REVIEW ARTICLE

Screening for Elevated Blood Pressure in Children and Adolescents

A Critical Appraisal

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Although screening for elevated blood pressure (BP) in adults is beneficial, evidence of its beneficial effects in children is not clear. Elevated BP in children is associated with atherosclerosis early in life and tracks across the life course. However, because of the high variability in BP, tracking is weak, and having an elevated BP in childhood has a low predictive value for having elevated BP later in life. The absolute risk of cardiovascular diseases associated with a given level of BP in childhood and the long-term effect of treatment beginning in childhood are not known. No study has experimentally evaluated the benefits and harm of BP screening in children. One modeling study indicates that BP screen-and-treat strategies in adolescents are moderately cost-effective but less cost-effective than population-wide interventions to decrease BP for the reduction of coronary heart diseases. The US National Heart, Lung, and Blood Institute and the European Society of Hypertension recommend that children 3 years of age and older have their BP measured during every health care visit. According to the US Preventive Services Task Force, there is no sufficient evidence to recommend for or against screening, but their recommendations have to be updated. Whether the benefits of universal BP screening in children outweigh the harm has to be determined. Studies are needed to assess the absolute risk of cardiovascular diseases associated with elevated BP in childhood, to evaluate how to simplify the identification of elevated BP, to evaluate the long-term benefits and harm of treatment beginning in childhood, and to compare universal and targeted screening strategies.

JAMA Pediatr. 2013;167(3):266-273. Published online January 7, 2013.
doi:10.1001/jamapediatrics.2013.438

Hypertension is a major risk factor for cardiovascular diseases (CVDs). Worldwide, 7.1 million deaths (13% of the global total) are due to elevated blood pressure (BP) in adults every year.[1]

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Until recently, hypertension was rarely searched for or diagnosed in children and adolescents. However, the approach toward elevated BP in childhood is changing because of the growing evidence that elevated BP in youth has detrimental lifelong cardiovascular effects.[2]

The BP level in childhood tracks to the BP level in adulthood, and children with elevated BP have a higher probability of developing hypertension as adults than do children with low BP.[3] This BP tracking is a major argument for being concerned with elevated BP early in life; since BP tracks, prevention and treatment of elevated BP early in life can result in a lifelong reduction of BP and of its associated conditions.

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Table 1. Key Questions That Need to be Addressed to Evaluate the Role of Screening for Elevated Blood Pressure in Children[a]

Question	Responses
1. Is elevated BP in children associated with CVD and mortality?	Association between childhood BP and surrogate markers of CVD was documented; no study was performed to quantify absolute CVD and mortality risk associated with childhood BP.
2. Is elevated BP in children associated with elevated BP later in life?	Yes
3. Is beginning treatment in childhood for elevated BP effective and safe?	Short-term efficacy to reduce childhood BP and safety was documented; long-term efficacy to decrease absolute CVD risk and safety is unknown.
4. Which method should be used to identify children with elevated BP?	Multiple BP readings at different visits are required.
5. Does screening for elevated BP in children reduce risk of CVD and mortality or improve quality of life?	No study has experimentally evaluated the benefits and harm of BP screening for children; one modeling study[29] indicates that BP screen-and-treat strategies for adolescents are moderately cost-effective but less cost-effective than population-wide interventions to decrease CHD risk.

Abbreviations: BP, blood pressure; CHD, coronary heart disease; CVD, cardiovascular disease.
[a] See also Figure 1.

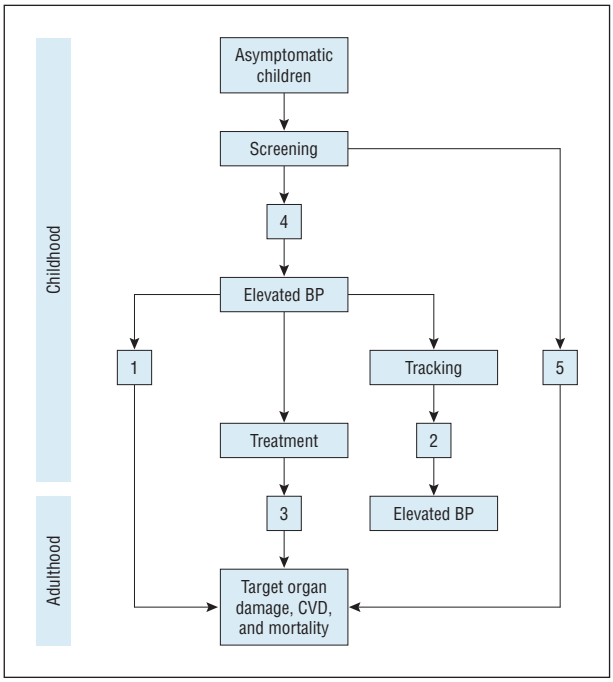

Figure 1. Analytic framework for evaluating the role of screening for elevated blood pressure (BP) in children (adapted from Sheridan et al[25]). Each number in a square corresponds to a key question that needs to be addressed (see Table 1). CVD indicates cardiovascular diseases.

Furthermore, elevated BP in childhood is associated with cardiac left ventricular hypertrophy[4] and a thickening of the carotid intima-media, a surrogate marker for atherosclerosis and a strong predictor of CVD.[5] Raised fibrous plaques of atherosclerosis have been observed in the aorta of children as young as 8 years of age, and the plaque extent has been shown to be associated with BP levels.[6]

Another reason for the interest in elevated BP in childhood is the increase in the prevalence of obesity. Because obesity is associated with elevated BP at all ages including childhood,[7-9] it is often assumed that the prevalence of hypertension has increased in youth in the last decades,[10,11] although such trends have not been observed in all populations.[12-15] Finally, although the clinical approach to the prevention of CVD relies on the identification and treatment of risk factors starting in mid-adulthood, a life-course approach to prevent the development of risk factors starting in childhood offers new avenues for the prevention of hypertension and CVD.[16,17]

In view of this evidence, universal BP screening beginning in childhood is advocated.[18-20] Undiagnosed elevated BP has become a matter of concern in children.[21,22] Screening for elevated BP may help identify children at increased risk of hypertension and CVD later in life and for whom early treatment could be beneficial.[23] Nevertheless, although there is strong evidence that screening for hypertension is beneficial for adults,[24,25] it is unclear whether screening is beneficial for children. Our aim is to critically appraise the evidence and recommendations regarding the screening for elevated BP in children and adolescents.

WHAT IS THE GOAL OF SCREENING FOR ELEVATED BP IN CHILDREN?

The aim of any screening is to identify individuals with an increased risk of disease relative to the general population or at an early stage of the disease with the aim of managing the identified condition.[26] Screening differs from standard clinical case finding; the latter consists of searching for diseases in individuals with medical problems, whereas the former is systematic and is conducted in apparently healthy individuals, that is, in individuals without specific signs or symptoms.[27] The UK National Screening Committee defined screening as "a process of identifying apparently healthy people who may be at increased risk of a disease or condition"; these people can then be offered "information, further tests and appropriate treatment to reduce their risk or any complications arising from the disease or condition."[28] As in adults, the primary goal of BP screening in asymptomatic children is to identify individuals at high risk of CVD due to elevated BP and to decrease this risk. The prevention of hypertension in adulthood should be seen as a secondary or intermediate goal of BP screening in children.

ANALYTIC FRAMEWORK AND KEY QUESTIONS

To evaluate the role of screening for elevated BP in children, we used the analytic framework proposed by the US Preventive Services Task Force (USPSTF) for reviewing the evidence regarding screening for hypertension in adults.[25] Five key questions, which we present, have to be addressed (**Table 1** and **Figure 1**).

Is Elevated BP in Children Associated With CVD and Mortality?

In adults, observational prospective studies have shown an increased risk of CVD and death associated with increased BP, and clinical trials have shown that lowering BP reduces the risk of CVD and death.[30,31] In a recent large nationwide cohort study in Sweden,[32] BP at the age of 18 years was shown to be associated with CVD mortality in later adulthood. No such evidence exists in persons younger than 18 years of age: although historical reports have shown that children with extremely high BP had a high short-term mortality,[33] no study has linked childhood BP to clinically manifest CVD in adulthood, and no trial was sufficiently long to show the effect of BP reduction in children on the reduction of CVD in adulthood.[19,34] However, several studies[6,35] have shown that elevated BP in childhood is associated with atherosclerosis later in life. For example, the Bogalusa Heart Study[6] showed that fibrous plaques were present in the aorta and coronary arteries of youth 2 to 39 years of age and that the extent of the lesions was positively correlated with systolic BP in childhood. In the Cardiovascular Risk in Young Finns Study,[36] BP in childhood was positively associated with the carotid intima-media thickness (a surrogate maker of hypertension end-organ damage) of young adults.

Overall, although it is reasonable to assume that children with elevated BP have an increased relative risk of CVD compared with children with low BP, there is no direct evidence to estimate the absolute risk of CVD associated with a given level of BP in childhood. In adults, the 5- or 10-year absolute risk of CVD increases with age and becomes important after mid-adulthood. There is little doubt that the 5- or 10-year risk is low in children compared with adults, but it has not yet been quantified. We also do not know the absolute CVD risk reduction following a given BP reduction during childhood. In all cases, the risk reduction will be smaller in children than in adults. It is necessary to quantify this risk in order to evaluate the effect of BP screening on children.

Nevertheless, irrespective of the magnitude of the contribution of childhood BP on the risk of adult CVD, elevated BP in children and adolescents has detrimental vascular consequences early in life, as shown by its associations with surrogate markers of vascular injury: for instance, increased arterial intima-media thickness,[37,38] impaired arterial compliance,[39] or retinal arteriolar narrowing.[40] Elevated BP is also associated with left ventricular hypertrophy in children and adolescents.[4,37]

Is Elevated BP in Children Associated With Elevated BP Later in Life?

The BP level tracks from childhood to adulthood: an individual at a given level (or rank) of BP tends to remain within the same level of BP throughout his or her life course. Therefore, children with elevated BP have a greater risk of having hypertension later in life than those with low BP.[3] However, within the same individual, BP is highly variable from minute to minute, from day to day, and from visit to visit, resulting in a relatively low degree of tracking. Furthermore, the within-individual BP variability is greater in childhood than in adulthood.[41,42] In a systematic review of studies assessing BP tracking from childhood to adulthood, the tracking coefficient correlation was, on average, 0.38 (range, −0.12 to 0.80) for systolic BP and 0.28 (range, −0.12 to 0.80) for diastolic BP.[3] Compared with the tracking of body mass index,[43] the tracking of BP is relatively weak.

A weak BP tracking results in a low predictive value of elevated BP in childhood for hypertension later in life.[23,42,44,45] For instance, in a universal BP screening program that was conducted in high schools in Dallas, Texas, 10% of 10th-grade students (15-16 years old) had elevated BP (≥95th percentile) at the initial examination, based on a single measurement.[46] Of these students with elevated BP, 17% had sustained elevated BP over 2 subsequent visits in the same year, that is, a positive predictive value of initial elevated BP for sustained elevated BP (over 1 year) of only 17%. Other studies indicate that the majority of children with elevated BP at a given visit have normal BP at subsequent visits a few weeks later, notably because of regression to the mean and habituation to the measurement procedure.[9,47,48] Over longer periods of time (eg, years), the positive predictive value of elevated BP at 1 visit is very low.

Averaging BP readings over several visits helps to account for BP variability, and this increases the degree of BP tracking and the predictive value of elevated BP.[42] Tracking would be stronger if it were possible to have a perfect measure of BP. For instance, for children 8 to 15 years of age who were followed up into young adulthood, BP was measured repeatedly at different visits, and after correction for the within-subject variability, the positive predictive value of childhood BP greater than the 95th percentile was 44% to 48% for systolic BP greater than the 90th percentile at 20 years of age.[44] The predictive value for elevated diastolic BP was 27% to 30%. Nevertheless, it is burdensome to obtain multiple BP readings at different visits and to estimate the average.

Is Beginning Treatment in Childhood for Elevated BP Effective and Safe?

Once a child has been identified as having elevated BP, a treatment is initiated and is expected to reduce BP, to prevent target organ damage, and, eventually, to decrease CVD risk. If an etiologic factor is involved, in case of secondary hypertension, the treatment should be targeted against the cause of hypertension. In most cases, a specific etiologic factor is not found, and the treatment aims initially to modify lifestyle.[19,20,34]

Lifestyle modifications consist of reducing the body weight in children who are overweight or obese, increasing physical activity and decreasing sedentary behaviors, and adopting a healthy diet (eg, decreased intake of saturated fats, sweetened drinks, and sodium and increased intake of fruits, vegetables, and whole grain products). For some of these measures, there is evidence for the short-term efficacy of reducing BP in children,[49-51] but the long-term efficacy is not known. There is no strong concern for the long-term safety of these lifestyle modifications.[51,52] Furthermore, lifestyle measures have ben-

eficial effects on several other conditions associated with elevated BP, including obesity, dyslipidemia, and hyperglycemia.

If the elevated BP is persistent despite lifestyle modifications or if the BP is very high, drug therapy is initiated. Clinical trials have demonstrated the short-term efficacy and safety of several classes of drugs for children.[34] For hypertensive children, BP control obtained by drug treatments was associated with less left ventricular hypertrophy.[53] However, no study has shown an effect on CVD end points. Furthermore, the long-term safety of drug treatment beginning in childhood is not known.[54] It has been hypothesized that a short period of treatment during childhood might cure hypertension or delay lifelong treatment.[23] There is no evidence to support this approach, which should be seriously evaluated.

Which Method Should Be Used to Identify Children With Elevated BP?

The goal of the screening test is to identify children with sustained elevated BP. Ideally, the test should be easy to perform, valid, and reliable. Key issues are the measurement method and the definition of elevated BP.

The measurement of BP requires standardized conditions and accurate instruments.[55] Office, ambulatory, and home BP can be measured in children. Office BP measured by a physician, a nurse, or a medical assistant is generally used for the screening of elevated BP. Blood pressure can also be measured by community pharmacists[56,57] or by school nurses.[9] The method of BP measurement is largely similar for adults and children.[20,34,58] The question whether to use oscillometric or auscultatory methods is still debated.[59] Traditionally, the auscultatory method is preferred for children.[19,20] Auscultatory methods are subject to specific observer biases (eg, rounding errors and expectation bias due to knowledge of previous readings), and the measurement devices need to be regularly calibrated.[55] Oscillometric devices should be clinically validated according to standard protocols,[55,60] and few devices have been validated for children.[58]

A major issue is the difficulty in defining the level of BP above which treatment is required in children.[29,61] Currently, the definition of elevated BP in children and adolescents is based on the normative distribution of office BP in children from the general population. Contrary to adults, norms for elevated BP in youth are not based on risk, and there are no studies assessing their ability in predicting CVD risk. The normative definition of elevated BP relies on the ranking of BP within a reference population: a child whose BP is above a given sex-, age-, and height-specific rank (percentile) is considered as having elevated BP.[19,20] These norms have been generated in specific populations (eg, US children). However, BP varies among populations (eg, higher values in European children compared with US children).[19] The diagnosis of hypertension, that is, sustained elevated BP, is based on multiple office BP measurements obtained on at least 3 different visits (**Figure 2**). An ambulatory BP measurement is used to confirm hypertension, to identify white coat hypertension, and to evaluate dipping nocturnal patterns.[19] Masked hypertension, that is, normal BP in the office and elevated BP out of the office, has also been reported in children.[19]

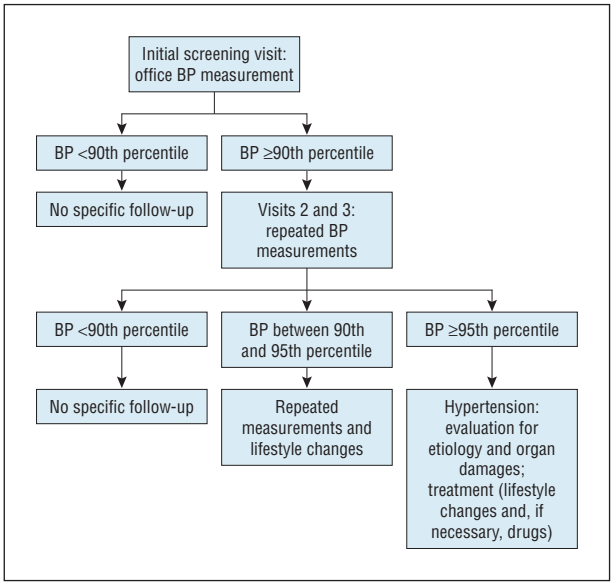

Figure 2. Diagnostic algorithm for hypertension in children and adolescents (adapted from Lurbe et al[19]). The diagnosis of hypertension requires having elevated blood pressure (BP) on at least 3 visits. Blood pressure below the 90th sex-, age-, and height-specific percentile is in the "normal" range, BP between the 90th percentile and the 95th percentile is in the "high-normal" or "prehypertension" range, and BP at or above the 95th percentile is in the "hypertension" range.

Several readings at multiple visits are required to have an accurate estimate of BP, but the best method for identifying elevated BP in children remains to be determined: efficiency and feasibility will depend on the number of visits, the number of readings at each visit, and the timing between visits. The optimal balance between the accuracy of BP determination and the predictive value of elevated BP (higher accuracy and better predictive value with multiple readings), on the one hand, and the feasibility and cost of the screening procedure (lower feasibility and higher cost with multiple readings), on the other, has to be identified.

Furthermore, current tables of normative BP values are difficult to use because of the multiple sex-, age-, and height-specific thresholds to define normal and elevated BP. Simpler tables or user-friendly formulae providing normal and abnormal BP values for children are needed.[62-64]

Another question is whether screening should be universal or targeted toward specific populations of children and adolescents at higher risk of hypertension. The prevalence of sustained elevated BP (elevated BP on at least 3 occasions) is low in children compared with adults, with estimations ranging from less than 1% to 4% in different populations.[9,21,47,48] A low prevalence decreases the positive predictive value of any screening procedure,[27] and the great majority of cases of elevated BP in children at initial screening will be false-positive cases. Any BP screening procedure will perform better in subgroups of children in which the prevalence of hypertension is high. For instance, it could be valuable to screen children who are obese or who have hypertensive parents.

Table 2. Cost-effectiveness Ratio of Different Screen-and-Treat and Population-wide Strategies for Elevated BP in Adolescents Compared With No Intervention[a,b]

Strategy	Cost per QALY Gained, $	
	Boys	Girls
Universal screening		
Exercise if elevated BP	66 000	123 000
Salt reduction if elevated BP	64 000	116 000
Pharmacological treatment or surgery if secondary hypertension or LVH	18 000	47 000
Targeted screening of overweight adolescents		
Weight loss if elevated BP	54 000	136 000
Exercise if elevated BP	64 000	123 000
Salt reduction if elevated BP	62 000	101 000
Policy/environmental intervention		
Increasing physical activity classes in schools	8000	29 000
Salt-reduction campaign	Cost saving (6000)	650

Abbreviations: BP, blood pressure; LVH, left ventricular hypertrophy; QALY, quality-adjusted life-year.

[a] Adapted from Wang et al.[29]

[b] The cost-effectiveness ratio of different screen-and-treat and population-wide (policy/environmental intervention) strategies for elevated BP in adolescents was assessed by the cost (in US dollars) per QALY gained. Estimates are highly sensitive to several assumptions, including annual decline in treatment effect, tracking coefficients, or proportion of secondary cases of hypertension.

Does Screening for Elevated BP in Children Reduce the Risk of CVD and Mortality or Improve Quality of Life?

Ideally, BP screening should lead to a clinically significant reduction in the absolute risk of CVD or of mortality or to an increase in the quality of life, and this should be evaluated by randomized controlled studies. No experimental study has been designed to assess directly the effect of BP screening in childhood on these outcomes.

The cost-effectiveness of routine BP screening of adolescents was estimated in a modeling study by Wang et al[29] (**Table 2**). A simulation model was used to project lifetime costs and cardiovascular outcomes for a cohort of 15-year-old US adolescents under various elevated BP prevention strategies: (1) no screening and no intervention, (2) screening and treatment of adolescents with elevated BP, and (3) population-wide intervention to reduce BP in adolescents. In this study,[29] the strategy of universal screening and treatment for elevated BP in adolescents was moderately cost-effective, at least for boys, but it was much less cost-effective than population-wide interventions (eg, salt reduction and increasing physical activity) for the reduction of coronary heart disease cases (Table 2). The strategy of universal screening with treatment given solely to adolescents with secondary hypertension or left ventricular hypertrophy and the strategy of targeted screening of overweight adolescents were more cost-effective than universal screening yet less cost-effective than population-based interventions.

POTENTIAL HARM OF SCREENING

All screening procedures cause harm and involve costs.[27,65-67] For children with a positive test result and their families, the potential detrimental effects of BP screening include the stress of being labeled hypertensive and the anxiety caused by the complications and costs of investigations to assess the causes and consequences of elevated BP.[68] The effects on a child's well-being, health, or quality of life of being told early in life that he or she has elevated BP are not known. Among children with negative test results, the potential detrimental effects include the anxiety, costs, and inconvenience generated by the screening test.[68] Children with a negative test result may lose their motivation to adopt healthy behaviors, even when they know that such behaviors may be beneficial at all BP levels and for several health outcomes.

Furthermore, even if the screening test is good for sorting children with or without sustained elevated BP (low rates of both false-positive and false-negative cases), it does not imply that the test is good at identifying children who would eventually develop CVD. Although elevated BP is a strong risk factor for CVD, screening for elevated BP is a weak screening test for the occurrence of CVD[26,69] because a large proportion of CVD cases occur in individuals with normal BP levels.[69] Many children with a positive test result and sustained elevated BP will not develop CVD. By analogy with what is observed with cancer screening,[70] these children are overdiagnosed because they have not developed CVD; they are only harmed by the screening because they are unnecessarily stressed, undergo unnecessary diagnostic procedures, and are submitted to unnecessary treatments. For adults, attempts have been made to better target individuals who will benefit most from treatment by the estimation of CVD risk based on the assessment of multiple risk factors and surrogate markers of CVD.[66] For children, tailoring the management of elevated BP according to the estimation of CVD risk has to be evaluated.

GUIDELINES AND RECOMMENDATIONS BY HEALTH PROFESSIONALS' SOCIETIES

The USPSTF, the National Heart, Lung, and Blood Institute, and several health professional societies recommend screening for elevated BP in adults 18 years of age or older.[24,25] According to the USPSTF, this is a grade "A" recommendation because there is a high level of certainty that the net benefit is substantial.[24]

For children and adolescents, there is no consensus. Some experts in the domain of pediatric hypertension strongly recommend screening for elevated BP in children,[71,72] but others do not.[61,73] In 2004, the National Heart, Lung, and Blood Institute recommended that children older than 3 years who are seen in medical care settings have their BP measured at least once during every health care visit.[20] In a recent

revision of its recommendations, the National Heart, Lung, and Blood Institute recommended no routine BP measurement between birth and 3 years and BP measurements every year in children and adolescents 3 to 17 years of age.[74] These recommendations are graded as "D" because they are based on expert consensus. The European Society of Hypertension recommends measuring BP in children older than 3 years who are seen in a medical setting.[19]

Nevertheless, according to the USPSTF, evidence is not sufficient to recommend for or against screening.[75] The USPSTF is in the process of updating its recommendations. None of these organizations recommends systematic BP screening in children outside of health care facilities (for instance, in the school setting). Routine BP measurements for children presenting to the emergency department are not adequate for identifying cases of elevated BP.[76]

CONCLUSIONS

Early identification and treatment of elevated BP in children has the potential to reduce the absolute CVD risk in adulthood. It could also reduce the risk of detrimental vascular consequences early in life and the risk of hypertension in adulthood. However, there is no evidence that universal screening for elevated BP conveys more benefits than harm for children.

Once a screening is implemented, it is difficult to convince people or health professionals that screening may be useless, if not harmful. In the case of screening for elevated BP in children, it is possible that the benefits will not occur for decades, while the harm[67] and costs[77] will be present systematically as soon as screening is initiated. Consistent with the recommendations of the USPSTF,[75] we find that it is reasonable not to recommend universal BP screening in children. However, we also lack definitive against screening because it is unclear whether the magnitude of potential harm outweighs the magnitude of potential benefits.

Coping with screening ahead of clear evidence is a difficult and sensitive public health challenge.[78] The final decision about whether to screen for elevated BP relies on the values children and parents place on each of the possible benefits and harms.[68] Nevertheless, in view of the lack of data on some critical questions regarding BP screening, it is not possible for individuals to make a genuinely informed or shared decision.[65,79] The absence of evidence may be conducive to the provision of excessive care.[80]

Therefore, to ascertain whether BP screening in children is a net good for public health,[65] studies are needed to estimate the absolute CVD risk associated with childhood BP; to evaluate how to simplify the identification of elevated BP; to evaluate the long-term benefits, harm, and costs of treatment beginning in childhood; and to compare the potential benefits, harm, and costs of universal and targeted BP screening in children. Ideally, a randomized control study should assess the effect on the occurrence of CVD of a BP screen-and-treat strategy in children. Owing to the low risk of CVD, a decades-long follow-up and a large sample size would be required to yield enough CVD cases to detect a difference between screened and nonscreened groups. It would be more feasible to assess the effect of BP screening on surrogate outcomes of CVD (eg, intima-media thickness or left ventricular thickness).

It can be concluded that, for now, there is no compelling evidence in favor of universal BP screening among healthy children. Standard clinical case findings with targeted identification of elevated BP according to the clinical context, for example, for the early identification of secondary causes of hypertension, may be advocated. At the population level, however, efforts should focus on the primordial prevention of elevated BP and other CVD risk factors[81] and on maintaining lifelong ideal cardiovascular health through environmental, policy, and educational approaches.[82]

Accepted for Publication: June 4, 2012.
Published Online: January 7, 2013. doi:10.1001/jamapediatrics.2013.438
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Author Contributions: *Study concept and design:* Chiolero, Bovet, and Paradis. *Acquisition of data:* Bovet. *Analysis and interpretation of data:* Chiolero. *Drafting of the manuscript:* Chiolero. *Critical revision of the manuscript for important intellectual content:* Bovet and Paradis. *Administrative, technical, and material support:* Chiolero, Bovet, and Paradis.
Conflict of Interest Disclosures: None reported.

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