children exceeding the threshold for high BP (inclusive of hypertension and prehypertension) between 1988 and 2008, reaching 12.6% among females and 19.2% among males in 2008 [23]. The discrepant results may reflect the higher prevalence of overweight and obesity in NHANES (33.3% among females and 35.1% among males, compared to 27.5% and 30.9% in this study); the amount of missing data was similar for NHANES and LSAC [24]. The NHANES data demonstrates an increased prevalence of children exceeding the threshold for high BP with increasing age, but the effect size is small (OR 1.12 per year) and that study included both younger and older children. Hence, age is likely to account for only a small part of the observed differences.

We also considered the possible impact of the recently released AAP guidelines on the classification of high BP. The reduced thresholds compared to the Fourth Report lead to a small absolute, but proportionally large, increase in the prevalence of children with values in the high BP range. The threshold for hypertension was now met in 5.4% of the population and elevated BP (prehypertension) in 3.7%. The greatest relative impact was among children with prehypertension, 70.3% of whom were

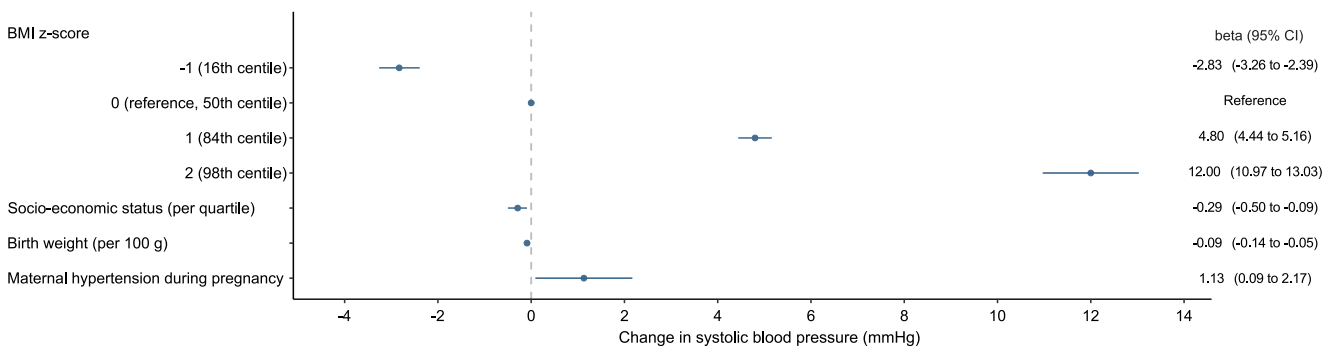


Fig. 3 Multivariable model for age, sex, and height adjusted BP. beta increase in systolic BP (mmHg) per unit increase in the covariate, CI confidence interval, BMI body mass index, BP blood pressure

re-classified as having stage 1 hypertension. This is consistent with both the 90th and 95th percentile reference values being reduced by a similar amount in the AAP guidelines (prehypertension also increased because these values have moved towards the center of the population distribution). Recent analysis of 5 to 18-year-old children participating in NHANES demonstrated a similar increase in the population-based prevalence of children exceeding the threshold for hypertension with application of the AAP 2017 guidelines (2.7 to 5.5%) [25].

Our findings regarding the relationship between BP and BMI among children add to previous findings by considering BMI as a continuous covariate, allowing for a description of the non-linear relationship with BP [22, 23]. Our estimate for the effect of birth weight is lower than previously reported [26]. However, many previous studies do not adjust for socioeconomic status and maternal blood pressure, which are associated with both birth weight and BP, and thus potentially important confounders [27]. Maternal hypertension during pregnancy may drive epigenetic programming or simply reflect the heritable component of blood pressure [28]. The finding that sport has a direct impact on BP beyond that of BMI, and after adjustment for confounders such as socioeconomic status, is consistent with trial data examining the impact of physical activity on BMI and BP in children [29, 30]. Increased television watching, neighborhood livability, being breast fed for at least 3 months, and a higher internalizing score (Strengths and Difficulties Questionnaire) were all associated with BP only in univariate analyses. This is consistent with the overall evidence base for the association between BP and these lifestyle factors in children, where fully adjusted analyses, larger studies, and trial data (for breast feeding) show no or weak evidence of an association; although it is difficult to resolve the role of covariates as confounders or mediators in complex observational data [31–33]. Such data does not preclude changes in these lifestyle measures being associated with BP.

There are some potential limitations to these data. Our method of taking multiple measurements at one visit, as opposed to over multiple visits, is consistent with other studies [8, 22, 23, 25, 34], but may have increased our estimates of prevalence, compared to the proportion of children that would require further investigation and clinical management of BP in clinical practice [23]. Other differences between the reference data used in the Fourth Report and AAP 2017 guidelines and this study, is the use of an oscillometric device to measure BP in this study, and the averaging of BP measurements rather than using the first measurement only. The first of these features is likely to slightly increase the observed BP in our study, and the second is to slightly reduce values on average [11, 35]. Overall, they are unlikely to have substantially impacted the results presented. Validation studies for the UA767 model of the A&D sphygmomanometer did not include participants below 15 years of age [36]. The prospective nature of LSAC

means that it has a better breadth and completeness of data on confounders than most comparable studies. However, we did not have data on salt intake or excretion, which are positively correlated with BP. One problem when analyzing data where there is such complete capture of potential explanatory variables is how to address the role of mediation. Another analytic approach, if we were to focus on the role of BMI or other variables as mediators, would be structural equation modeling. However, this requires a clear understanding of, or strong assumptions about, the underlying causal pathway. In addition, intermediate confounding is likely to be common and is difficult to adjust for [37]. For example, neighborhood livability might be considered an intermediate confounder, where BMI mediates some of the relationship between socioeconomic status and BP, but livability also mediates some of this relationship and confounds the association between BMI and BP. Regardless of the analytic technique, and as applies to the analyses presented here, one cannot infer causality from cross-sectional, observational data. Given the limited age range of participants, caution should be applied in generalizing these results to young children or older adolescents.

The reclassification of children with stage 1 hypertension under the AAP guidelines has important implications, because this is the threshold at which treatment, initially nonpharmacologic whether children are obese or not, is recommended [7]. The approach of the AAP to exclude overweight children from the reference population is not unreasonable. However, truncating the BMI range of the reference population means that it cannot have the normal distribution one would expect in an a physiologically healthy reference population. It is likely that this issue will remain controversial until there are sufficient data to allow the derivation of risk-based thresholds. We show that the relationship between BP and BMI was not linear, with an increasing gradient for BMI approaching the overweight and obese range. This means that for populations with a mean BMI z score above zero and increasing, that the rate of increase in hypertension over time is likely to accelerate. The persistence of BMI and birth weight as significant variables in the final multivariable model may be because they represent convergent points mediating complex, multifactorial causal pathways to hypertension. Regardless, they are potential targets for interventional trials aiming to reduce the prevalence of hypertension. In combination with published trial data, our large-scale observational evidence would support the concept of interventions that encourage sporting participation. These interventions should specifically include socioeconomically disadvantaged children who are not only at higher risk of hypertension, but also face barriers to both involvement in organized sport and receiving appropriate treatment for hypertension [34, 38].

In summary, 9.1% of 10 to 12-year Australian children exceed the AAP thresholds for elevated BP or hypertension, compared to 6.1% using the previous reference standard, the

Fourth Report. BMI is a strong predictor of BP, but the relationship is not linear. Birth weight, socioeconomic status, maternal hypertension during pregnancy, and sporting participation are all associated with BP when adjusted for one another and BMI.

Acknowledgements The Growing Up in Australia, the Longitudinal Study of Australian Children, is conducted in partnership between the Department of Social Services (DSS), the Australian Institute of Family Studies (AIFS), and the Australian Bureau of Statistics (ABS). The findings and views reported in this paper are those of the author and should not be attributed to DSS, AIFS, or the ABS.

Funding Nicholas Larkins work on this project was funded by a Postgraduate Scholarship from the National Health and Medical Research Council (NHMRC; GNT1114218). Armando Teixeira-Pinto is partially supported by the NHMRC Program Grant BeatCKD (APP1092957). David Burgner is supported by a NHMRC Senior Research Fellowship (1064629) and is a National Heart Foundation Future Fellow (100026). For the remaining authors, none were declared.

Compliance with ethical standards

Written informed consent was provided by families and the study was approved by the Australian Institute of Family Studies Ethics Committee.

Conflicts of interest The authors declare that they have no conflict of interest.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

References

- Olsen MH, Angell SY, Asma S, Boutouyrie P, Burger D, Chirinos JA, Damasceno A, Delles C, Gimenez-Roqueplo A-P, Hering D, López-Jaramillo P, Martinez F, Perkovic V, Rietzschel ER, Schillaci G, Schutte AE, Scuteri A, Sharmar JE, Wachtell K, Wang JG (2016) A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the Lancet Commission on hypertension. *Lancet* 388:2665–2712
- Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, White IR, Caulfield MJ, Deanfield JE, Smeeth L, Williams B, Hingorani A, Hemingway H (2014) Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet* 383:1899–1911
- Larkins N, Craig J (2018) Cohort studies, meta-analyses, and clinical trials in childhood hypertension. In: Flynn J, Ingelfinger J, Redwine K (eds) *Pediatric hypertension*. Springer, Cham, pp 819–839
- Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, Amann M, Anderson HR, Andrews KG, Aryee M, Atkinson C, Bacchus LJ, Bahalim AN, Balakrishnan K, Balmes J, Barker-Collo S, Baxter A, Bell ML, Blore JD, Blyth F, Bonner C, Borges G, Bourne R, Boussinesq M, Brauer M, Brooks P, Bruce NG, Brunekeef B, Bryan-Hancock C, Bucello C, Buchbinder R, Bull F, Burnett RT, Byers TE, Calabria B, Carapetis J, Carnahan E, Chafe Z, Charlson F, Chen H, Chen JS, Cheng AT, Child JC, Cohen A, Colson KE, Cowie BC, Darby S, Darling S, Davis A, Degenhardt L, Dentener F, Des Jarlais DC, Devries K, Dherani M, Ding EL, Dorsey ER, Driscoll T, Edmond K, Ali SE, Engell RE, Erwin PJ, Fahimi S, Falder G, Farzadfar F, Ferrari A, Finucane MM, Flaxman S, Fowkes FG, Freedman G, Freeman MK, Gakidou E, Ghosh S, Giovannucci E, Gmel G, Graham K, Grainger R, Grant B, Gunnell D, Gutierrez HR, Hall W, Hoek HW, Hogan A, Hosgood HD 3rd, Hoy D, Hu H, Hubbell BJ, Hutchings SJ, Ibeanusi SE, Jacklyn GL, Jasrasaria R, Jonas JB, Kan H, Kanis JA, Kassebaum N, Kawakami N, Khang YH, Khatibzadeh S, Khoo JP, Kok C, Laden F, Lalloo R, Lan Q, Lathlean T, Leasher JL, Leigh J, Li Y, Lin JK, Lipshultz SE, London S, Lozano R, Lu Y, Mak J, Malekzadeh R, Mallinger L, Marcenes W, March L, Marks R, Martin R, McGale P, McGrath J, Mehta S, Mensah GA, Merriman TR, Micha R, Michaud C, Mishra V, Mohd Hanafiah K, Mokdad AA, Morawska L, Mozaffarian D, Murphy T, Naghavi M, Neal B, Nelson PK, Nolla JM, Norman R, Olives C, Omer SB, Orchard J, Osborne R, Ostro B, Page A, Pandey KD, Parry CD, Passmore E, Patra J, Pearce N, Pelizzari PM, Petzold M, Phillips MR, Pope D, Pope CA 3rd, Powles J, Rao M, Razavi H, Rehfuss EA, Rehm JT, Ritz B, Rivara FP, Roberts T, Robinson C, Rodriguez-Portales JA, Romieu I, Room R, Rosenfeld LC, Roy A, Rushton L, Salomon JA, Sampson U, Sanchez-Riera L, Sanman E, Sapkota A, Seedat S, Shi P, Shield K, Shivakoti R, Singh GM, Sleet DA, Smith E, Smith KR, Stapelberg NJ, Steenland K, Stöckl H, Stovner LJ, Straif K, Straney L, Thurston GD, Tran JH, Van Dingenen R, van Donkelaar A, Veerman JL, Vijayakumar L, Weintraub R, Weissman MM, White RA, Whiteford H, Wiersma ST, Wilkinson JD, Williams HC, Williams W, Wilson N, Woolf AD, Yip P, Zielinski JM, Lopez AD, Murray CJ, Ezzati M, AlMazroa MA, Memish ZA (2012) A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 380:2224–2260
- Johnson CL, Dohrmann SM, Burt VL, Mohadjer LK (2014) National Health and nutrition examination survey: sample design, 2011–2014. *Vital Health Stat* 2(162):1–33
- National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (2004) The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics* 114:555–576
- Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, de Ferranti SD, Dionne JM, Falkner B, Flinn SK, Gidding SS, Goodwin C, Leu MG, Powers ME, Rea C, Samuels J, Simasek M, Thaker VV, Urbina EM (2017) Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics* 140:e20171904
- Rosner B, Cook N, Portman R, Daniels S, Falkner B (2008) Determination of blood pressure percentiles in normal-weight children: some methodological issues. *Am J Epidemiol* 167:653–666
- Soloff C, Lawrence D, Johnstone R (2005) LSAC technical paper number 1: sample design. Australian Institute of Family Studies, Melbourne
- Bronfenbrenner U, Morris PA (2007) The bioecological model of human development. In: Damon W, Lerner R (eds) *Handbook of child psychology*. John Wiley & Sons, Hoboken, pp 793–828
- Duncombe SL, Voss C, Harris KC (2017) Oscillometric and auscultatory blood pressure measurement methods in children: a systematic review and meta-analysis. *J Hypertens* 35:213–224
- Šuláková T, Šuláková A, Strnadel J, Pavlíček J, Obermannová B, Feber J (2016) Can auscultatory blood pressure normative values be used for evaluation of oscillometric blood pressure in children? *J Clin Hypertens* 19:381–387
- Ogden CL, Kuczmarski RJ, Flegal KM, Mei Z, Guo S, Wei R, Grummer-Strawn LM, Curtin LR, Roche AF, Johnson CL (2002) Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. *Pediatrics* 109:45–60

14. Barlow SE, the Expert Committee (2007) Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics* 120:S164–S192
15. Blakemore T, Strazdins L, Gibbings J (2009) Measuring family socioeconomic position. *Aust Soc Policy* 8:121–168
16. Goodman A, Lamping DL, Ploubidis GB (2010) When to use broader internalising and externalising subscales instead of the hypothesised five subscales on the Strengths and Difficulties Questionnaire (SDQ): data from British parents, teachers and children. *J Abnorm Child Psychol* 38:1179–1191
17. Norton A, Monahan K, Branch PE (2015) The Longitudinal Study of Australian Children: LSAC Technical paper No.15, Wave 6 Weighting and Non-Response. Australian Institute of Family Studies, Melbourne
18. Royston P, Ambler G, Sauerbrei W (1999) The use of fractional polynomials to model continuous risk variables in epidemiology. *Int J Epidemiol* 28:964–974
19. Morris TP, White IR, Carpenter JR, Stanworth SJ, Royston P (2015) Combining fractional polynomial model building with multiple imputation. *Stat Med* 34:3298–3317
20. Little RJA, Rubin DB (2014) *Statistical analysis with missing data*. John Wiley & Sons, Hoboken
21. Australian Bureau of Statistics (ABS) (2015) *National Health Survey: First Results, 2014–15*. ABS, Canberra
22. Larkins NG, Teixeira-Pinto A, Craig JC (2015) The prevalence and predictors of hypertension in a National Survey of Australian children. *Blood Press* 27:41–47
23. Rosner B, Cook NR, Daniels S, Falkner B (2013) Childhood blood pressure trends and risk factors for high blood pressure: the NHANES experience 1988–2008. *Hypertension* 62:247–254
24. Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS) (2014) National health and nutrition examination survey data. In: US Department of Health and Human Services. Centers for Disease Control and Prevention, Hyattsville
25. Sharma AK, Metzger DL, Rodd CJ (2018) Prevalence and severity of high blood pressure among children based on the 2017 American Academy of Pediatrics guidelines. *JAMA Pediatr* 172:557–565
26. Huxley R, Shiell A, Law C (2000) The role of size at birth and postnatal catch-up growth in determining systolic blood pressure: a systematic review of the literature. *J Hypertens* 18:815–831
27. Edvardsson VO, Steinhorsdottir SD, Eliasdottir SB, Indridason OS, Palsson R (2012) Birth weight and childhood blood pressure. *Curr Hypertens Rep* 14:596–602
28. Davis EF, Lewandowski AJ, Aye C, Williamson W, Boardman H, Huang RC, Mori TA, Newnham J, Beilin LJ, Leeson P (2015) Clinical cardiovascular risk during young adulthood in offspring of hypertensive pregnancies: insights from a 20-year prospective follow-up birth cohort. *BMJ Open* 5:e008136
29. Hansen HS, Froberg K, Hyldebrandt N, Nielsen JR (1991) A controlled study of eight months of physical training and reduction of blood pressure in children: the Odense schoolchild study. *BMJ* 303:682–685
30. Farpour-Lambert NJ, Aggoun Y, Marchand LM, Martin XE, Herrmann FR, Beghetti M (2009) Physical activity reduces systemic blood pressure and improves early markers of atherosclerosis in pre-pubertal obese children. *J Am Coll Cardiol* 54:2396–2406
31. Kramer MS, Matush L, Vanilovich I, Platt RW, Bogdanovich N, Sevkovskaya Z, Dzikovich I, Shishko G, Collet J-P, Martin RM, Smith GD, Gillman MW, Chalmers B, Hodnett E, Shapiro S (2007) Effects of prolonged and exclusive breastfeeding on child height, weight, adiposity, and blood pressure at age 6.5y: evidence from a large randomized trial. *Am J Clin Nutr* 86:1717–1721
32. Martin RM, Gunnell D, Smith GD (2005) Breastfeeding in infancy and blood pressure in later life: systematic review and meta-analysis. *Am J Epidemiol* 161:15–26
33. Lazarou C, Panagiotakos DB, Matalas AL (2009) Lifestyle factors are determinants of children's blood pressure levels: the CYKIDS study. *J Hum Hypertens* 23:456–463
34. Duru OK, Vargas RB, Kermah D, Pan D, Norris KC (2007) Health insurance status and hypertension monitoring and control in the United States. *Am J Hypertens* 20:348–353
35. Veloudi P, Blizzard CL, Srikanth VK, Schultz MG, Sharman JE (2018) Influence of blood pressure level and age on within-visit blood pressure variability in children and adolescents. *Eur J Pediatr* 117:205–210
36. Rogoza AN, Pavlova TS, Sergeeva M (2000) Validation of A&D UA-767 device for the self-measurement of blood pressure. *Blood Press Monit* 5:227–231
37. Richiardi L, Bellocco R, Zugna D (2013) Mediation analysis in epidemiology: methods, interpretation and bias. *Int J Epidemiol* 42:1511–1519
38. Brockman R, Jago R, Fox KR, Thompson JL, Cartwright K, Page AS (2009) “Get off the sofa and go and play”: family and socioeconomic influences on the physical activity of 10–11 year old children. *BMC Public Health* 9:253