

## Epidemiology of elevated blood pressure in youth and its utility for predicting adulthood outcomes: A review

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### Abstract

Elevated blood pressure has been demonstrated to track from youth to adulthood and some have demonstrated an association between early-life blood pressure and subsequent atherosclerosis and cardiovascular disease. In addition, reports regarding the strength of tracking are inconsistent and the modifiable risk factors that affect the trajectory of blood pressure from youth to adulthood remain unclear. This paper comprehensively evaluated the existing classifications of youth hypertension and the current trends of youth hypertension. Further, evidence for the consequences of hypertension in youth has been comprehensively evaluated. Importantly, a review of the studies examining tracking from youth to adulthood has been performed and a number of studies investigating the factors affecting tracking has also been investigated. The overall consideration of this body of literature highlights the vital importance of identifying hypertension in youth to prevent complications in adulthood. Adiposity is regarded to be a factor affecting the progression of hypertension from youth to adulthood yet there is little evidence available for other modifiable factors. It is apparent that further research is necessary within this field in order to create effective preventative strategies to target youth hyper-

tension.

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**Key words:** Pediatric; Children; Blood pressure; Hypertension; Epidemiology; Atherosclerosis

**Core tip:** Elevated blood pressure in youth predicts adult hypertension and end-stage organ damage but most youth with elevated blood pressure are left undiagnosed. In this review, we examine current classifications of youth blood pressure, recent trends in youth blood pressure, the adult consequences of elevated youth blood pressure, and lifestyle factors associated with improved blood pressure status from youth to adulthood. We show that identification of youth with elevated blood pressure may prove effective in preventing associated adult complications and that youth with elevated blood pressure may benefit most from interventions aimed at improvements to adiposity between youth and adulthood.

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### INTRODUCTION

It has been established that atherosclerosis begins at an early age and progresses silently throughout the life span before clinical complications such as myocardial infarction, stroke, and peripheral vascular disease present<sup>[1]</sup>. Substantial evidence supports the role of elevated blood pressure levels (including hypertension and prehypertension) as an important contributor to cardiovascular disease in adults and as such, has received increasing in-

terest as the target of consensus statements for pediatric screening and treatment<sup>[2]</sup>. The basis of these documents is that prevention, and treatment, of elevated blood pressure beginning in childhood or adolescence (from age 5-year to 18-year, herein termed youth) may reduce the lifetime risk of atherosclerotic cardiovascular disease. In this review, we summarize the epidemiology of youth hypertension and provide an overview of important findings from studies on blood pressure that span youth to adulthood.

## CLASSIFICATION OF YOUTH BLOOD PRESSURE LEVELS

A number of criteria and definitions have been proposed for the classification of blood pressure levels in youth; albeit mostly for use among North American populations<sup>[3-5]</sup>. The most widely accepted standard is that devised by the National High Blood Pressure Education Program (NHBPEP) in 1987 and revised in their fourth report in 2004<sup>[4,6,7]</sup>. This classification defines high blood pressure on the basis of age, sex and height percentiles. Prehypertension, signifying blood pressure only marginally elevated above normal levels, is defined as systolic or diastolic blood pressure between the 90<sup>th</sup> and 95<sup>th</sup> age-, sex-, and height- specific percentiles and hypertension is defined as systolic or diastolic blood pressure between the age-, sex- and height- specific 95<sup>th</sup> and 100<sup>th</sup> percentiles. Elevated blood pressures must be confirmed on repeated visits. However, the NHBPEP scale may be poorly applicable both as a population-screening tool and for application to the clinical setting due to its complex design. For example, the NHBPEP classification contains over 950 critical values [*i.e.*, 7 height percentiles, 2 measures (systolic and diastolic blood pressure), 17 age-groups (1-17 years), for males and females, each for prehypertension and hypertension], compared with simplified classifications that have been subsequently proposed by Kaelber *et al*<sup>[8]</sup> and Mitchell *et al*<sup>[9]</sup> that are based on the NHBPEP cut-points but contain only 64 and 10 critical values respectively. Using data from the Cardiovascular Risk in Young Finns Study that collected data from participants when aged 3-18 years and followed them up more than 20 years later, Aatola *et al*<sup>[10]</sup> compared the predictive utility of the NHBPEP classification of elevated youth blood pressure with the two simplified versions proposed by Kaelber *et al*<sup>[8]</sup> and Mitchell *et al*<sup>[9]</sup>. They concluded that the simplified classifications, which only account for combinations of age and sex but not height, had similar predictive utility for pulse wave velocity measured in adulthood than the NHBPEP classification, which considers age, sex and height percentiles. Therefore, the simplified definitions, if proven to show similar predictive utility for other outcomes, would largely overcome the complexity of the NHBPEP classification as a potential barrier to its implementation in the clinical and population-based settings. As with classifications of blood pressure in adulthood, the cut-point definitions used to denote someone

of apparent increased risk, although practical, do not acknowledge that there is a continuous relationship between youth blood pressure levels and adult end-organ damage<sup>[11-13]</sup>.

In the diagnosis of paediatric hypertension it is also important to consider alternate secondary causes, particularly if blood pressure values are excessively high. Secondary hypertension is more common in childhood than adulthood and can be attributable to conditions such as pheochromocytoma, bronchopulmonary dysplasia, coarctation of the aorta, renal artery stenosis and other renal abnormalities. Nevertheless, estimates of secondary hypertension prevalence in youth are still relatively lower than combined essential hypertension and prehypertension in childhood and this review will only consider the latter<sup>[14]</sup>.

## TRENDS IN YOUTH BLOOD PRESSURE

Though not all available data are concordant<sup>[15-19]</sup>, the prevalence of elevated blood pressure in youth appears to be increasing<sup>[20-25]</sup>. The increasing trend in pediatric prehypertension and hypertension is widely attributed to the childhood obesity epidemic<sup>[26-31]</sup>. Though the worldwide prevalence of elevated blood pressure in youth is unknown, the most recent data from the nationally representative United Kingdom National Health and Examination Survey suggested a 27% increase in elevated blood pressure (prehypertension or hypertension) among youth from 1999-2008<sup>[28]</sup>. These data indicated that among youth aged 8-17 years 10% were prehypertensive and 3.7% were hypertensive<sup>[30]</sup>. These values are probably underestimates of the true prevalence of pediatric prehypertension and hypertension due to misclassification and under diagnosis<sup>[27,32-37]</sup>. Upon examination of medical records from 507 youth, Hansen *et al*<sup>[36]</sup> illustrated these inconsistencies by showing that despite adequate examination, more than 74% of those who satisfied the criteria for hypertension had no diagnosis. The reasons for this were speculated to include poor clinician knowledge of the existing guidelines and cut-points, and lack of awareness of the patient's previous readings. We hypothesize that the complexities of the NHBPEP classification probably added to the poor clinician knowledge and that blood pressure measurements were likely secondary to the primary reason for the patient's clinic attendance.

## IMPORTANCE OF IDENTIFYING YOUTH HYPERTENSION

Formerly, the presence of elevated blood pressure in youth was considered to be benign unless related to secondary causes. However, there is now sound evidence showing that high blood pressure in youth indicates higher likelihood of hypertension as an adult<sup>[38]</sup>. Additional research has indicated that pathological changes, such as markers of atherosclerosis and changes in left ventricular morphology, measured concurrently or in

adulthood, are associated with elevated youth blood pressure<sup>[10-13,39-55]</sup>. These changes are largely asymptomatic and are detectable prior to signs of end-organ damage such as nephropathy and retinopathy. Two of these studies, the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study<sup>[41,56,57]</sup> and the Bogalusa Heart Study<sup>[39,47-50]</sup> have shown autopsy evidence of accelerated atherosclerosis among children and adolescents with indicators of elevated blood pressure measured both post mortem (PDAY) and ante mortem (Bogalusa). In addition, elevated pulse pressure in youth has been associated with adverse changes in left ventricular morphology in youth and increased atherosclerosis in adulthood<sup>[11,45]</sup>. Most importantly, a recent study indicated that levels of carotid intima-media thickness (CIMT), a preclinical marker of atherosclerosis, is similar among those that normalize their elevated blood pressure in the time between youth and adulthood to those who did not have elevated blood pressure in youth or adulthood<sup>[58,59]</sup>. This reversal has not been demonstrated to the same extent in those who normalize their blood pressure during adulthood and thus confirms the importance of identifying elevated blood pressure in youth<sup>[41]</sup>.

The link between elevated blood pressure and premature mortality (all-cause and cardiovascular) in adulthood is well documented<sup>[60]</sup>. Predictably, it is hypothesized that elevated blood pressure in youth is associated with premature mortality from cardiovascular disease although only one study was found to have examined this association<sup>[29]</sup>. This recent publication showed a relationship between youth hypertension and premature mortality from endogenous causes<sup>[29]</sup>. Interestingly, some have also reported a higher incidence of specific cardiovascular diseases, primarily stroke, in adolescence and early adulthood in association with essential hypertension<sup>[61]</sup>.

## TRACKING OF BLOOD PRESSURE FROM YOUTH TO ADULTHOOD

Tracking is a term used in epidemiological research to refer to the ability of an individual to maintain their approximate blood pressure rank relative to the rest of a cohort over a period of time<sup>[62-64]</sup>. The primary aim of tracking investigations is to determine the extent to which future blood pressure elevations can be identified from blood pressure measurements in youth. If these studies demonstrate significant tracking they have the potential to inform clinical practice, particularly regarding primary prevention in youth.

Tracking of blood pressure from youth to adulthood has been investigated in a number of longitudinal studies and has been the focus of two systematic reviews with meta-analysis. Chen *et al.*<sup>[38]</sup> conducted a systematic review and meta-analysis that included 50 cohort studies. Studies were selected on the basis of a sample size > 50, reporting of tracking correlation coefficients, baseline ages < 18 years and publication in English, Chinese or Japanese. Mean tracking coefficients were 0.38 for systolic blood

pressure and 0.28 for diastolic blood pressure. Tracking was shown to be stronger among males compared with females for both systolic blood pressure and diastolic blood pressure. Toschke *et al.*<sup>[65]</sup> produced a meta-analysis from 29 studies and presented similar findings to that of Chen. Their results showed a mean correlation coefficient of 0.37 for systolic blood pressure and 0.31 for diastolic blood pressure. However, both papers included results from tracking studies within youth. Overall, these two reviews and several studies<sup>[66-71]</sup> concluded that the strength of tracking merits population-based prevention aimed at decreasing elevated blood pressure in children, and regular blood pressure screening in an attempt to identify those youth at risk of developing elevated levels in adulthood and whom may benefit from early detection. However, some did not agree with these recommendations<sup>[72-74]</sup>. Woelk<sup>[75]</sup> published a review indicating that tracking was too weak to justify blood pressure screening in youth. They emphasized the need for studies with a longer follow-up period, increased numbers of blood pressure observations and using a statistical model that does not infer linearity. While methodological concerns play an important role in the degree to which blood pressure measures track, these studies do not consider that some of the inherent loss of tracking could be as a direct result of individuals enacting changes to their lifestyle during the period of observation that may place them on a different trajectory<sup>[62,76]</sup>.

## FACTORS AFFECTING TRACKING OF BLOOD PRESSURE FROM YOUTH TO ADULTHOOD

There are several factors hypothesized to modify the tracking of blood pressure from youth to adulthood although few studies have investigated them, particularly as they relate to modifiable factors. However, in the absence of long-term clinical trials of blood pressure interventions, these results are particularly important as they could identify potential lifestyle-related targets for primary prevention strategies to lower blood pressure or maintain a healthy blood pressure at a population level or resolve an elevated blood pressure at an individual level<sup>[62]</sup>.

The predominance of literature investigating modifiable risk factors has focused on the association between single measurements in youth, such as body mass index (BMI), and their association with adult blood pressure measurements. Nevertheless, a small number of studies were identified that demonstrate how a change in risk factor levels from youth to adulthood are related to changes in blood pressure trajectory. These studies have primarily focused on adiposity and are outlined in Table 1.

For adiposity, the most comprehensive data were from Juhola *et al.*<sup>[59]</sup> that used data from four large prospective studies (the Muscatine, Bogalusa, Young Finns and CDAH studies). They examined change in BMI z-score between youth and adulthood in respect to the youth-

**Table 1 Summary of studies investigating modifiable factors affecting blood pressure tracking from childhood to adulthood<sup>1</sup>**

Ref.	Study	Location	No.	Factors
Juhola <i>et al</i> <sup>[59]</sup>	i3C Consortium	Finland, Australia, United States	4210	Adiposity (BMI)
Dekkers <i>et al</i> <sup>[77]</sup>	Not specified	United States	745	Adiposity (BMI)
Klumbiene <i>et al</i> <sup>[71]</sup>	The Longitudinal Study of Juvenile Hypertension in Lithuania	Lithuania	505	Adiposity (BMI, weight)
Lambrechtsen <i>et al</i> <sup>[80]</sup>	Odense Schoolchild Study	Denmark	1369	Adiposity (weight), physical fitness
Macedo <i>et al</i> <sup>[79]</sup>	Not specified	Portugal	222	Adiposity (BMI, weight)
Yong <i>et al</i> <sup>[72]</sup>	The Dormont High School Study	United States	202	Adiposity (weight)
Lauer <i>et al</i> <sup>[78]</sup>	The Muscatine Study	United States	2165	Adiposity (weight, BMI, skin fold thickness and waist circumference), bone density

<sup>1</sup>Studies sorted by publication year (latest to earliest). BMI: Body mass index; i3C Consortium: International Childhood Cardiovascular Cohort Consortium.

adult blood pressure groups of control (normal blood pressure as a youth and adult), resolution (elevated blood pressure in youth but not as an adult), incident (normal blood pressure in youth but elevated in adulthood), and persistent (elevated blood pressure in both youth and adulthood). This revealed that those in the incident and persistent hypertension groups had increased their BMI z-score relative to those that resolved their hypertensive status or those in the control group. Moreover, those that resolved their elevated blood pressure status has a greater mean decrease in their BMI z-score compared with the control group. This illustrates that adiposity, measured using BMI, has a significant affect on blood pressure tracking from youth to adulthood. Dekkers *et al*<sup>[77]</sup>, Klumbiene *et al*<sup>[71]</sup>, Lauer *et al*<sup>[78]</sup> and Macedo *et al*<sup>[79]</sup> had similar findings in relation to BMI change. Yong *et al*<sup>[72]</sup>, Macedo *et al*<sup>[79]</sup>, Lauer *et al*<sup>[78]</sup> and Lambrechtsen *et al*<sup>[80]</sup> also demonstrated an association between weight change and blood pressure trajectory change from youth to adulthood.

Lauer *et al*<sup>[78]</sup> additionally examined skin fold thickness, waist circumference and bone density and demonstrated that resolution of hypertensive blood pressure or the maintenance of low blood pressure in youth was associated with lesser skin fold thickness and waist circumference and lesser bone age.

Lambrechtsen *et al*<sup>[80]</sup> further demonstrated that change in physical fitness was related to change in blood pressure tracking from youth to adulthood. The results of logistic regression to predict a rise in blood pressure quartile revealed odd's ratios were higher for models accounting for weight change (OR = 1.05, 95%CI: 1.03-1.07) or physical fitness (OR = 1.04, 95%CI: 1.01-1.07) in addition to baseline blood pressure alone (OR = 0.94, 95%CI: 0.89-0.96). This revealed the utility of these factors in predicting future blood pressure status and also indicates their potential for further research into prevention and risk reduction.

Overall, there is little research to indicate how changes in modifiable factors impact tracking of blood pressure levels from youth to adulthood, particularly those that may lead to improved blood pressure status. However, there are a number of other modifiable factors that are likely to influence blood pressure tracking. These include; diet, physical activity, muscular fitness, smoking, alcohol

consumption, hormonal contraceptive use and socioeconomic status. There is significant cross-sectional research to suggest that these factors in youth are significantly associated with blood pressure levels in adulthood. Nevertheless, further study is necessary to determine how changes in these factors affect blood pressure tracking.

## PATHOBIOLOGICAL MECHANISMS OF OBESITY AND ELEVATED BP IN YOUTH

Though the association of excess adiposity levels on blood pressure values from youth to adulthood has been well documented, the exact mechanism of this relationship remains uncertain. Adiposity is proposed to affect youth BP levels through a number of processes including; the renin-angiotensin system, hormonal changes and pro-inflammatory changes to the endothelium<sup>[81]</sup>. Although closely related, youth elevated BP and youth obesity is also known to have independent effects on the early development and progression of atherosclerosis<sup>[11,82,83]</sup>. Raitakari *et al*<sup>[11]</sup> reported a significant association between youth BMI and adult CIMT and systolic BP and adult CIMT in univariable models. However, the effect of both BMI and systolic BP were somewhat attenuated in a multivariable model of risk factor load and CIMT, though both remained independent predictors. These data suggest that part of the effect of youth BMI and BP in the development of atherosclerosis is from a common pathway. It has been shown that the presence of multiple risk factors accelerates atherosclerosis development in the young, but the effect appears mostly additive rather than synergistic<sup>[39]</sup>. And though it has been shown that blood lipids interact with BMI such that among those children who are overweight or obese having an adverse lipid level substantially increases risk of developing a high CIMT in adulthood whereas normal weight children with adverse blood lipids do not have increased risk<sup>[84]</sup>, the same has not been shown for BP<sup>[84]</sup>. Though it appears that both youth BMI and BP are independently contributing to adult markers of atherosclerosis, more data are needed to fully determine whether the presence of these risk factors in youth are working synergistically in increasing cardiovascular risk.

## CONCLUSION

Paediatric hypertension is an increasingly important issue and requires greater attention and awareness in the clinical and research domains. This review has entailed literature regarding the epidemiology of youth blood pressure and some of its predictive utility for end-organ damage both in youth and later, in adulthood. We identified that while tracking of blood pressure levels from youth to adulthood is significant, resolution of elevated youth blood pressure by adulthood can largely attenuate the risk of some end-organ damage in youth - but the factors associated with resolution of elevated youth blood pressure are largely unstudied. Examination of multiple important modifiable factors, such as smoking, diet, socioeconomic status and fitness measures could provide vital information of significance to primary prevention guidelines and give clues as to changes that may precede secular declines in elevated blood pressure levels among youth. Furthermore, there is substantial scope for research into the utility and predictive value of other blood pressure measurements such as pulse pressure, mean arterial pressure, and mid blood pressure. In particular, pulse pressure and mid blood pressure are becoming increasingly important in adult blood pressure research and accordingly it is anticipated that these measures will be of increased interest in the pediatric population.

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