JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Screening for Hypertension in Children and Adolescents
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Childhood hypertension can result in adverse outcomes during adulthood; identifying and treating primary and secondary childhood hypertension may reduce such risks.

OBJECTIVE To update the evidence on screening and treatment of hypertension in childhood and adolescence for the US Preventive Services Task Force.

DATA SOURCES PubMed, Cochrane Library, International Pharmaceutical Abstracts, EMBASE, and trial registries through September 3, 2019; bibliographies from retrieved articles, experts, and surveillance of the literature through October 6, 2020.

STUDY SELECTION Fair- or good-quality English-language studies evaluating diagnostic accuracy of blood pressure screening; cohort studies assessing the association of hypertension in childhood and adolescence with blood pressure or other intermediate outcomes in adulthood; randomized clinical trials (RCTs) or meta-analyses of pharmacological and lifestyle interventions.

DATA EXTRACTION AND SYNTHESIS Two reviewers independently assessed titles/abstracts and full-text articles, extracted data, and assessed study quality; the evidence was synthesized qualitatively.

MAIN OUTCOMES AND MEASURES Sensitivity, specificity, and measures of association between childhood and adulthood blood pressure; reduction of childhood blood pressure; adverse effects of treatments.

RESULTS Forty-two studies from 43 publications were included (N>12 400). No studies evaluated the benefits or harms of screening and the effect of treating childhood hypertension on outcomes in adulthood. One study reported a sensitivity of 0.82 and a specificity of 0.70 for 2 office-based blood pressure measurements. Twenty observational studies suggested a significant association between childhood hypertension and abnormal blood pressure in adulthood (odds ratios, 1.1-4.5; risk ratios, 1.45-3.60; hazard ratios, 2.8-3.2). Thirteen placebo-controlled RCTs and 1 meta-analysis assessed reductions in systolic (SBP) and diastolic blood pressure from pharmacological treatments. Pooled reductions of SBP were −4.38 mm Hg (95% CI, −7.27 to −2.16) for angiotensin-converting enzyme inhibitors and −3.07 mm Hg (95% CI, −4.99 to −1.44) for angiotensin receptor blockers. Candesartan reduced SBP by −6.56 mm Hg ($P < .001$; n = 240). β-Blockers, calcium channel blockers, and mineralocorticoid receptor antagonists did not achieve significant reductions over 2 to 4 weeks. SBP was significantly reduced by exercise over 8 months (−4.9 mm Hg, $P \leq .05$; n = 69), by dietary approaches to stop hypertension over 3 months (−2.2 mm Hg, $P < .01$; n = 57), and by a combination of drug treatment and lifestyle interventions over 6 months (−7.6 mm Hg; $P < .001$; n = 95). Low-salt diet did not achieve reductions of blood pressure.

CONCLUSIONS AND RELEVANCE Observational studies indicate an association between hypertension in childhood and hypertension in adulthood. However, the evidence is inconclusive whether the diagnostic accuracy of blood pressure measurements is adequate for screening asymptomatic children and adolescents in primary care.

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The American Academy of Pediatrics defines hypertension in children aged 1 to 13 years as auscultatory systolic or diastolic blood pressure measurements that, according to 3 separate measurements, are either at or above 130/80 mm Hg or equal to or above the 95th percentile for children of the same sex and age or height (**Table 1**).[1] In adolescents 13 years or older, thresholds mirror guidelines for adults.[1] Primary hypertension does not have an identifiable cause; secondary hypertension is most commonly caused by renal or renovascular disease, endocrine disorders, cardiac abnormalities, or genetic disorders.[2] In asymptomatic children, hypertension may be the only sign of such an underlying condition. The overall prevalence of hypertension in children and adolescents in studies conducted between 1999 and 2014 in the US ranged between 1.6% and 3.6%.[3-6]

Children with primary hypertension are at higher risk of developing adverse intermediate cardiovascular outcomes, such as increased left ventricular mass, carotid intima-media thickness, and increased pulse wave velocity.[7] The association between such intermediate outcomes in childhood and health outcomes in adulthood, however, is unclear. Screening for hypertension in childhood and adolescence may lead to earlier treatment, therefore reducing the risk of adult hypertension and cardiovascular complications.

This review was conducted to inform the US Preventive Services Task Force (USPSTF) in preparing an updated recommendation statement. Based on an updated systematic review,[8] in 2013 the USPSTF concluded that the evidence was insufficient to assess the balance of benefits and harms of screening for primary hypertension in asymptomatic children and adolescents to prevent subsequent cardiovascular disease in childhood and adulthood (I statement).[9]

Methods

Scope of the Review

The analytic framework and key questions (KQs) that guided the review are shown in **Figure 1**. Detailed methods, evidence tables, and contextual information are available in the full evidence report.[11]

Compared with the previous review,[8] the population of interest was extended to children and adolescents with secondary hypertension, excluded pharmacological dose-ranging studies without a placebo group, and excluded results on harms from placebo-controlled withdrawal phases of trials.

Data Sources and Searches

PubMed, the Cochrane Library, International Pharmaceutical Abstracts, and EMBASE were searched for English-language articles published from June 1, 2012, through September 3, 2019. Because the previous review for the USPSTF did not include secondary hypertension, PubMed was searched from inception through September 3, 2019, and studies that the previous report excluded for "ineligible population" were rescreened. ClinicalTrials.gov, Cochrane Clinical Trials Registry, the World Health Organization International Clinical Trials Registry Platform, and Health Services Research Projects in Process were also searched. To supplement electronic searches (eMethods in the Supplement), reference lists of pertinent articles and studies suggested by reviewers were searched. Ongoing surveillance was conducted through article alerts and targeted searches of journals to identify major studies published in the interim that may affect the conclusions or understanding of the evidence and the related USPSTF recommendation. The last surveillance was conducted on October 6, 2020.

Study Selection

Two investigators independently reviewed titles, abstracts, and full-text articles using prespecified inclusion criteria for each KQ (eMethods in the Supplement); disagreements about inclusion were resolved by discussion or by a third reviewer. Briefly, eligible populations were asymptomatic children and adolescents for KQs 1 through 3 and participants with elevated blood pressure or hypertension for KQs 4 through 8. For KQ1 and KQ3, any study that compared screening with no screening was eligible for inclusion. For KQ2, studies reporting diagnostic test accuracy of blood pressure measurements that used a confirmed clinical diagnosis (ie, after diagnostic workup) of abnormal blood pressure as the reference test were included. For KQ4, eligible studies were longitudinal cohort studies that assessed the association of abnormal blood pressure during childhood and adult hypertension or other intermediate outcomes during adulthood. For KQs 5 through 8 on the effectiveness and harms of treatments, randomized clinical trials (RCTs) and large, controlled, observational studies (sample size >1000) were included; for KQ8 on harms, uncontrolled before-after studies were also accepted. For effectiveness, hypertension-related health outcomes (eg, cardiovascular events, end-stage kidney disease, or mortality) or intermediate outcomes (eg, blood pressure, left ventricular hypertrophy, or microalbuminuria) were of interest. For harms, labeling, anxiety, school absenteeism, and any treatment-related harms were included.

English-language studies that met all study selection criteria and that were of fair or good methodological quality (eMethods in the Supplement) were included. Studies included in the prior 2013 review were reassessed against the study selection and methodological quality criteria for this update.

Data Extraction and Quality Assessment

For each included study, 1 reviewer abstracted relevant study characteristics (ie, population, intervention, comparator) and data for eligible outcomes into a structured form. A second reviewer checked all data for completeness and accuracy. In cases of ambiguous or missing data, study authors were contacted. Two senior reviewers independently assessed each study's methodological quality using predefined criteria established by the USPSTF (eMethods in the Supplement).[12] Disagreements in study quality ratings were resolved through discussion or with an independent assessment from a third senior investigator. Studies reporting multiple outcomes may have been assigned different quality ratings for different outcomes.

Data Synthesis and Analysis

Study characteristics and results of included studies were summarized in tabular or narrative format. Findings for all KQs were synthesized qualitatively. The strength of evidence was assessed based on the Agency for Healthcare Research and Quality *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*, which specifies the assessment of study limitations, directness, consistency, precision, and reporting bias for each intervention

Table 1. Thresholds for Diagnosing Abnormal Blood Pressure in Children and Adolescents

Age, y	Elevated blood pressure	Hypertension	
		Stage 1	Stage 2
1-13	The lower of: 90th-94th percentiles or Systolic 120-129 mm Hg Diastolic <80 mm Hg	The lower of: ≥95th percentile to <95th percentile + 12 mm Hg or Systolic 130-139 mm Hg Diastolic 80-89 mm Hg	The lower of: ≥95th percentile + 12 mm Hg or Systolic ≥140 mm Hg systolic Diastolic ≥90 mm Hg
≥13	Systolic 120-129 mm Hg Diastolic <80 mm Hg	Systolic 130-139 mm Hg Diastolic 80-89 mm Hg	Systolic ≥140 mm Hg Diastolic ≥90 mm Hg

comparison and major outcome of interest.[13] Two senior reviewers independently developed initial strength-of-evidence assessments for each relevant outcome and comparison across the KQs; disagreements were resolved through discussion and the independent assessment of a third senior reviewer.

Results

Forty-two studies (N>12 400) from 43 publications were included (**Figure 2**). One study was conducted among children 11 years or younger,[14] 2 studies enrolled adolescents between the ages of 12 and 18 years,[15,16] and the remaining studies included mixed populations of children and adolescents or did not report the age range at baseline.[17,18] Because of slightly revised inclusion criteria, 4 RCTs from the previous report were excluded.[19-22] The update included 1 study of test accuracy (KQ2),[23] 20 studies evaluated the association between abnormal blood pressure in childhood and abnormal blood pressure or other intermediate outcomes in adulthood (KQ4),[17,18,24-41] 20 RCTs[14-16,42-58] and a meta-analysis[59] assessed the effectiveness of pharmacological and nonpharmacological interventions (KQ5), and 7 RCTs provided data on harms (KQ8).[42-47,55]

Benefits of Screening

Key Question 1. Does screening for high blood pressure (ie, persistently elevated blood pressure or hypertension) in children and adolescents delay the onset of or reduce adverse health outcomes related to high blood pressure?

No studies were identified.

Accuracy of Screening

Key Question 2. What is the diagnostic accuracy of screening tests for high blood pressure in children and adolescents?

One fair-quality diagnostic test accuracy study (n = 247) assessed the sensitivity of 2 office-based blood pressure measurements, 1 to 2 weeks apart.[23] Study characteristics are described in eTable 1 in the Supplement, and study methodological quality is presented in eTable 2 in the Supplement. The study enrolled healthy volunteers or patients referred for abnormal blood pressure who were 11 to 19 years old. Abnormal blood pressure for office-based measurements was defined according to the previous American Academy of Pediatrics recommendation.[60] The reference standard was 26-hour ambulatory blood pressure monitoring (ABPM) at 20-minute intervals. Using systolic blood pressure (SBP) at the 90th percentile as a threshold, the sensitivity of 2 office-based blood pressure measurements was 0.82 (95% CI not reported) with a specificity of 0.70 (95% CI not reported) compared with ABPM.

Harms of Screening

Key Question 3. What are the adverse effects, such as labeling and anxiety, of screening for high blood pressure in children and adolescents?

No studies were identified.

Association of Childhood and Adult Hypertension

Key Question 4. What is the association between high blood pressure in children and adolescents and high blood pressure and other intermediate outcomes in adults?

Association Between Childhood and Adulthood Abnormal Blood Pressure

Twenty publications reported on the association between abnormal blood pressure in childhood and abnormal blood pressure or other intermediate outcomes in adulthood.[17,18,24-41] Two studies did not report the age range of study participants at baseline[17,18]; all other studies included mixed populations of children (mostly 3 to 11 years) and adolescents (12 to 18 years) at baseline. These studies drew from 9 databases (4 based in the US [1 unnamed cohort of school children in Boston, Massachusetts,[24] the Fels Longitudinal Study,[25,26] Bogalusa Heart Study,[27-31,40] and Muscatine Study[17,18]], 2 based in Australia [Childhood Determinants of Adult Health study,[39] Insulin study[61]], 1 based in Eastern Europe [Kaunas study[62]], 1 based in Finland [Young Finns[32-37]], and 1 based in New Zealand [the Dunedin Multidisciplinary Health and Development Study[38]]) that followed up cohorts of children into adulthood. The mean duration of follow-up ranged from 10 to 33 years. Study characteristics are summarized in eTable 3 in the Supplement. The risk of bias of these studies was not rated because risk-of-bias tools are designed to identify potential biases in causal inference rather than validity of associations.

Studies used various definitions of childhood and adulthood abnormal blood pressure (**Table 2**). Despite varying definitions, studies were generally consistent in demonstrating an association between abnormal blood pressure in childhood and abnormal blood pressure in adulthood.

The only study[40] that used current definitions applied the 2017 American Academy of Pediatrics guidelines[1] to categorize childhood blood pressure and the American Heart Association standards[63] for adulthood blood pressure. It used data from the Bogalusa Heart Study,[40] which followed up 3940 children over 25 years, on average. Children with elevated blood pressure had an increased risk (adjusted risk ratio [RR], 1.45 [95% CI, 1.30 to 1.61]) for developing hypertension as adults.

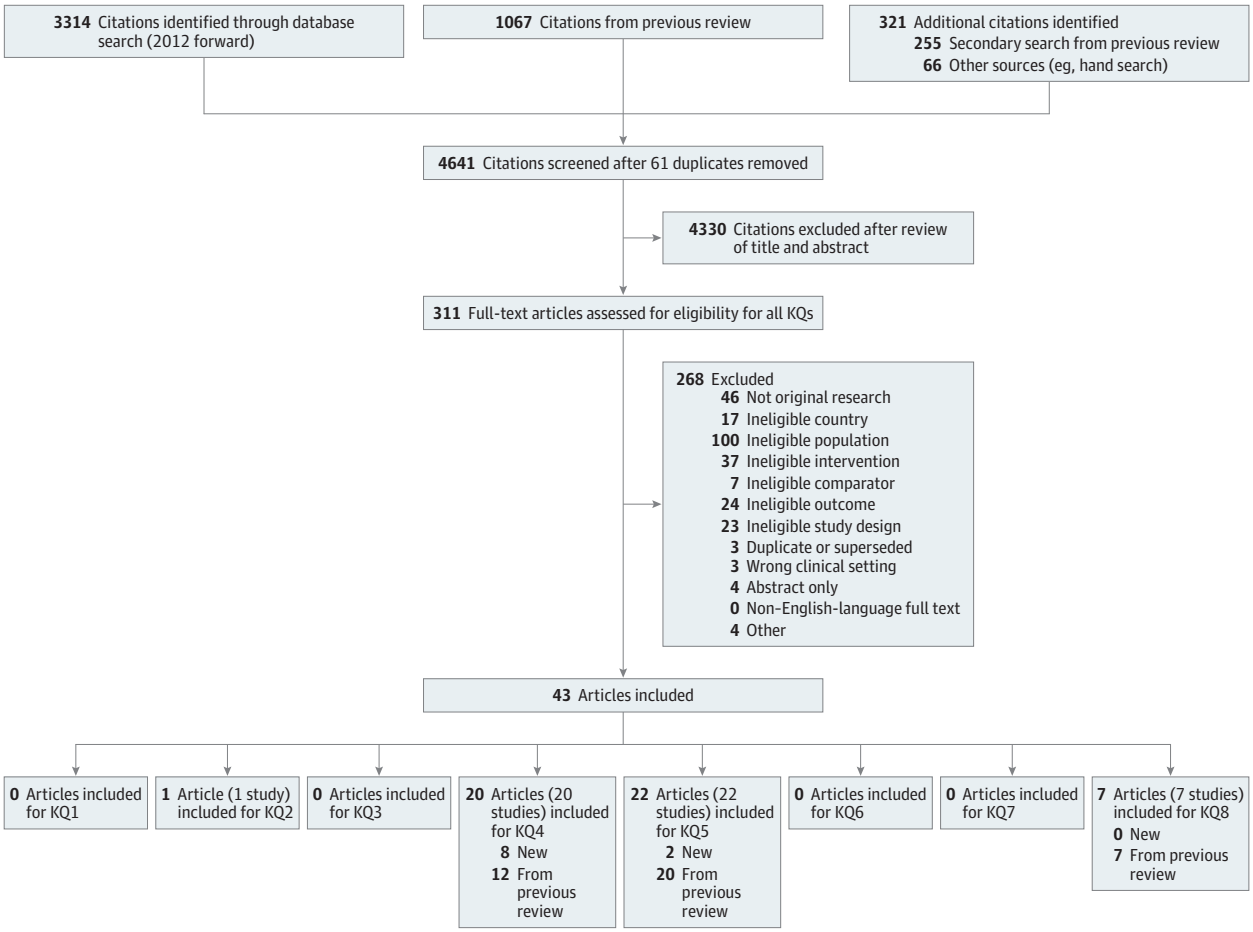
Nine studies relying on prior definitions of abnormal childhood or adulthood blood pressure also consistently found results for

Figure 1. Analytic Framework: Screening for Hypertension in Children and Adolescents

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display key questions addressed by the review to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions to outcomes. A dashed line indicates a health outcome that precedes subsequent outcomes. Refer to the USPSTF procedure manual for further details.[10]

[a] Includes left ventricular hypertrophy, urinary albumin excretion (microalbuminuria), intima-media thickness (measured at carotid arteries, femoral arteries, or both), and retinal vascular changes.

Figure 2. Literature Search Flow Diagram: Screening for Hypertension in Children and Adolescents



Abbreviation: KQ, key question.

associations between abnormal blood pressure in childhood and abnormal blood pressure in adulthood, regardless of the definition of hypertension and methods of measurement (Table 2).[31,33-40] Likewise, studies with nonstandard definitions of abnormal blood pressure (usually thresholds based on percentiles within the study cohort) reported associations between abnormal childhood and adulthood blood pressure (Table 2).[17,18,24-27,30] Studies reported different measures of association such as odds ratios (ranging from 1.1 [95% CI, 0.5 to 2.4] to 4.5 [95% CI, 1.1 to 17.7]), RRs (ranging from 1.45 [95% CI, 1.30 to 1.61] to 3.60 [95% CI, 1.38 to 9.40]), and hazard ratios (ranging from 2.8 [95% CI, 2.0 to 3.9] to 3.2 [95% CI, 2.1 to 5.0]).

Association Between Abnormal Childhood Blood Pressure and Other Intermediate Outcomes in Adulthood

Seven studies[28,29,31,32,36,40,41] examined the relationship between abnormal childhood or adolescent (age range, 3-18 years) blood pressure and intermediate outcomes (other than blood pressure) in adults. Only 1 study used current definitions of hypertension in children.[40] Regardless of definitions used, 6 studies generally reported statistically significant associations between abnormal childhood blood pressure and carotid intima-media thickness in adults.[29,31,32,36,39,41] The largest analysis (n = 4210), the International Childhood Cardiovascular Cohort Consortium (i3C), pooled results from 4 databases (Bogalusa Heart Study, Muscatine Study, Young Finns Study, and the Childhood Determinants of Adult Health study) and used the previous definition of the American Academy of Pediatrics to define childhood abnormal blood pressure and current American Heart Association standards for adult abnormal blood pressure.[39] Based on a follow-up of 23 years, the study found that individuals who had persistently elevated blood pressure from childhood to adulthood had a significantly higher risk of carotid intima-media thickness (RR, 1.76 [95% CI, 1.21 to 2.56]).[39] Individuals whose abnormal blood pressure normalized during childhood did not have a significantly increased risk (RR, 1.20 [95% CI, 0.86 to 1.67]).

Two studies (age range, 3-18 years) reported significant associations between abnormal childhood and adolescent blood pressure and adult left ventricular hypertrophy.[31,40] Based on definitions, the magnitude of associations varied (RRs ranged from 1.30 to 1.59; hazard ratios ranged from 1.92 to 3.41).

Single studies (range of mean age, 10.0-10.9 years) reported significant associations between abnormal childhood and adolescent blood pressure and subclinical cardiovascular disease,[31] higher

Table 2. Associations Between High Blood Pressure in Childhood and Adulthood Across Different Definitions of Hypertension

Standard	Adult hypertension standards		Nonstandard adult hypertension definitions
	Current[a]	Prior[b]	
Current childhood hypertension standards[1]	1 publication[40] (n = 3940) RRs range from 1.45 to 1.66 (all statistically significant)	1 publication[40] (n = 3940) RRs range from 1.62 to 1.98 (all statistically significant)	0 publications
Prior childhood hypertension standards[60]	2 publications[37,39,40] (n >5480) RRs range from 1.49 to 1.65 (all statistically significant) Sensitivity, 0.55-0.56 Specificity, 0.63-0.64 PPV, 0.53-0.73	6 publications[31,33,34,36,38,40] (n >4127) RRs range from 1.53 to 1.95 (all statistically significant) HRs range from 2.8 to 3.2 (all statistically significant) PPV, 0.11-0.58 AUC range, 0.60-0.63 Sensitivity, 0.05-0.37 Specificity, 0.87-0.99	1 publication[35] (n = 2625) OR, 2.12 (95% CI, 1.82 to 2.61)
Nonstandard childhood hypertension definitions	0 publications	0 publications	7 publications[17,18,24-27,30] (n = 4790) ORs and RRs range from 1.1 to 9.0, generally excluding the null Sensitivity, 0-0.66 Specificity, 0.77-1.00

Abbreviations: AUC, area under the receiver operating characteristic curve; HR, hazard ratio; OR, odds ratio; PPV, positive predictive value; RR, relative risk.

[a] Abnormal blood pressure defined as SBP greater than 120 mm Hg and DPB greater than 80 mm Hg or self-reporting of antihypertensive medication use.[63]

[b] Hypertension defined as SBP 140 mm Hg or greater or DBP 90 mm Hg or greater or self-reported antihypertensive medication use.[64]

aorta-femoral pulse wave velocity,[31] and microalbuminuria, particularly in Black participants.[28]

Effectiveness of Treatment

Key Question 5. What is the effectiveness of drug, nondrug, and combination interventions for treating high blood pressure in children and adolescents?

Twenty RCTs (21 publications)[14-16,42-58,65] and 1 meta-analysis[59] met inclusion criteria for KQ5. Study characteristics are summarized in eTable 4 in the Supplement, and individual study methodological quality is presented in eTable 5 and 6 in the Supplement.

Pharmacological Treatments

Thirteen RCTs with data on more than 2300 participants assessed the efficacy of pharmacological interventions, including angiotensin-converting enzyme inhibitors (enalapril,[48] fosinopril,[47] lisinopril[49]), angiotensin receptor blockers (candesartan,[43] losartan,[50] olmisartan,[51] telmisartan,[45] valsartan[53]), β-blockers (metoprolol succinate extended release [ER]),[42] a combination of bisoprolol fumarate and hydrochlorothiazide,[46] calcium channel blockers (amlodipine,[54] felodipine ER[44]), and a mineralocorticoid receptor antagonist (eplerenone[52]). All studies were conducted in mixed populations of children and adolescents. None of the studies provided efficacy outcomes beyond 4 weeks. Telmisartan and a combination of bisoprolol with hydrochlorothiazide are currently not approved by the US Food and Drug Administration for the treatment of children and adolescents.

Most studies excluded children or adolescents with severe hypertension (mostly defined as SBP >20 mm Hg or diastolic blood pressure [DBP] >10 mm Hg above the 99th percentile) or secondary hypertension. The meta-analysis included 12 of the 13 RCTs.[59] It combined treatment groups of individual drugs regardless of the dose. Pooled reductions of SBP were −4.38 mm Hg (95% CI, −7.27 to −2.16) for angiotensin-converting enzyme inhibitors, −3.07 mm Hg (95% CI, −4.99 to −1.44) for angiotensin receptor blockers, −3.2 mm Hg (95% CI, −8.69 to −2.23) for β-blockers, −3.1 mm Hg (95% CI, −6.52 to 0.45) for calcium channel blockers, and −0.12 mm Hg (95% CI, −3.69 to 3.46) for mineralocorticoid receptor antagonists.[59] The study that was not included in the meta-analysis assessed candesartan in 240 children and adolescents aged 6 to 17 years over 4 weeks.[43] Compared with placebo, candesartan led to significantly greater reductions in SBP (−6.56 mm Hg [95% CI not reported]; $P < .001$) and DBP (−4.76 mm Hg [95% CI not reported]; $P = .003$).

Pharmacological Treatments Combined With Lifestyle Interventions

In a 6-month, open-label, poor-quality trial (conducted from 1979 to 1981 in the US), a combination of low-dose propranolol/chlorthalidone and an educational program directed toward dietary and exercise modifications for children and parents significantly decreased SBP (−7.6 mm Hg; $P < .001$) and DBP (−6.9 mm Hg; $P < .01$).[55,65] However, propranolol, like other β-blockers, is no longer recommended as a first-line therapy because of the adverse events profile and the lack of association in adults with improved health outcomes.[1]

Lifestyle Interventions

Six RCTs assessed the effectiveness of physical exercise,[14,16] dietary interventions,[56-58] and progressive muscle relaxation.[15]

Significant decreases in SBP and DBP were achieved by 3 extra weekly school lessons of physical education in hypertensive children (n = 69) aged 9 to 11 years over 8 months (SBP, −4.9 mm Hg [$P < .05$]; DBP, −3.8 mm Hg [$P < .05$])[14]; by combined resistance and aerobic exercise over 12 weeks for obese, adolescent girls (n = 40; SBP, −8.3 mm Hg [$P < .05$]; DBP, data not reported)[16]; and by a DASH (Dietary Approaches to Stop Hypertension)–type diet for overweight adolescents (n = 57) over 3 months (SBP, −2.2 mm Hg [$P < .01$]; DBP, −2.8 mm Hg [$P < .05$]).[56]

Low-sodium diet[57,58] and progressive muscle relaxation[15] did not achieve significant decreases in SBP and DBP.

Effectiveness of Treatments During Childhood to Reduce Blood Pressure in Adulthood

Key Question 6. What is the effectiveness of drug, nondrug, and combination interventions initiated for the treatment of high blood pressure in children and adolescents for reducing blood pressure and improving other intermediate outcomes in adults?

No studies were identified.

Effectiveness of Treatments During Childhood to Reduce Adverse Health Outcomes in Adulthood

Key Question 7. What is the effectiveness of drug, nondrug, and combination interventions initiated for the treatment of high blood pressure in children and adolescents for reducing adverse health outcomes related to high blood pressure in adults?

No studies were identified.

Harms of Treatment

Key Question 8. What are the adverse effects of drug, nondrug, and combination interventions for treating high blood pressure in children and adolescents?

Seven RCTs[42-47,55] provided results on harms of interventions. eTable 7 in the Supplement summarizes study characteristics; eTable 8 in the Supplement presents the methodological quality of individual studies.

Pharmacological Treatments

The included RCTs assessed the risk of harms of ER metoprolol succinate,[42] candesartan,[43] felodipine ER,[44] fosinopril,[47] telmisartan,[45] and a combination of bisoprolol fumarate and hydrochlorothiazide[46] based on data for 909 participants. Overall, risks of experiencing any adverse event and risks of specific adverse events were similar between active treatments and placebo over 2 to 4 weeks.

Pharmacological Treatments Combined With Lifestyle Interventions

No differences in adverse events were reported in the trial with a 6-month follow-up of low-dose propranolol/chlorthalidone in combination with an educational program (see KQ5).[55]

Lifestyle Interventions

No data were reported.

Discussion

This evidence report reviewed studies on the diagnostic accuracy of screening tests for abnormal blood pressure in children and adolescents, studies on the association between childhood and adulthood blood pressure, and studies evaluating the benefits and harms of treatments for abnormal blood pressure in children and adolescents. **Table 3** summarizes the evidence by KQ and provides an assessment of the strength of evidence. Compared with the 2013 review for the USPSTF on this topic, 13 RCTs and 1 meta-analysis were added and 4 RCTs were excluded.

No studies evaluated the benefits or harms of screening and the effect of treating childhood hypertension on intermediate and health outcomes in adulthood. The strength of evidence was assessed as low for the single study that reported on the test accuracy of office-based blood pressure measurements. Results of this study might have limited applicability to a screening population because the study population also included children with known hypertension. Overall, the prevalence of hypertension in this population was 29%.

The strength of evidence was low for an association between childhood hypertension and abnormal blood pressure or other intermediate outcomes in adulthood. Studies were very heterogeneous regarding definitions of childhood and adulthood hypertension, the underlying prevalence of hypertension, and outcome measures. Nevertheless, findings consistently demonstrated an association between abnormal childhood and abnormal adulthood blood pressure.

Evidence of moderate strength indicated efficacy and good tolerability of pharmacological interventions, but these studies were mostly limited to participants with primary hypertension. Moreover, none of the drugs were evaluated in more than 1 study. The magnitude of the antihypertensive effects varied across agents and was not always significantly different from that of placebo. The mean age of children in these studies ranged from aged 12 to 14 years; the generalizability of results to younger children or children with secondary hypertension is unknown. For physical exercise and a DASH-type diet, the strength of evidence was low for reducing blood pressure. The evidence was rated as moderate and low for no effect of low-sodium diet and progressive muscle relaxation, respectively.

Limitations

The main limitation of the methodological approach in this review is that it was limited to literature searches for English-language studies. This strategy might have missed studies conducted in Hispanic children, who have a higher risk for obesity and primary hypertension than non-Hispanic White children.

This review also has several limitations regarding its evidence base. First, no available evidence that directly evaluated the health benefits and harms of screening (KQ1 and KQ3) was identified. Likewise, no evidence on the effect of treating childhood hypertension on intermediate and health outcomes in adulthood could be detected (KQ6 and KQ7). Second, for diagnostic test accuracy of blood pressure measurements (KQ2), there was only 1 study with limited applicability. In addition, thresholds and classifications of hypertension in children are based on normative values and not on health outcomes, like in adults. It is still unclear whether such distribution-based thresholds can adequately distinguish between children with and without hypertension. Furthermore, the exact diagnostic workup in children who screen positive is not well established. Although ABPM is recommended to confirm office-based measurements, normative values and thresholds for hypertension for ABPM are not well founded in children and adolescents. Third, pharmacological treatment studies were small and of very short duration (2 to 4 weeks). No conclusions about the beneficial and harmful effects of long-term pharmacological treatments can be drawn. The mean age of children in these studies ranged from aged 12 to 14 years; the generalizability of results to younger children or children with secondary hypertension is unknown. Fourth, many of the trials included

Table 3. Summary of Evidence for Screening for Hypertension in Children and Adolescents

	No. of studies (No. of participants)	Summary of findings	Consistency/precision	Other limitations	EPC assessment of strength of evidence	Applicability
KQ1: Direct benefits of screening						
	No studies identified	NA	NA	NA	NA	NA
KQ2: Diagnostic test accuracy						
Sensitivity and specificity	1 cross-sectional study[23] (247)	Sensitivity of office-based BP measurements, 81.6% Specificity, 70.3%	Consistency unknown (single study body of evidence)/imprecise	Body of evidence limitations: moderate Reporting bias: not detected	Low for diagnostic test accuracy measures	Limited applicability; only 2 office-based measurements: population included children with known abnormal blood pressure
KQ3: Harms of screening—No studies identified						
	No studies identified	NA	NA	NA	NA	NA
KQ4: Association between high BP in children and high BP or intermediate outcomes in adults						
Association between BP in children and adults	20 longitudinal cohort studies[17,18,24-39] (>9687)[a]	Low to moderate sensitivity and PPV for relationship between childhood and adult abnormal BP; results consistent despite variable definitions	Consistent/imprecise	Body of evidence limitations: high Reporting bias: NA	Low for association between abnormal BP in childhood and abnormal BP in adulthood	Applicability varies because prevalence of hypertension is widely variable
Association between BP in children and intermediate outcomes in adults	7 longitudinal cohort studies[28,29,31,32,36,40,41] (>5925)[a]	OR for CIMT, 1.24; HRs range from 2.03 to 3.07 Weak correlations between abnormal BP in childhood and CIMT in adulthood (ranging from 0.04 to 0.16)	Consistent/imprecise	Body-of-evidence limitations: high Reporting bias: NA	Low for CIMT	Applicability varies because prevalence of hypertension is widely variable
KQ5: Effectiveness of interventions						
	13 RCTs[42-54] (2476)	Reductions of SBP for: ACE inhibitors: −4.38 mm Hg ARBs: −3.07 mm Hg β-Blockers: −3.20 mm Hg Calcium channel blockers: −3.10 mm Hg Mineralocorticoid receptor antagonists: −0.12 mm Hg All comparisons with placebo after 2 to 4 wk	Consistent/imprecise	Body-of-evidence limitations: moderate Reporting bias: not detected	Moderate for benefit	Applies to children and adolescents aged 6 to 18 y with BP above the 95th percentile; severe hypertension and secondary hypertension were excluded from most studies; study durations up to 4 wk; no long-term studies
Pharmacological + lifestyle intervention	1 RCT[55,65] (141)	Statistically significant reductions of SBP (−7.6 mm Hg) and DBP (−6.9 mm Hg) compared with control after 6 mo	Consistency unknown (single study body of evidence)/precise	Body-of-evidence limitations: high Reporting bias: not detected	Low for benefit	Applies to children and adolescents aged 8 to 18 y with BP above the 90th percentile
Low-sodium diet	2 RCTs[57,58] (313)	No clinically relevant differences in DBP or SBP compared with control	Consistent/imprecise	Body-of-evidence limitations: moderate Reporting bias: not detected	Moderate for no benefit	Applies to children and adolescents age 11 to 18 y with BP above the 85th percentile

(continued)

Table 3. Summary of Evidence for Screening for Hypertension in Children and Adolescents (continued)

	No. of studies (No. of participants)	Summary of findings	Consistency/precision	Other limitations	EPC assessment of strength of evidence	Applicability
DASH diet	1 RCT[56] (57)	Statistically significant reduction of SBP (−2.2 mm Mg; $P < .01$) and DBP (−2.8 mm Hg; $P < .05$) at the end of intervention (3 mo) compared with control At 6-mo follow-up, similar BP measurements between treatment and control groups (SBP, 120.1 vs 120.0 mm Hg; DBP, 75.2 vs 76.4 mm Hg)	Consistency unknown (single study body of evidence)/imprecise	Body-of-evidence limitations: moderates Reporting bias: not detected	Low for benefit	Applies to children and adolescents age 11 to 18 y with BP above the 90th percentile
Physical exercise	2 RCTs[14,16] (109)	Statistically significant reductions in SBP (−4.9 mm Hg; $P < .05$) and DBP (−3.8 mm Hg; $P < .05$) in children aged 9 to 11 years after 8 mo Statistically significant reduction in SBP (−8.3 mm Hg; $P < .05$) but not DBP (data not reported) in obese adolescent girls after 3 mo	Consistent/imprecise	Body-of-evidence limitations: moderate Reporting bias: not detected	Low for benefit	Applies to children age 9 to 11 y with BP above the 95th percentile and obese adolescent girls with elevated BP
Progressive muscle relaxation	1 RCT[15] (159)	No clinically relevant differences in SBP or DBP compared with control	Consistency unknown (single study body of evidence)/imprecise	Body-of-evidence limitations: moderate Reporting bias: not detected	Low for no benefit	Applies to children and adolescents age 13 to 17 y with BP above the 85th percentile
KQ6: Effectiveness of interventions on intermediate outcomes in adulthood—No studies identified						
	No studies identified	NA	NA	NA	NA	NA
KQ7: Effectiveness of interventions on health outcomes in adulthood						
	No studies identified	NA	NA	NA	NA	NA
KQ8: Harms of interventions						
Pharmacological interventions	6 RCTs[42-45,47] (909)	Similar risks of overall adverse events between pharmacological treatments (β-blocker, calcium channel blockers, ACE inhibitors, or ARBs) and placebo over 2 to 4 wk	Consistent/very imprecise	Body-of-evidence limitations: moderate	Low for similar harms	Applies to children and adolescents age 6 to 18 y with BP above the 95th percentile; severe hypertension and secondary hypertension were excluded; study durations up to 4 wk; no long-term studies
Pharmacological treatments combined with lifestyle interventions	1 RCT[55] (150)	Similar risks of overall adverse events between pharmacological treatment (propranolol + chlorothalidone) plus lifestyle interventions and no intervention	NA/very imprecise	Body-of-evidence limitations: moderate Indirectness: propranolol not recommended anymore as first line treatment	Very low for similar harms	Applies to children and adolescents aged 6 to 18 y with BP above the 90th percentile

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CIMT, carotid intima-media thickness; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; HR, hazard ratio; KQ, key question; NA, not applicable; PPV, positive predictive value; RCT, randomized clinical trial; SBP, systolic blood pressure.

[a] Studies drew from overlapping cohorts and may include the same participants.

children and adolescents and did not analyze the results separately for these 2 groups. Fifth, although target organ damage because of elevated blood pressure in children is quite common, a causal association with cardiovascular events later in life is difficult to establish.[66,67] The ongoing i3C Outcomes study might be able to provide more solid and more direct evidence regarding the association between childhood hypertension and adult cardiovascular events.[68]

Conclusions

Observational studies indicate an association between hypertension in childhood and hypertension in adulthood. However, the evidence is inconclusive whether the diagnostic accuracy of blood pressure measurements is adequate for screening asymptomatic children and adolescents in primary care.

ARTICLE INFORMATION

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Concept and design: Gartlehner, Vander Schaaf, Clark, Viswanathan.
Acquisition, analysis, or interpretation of data: Gartlehner, Vander Schaaf, Orr, Kennedy, Clark, Viswanathan.
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Editorial Disclaimer: This evidence report is presented as a document in support of the accompanying USPSTF Recommendation Statement. It did not undergo additional peer review after submission to *JAMA*.

REFERENCES

1. Flynn JT, Kaelber DC, Baker-Smith CM, et al; Subcommittee on Screening and Management of High Blood Pressure in Children. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3):e20171904. doi:10.1542/peds.2017-1904

2. Flynn JT, Pierce CB, Miller ER III, et al; Chronic Kidney Disease in Children Study Group. Reliability of resting blood pressure measurement and classification using an oscillometric device in children with chronic kidney disease. *J Pediatr*. 2012;160(3):434-440. doi:10.1016/j.jpeds.2011.08.071

3. Kaelber DC, Liu W, Ross M, et al; Comparative Effectiveness Research Through Collaborative Electronic Reporting (CER2) Consortium. Diagnosis and medication treatment of pediatric hypertension: a retrospective cohort study. *Pediatrics*. 2016;138(6):e20162195. doi:10.1542/peds.2016-2195

4. Dobson CP, Eide M, Nylund CM. Hypertension prevalence, cardiac complications, and antihypertensive medication use in children. *J Pediatr*. 2015;167(1):92-97. doi:10.1016/j.jpeds.2015.04.016

5. McNiece KL, Poffenbarger TS, Turner JL, Franco KD, Sorof JM, Portman RJ. Prevalence of hypertension and pre-hypertension among adolescents. *J Pediatr*. 2007;150(6):640-644. doi:10.1016/j.jpeds.2007.01.052

6. Xi Y, Jiang X, Li R, Chen M, Song W, Li X. The levels of human milk microRNAs and their association with maternal weight characteristics. *Eur J Clin Nutr*. 2016;70(4):445-449. doi:10.1038/ejcn.2015.168

7. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation*. 2008;117(25):3171-3180. doi:10.1161/CIRCULATIONAHA.107.730366

8. Thompson M, Dana T, Bougatsos C, Blazina I, Norris SL. Screening for hypertension in children and adolescents to prevent cardiovascular disease. *Pediatrics*. 2013;131(3):490-525. doi:10.1542/peds.2012-3523

9. Moyer VA; US Preventive Services Task Force. Screening for primary hypertension in children and adolescents: U.S. Preventive Services Task Force recommendation statement. *Pediatrics*. 2013;132(5):907-914. doi:10.1542/peds.2013-2864

10. US Preventive Services Task Force. Procedure Manual. Published 2015. Accessed February 4, 2020. https://www.uspreventiveservicestaskforce.org/uspstf/procedure-manual

11. Gartlehner G, Vander Schaaf EB, Orr C, Kennedy SM, Clark R, Viswanathan M. *Screening for High Blood Pressure in Children and Adolescents: Systematic Review for the U.S. Preventive Services Task Force*. Evidence Synthesis No. 193. Agency for Healthcare Research and Quality; 2020. AHRQ publication 20-05261-EF-1.

12. Harris RP, Helfand M, Woolf SH, et al; Methods Work Group, Third US Preventive Services Task Force. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med*. 2001;20(3)(suppl):21-35. doi:10.1016/S0749-3797(01)00261-6

13. Agency for Healthcare Research and Quality. *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Agency for Healthcare Research and Quality; 2014. AHRQ publication 10(14)-EHC063-EF.

14. Hansen HS, Froberg K, Hyldebrandt N, Nielsen JR. A controlled study of eight months of physical training and reduction of blood pressure in children: the Odense schoolchild study. *BMJ*. 1991;303(6804):682-685. doi:10.1136/bmj.303.6804.682

15. Ewart CK, Harris WL, Iwata MM, Coates TJ, Bullock R, Simon B. Feasibility and effectiveness of school-based relaxation in lowering blood pressure. *Health Psychol*. 1987;6(5):399-416. doi:10.1037/0278-6133.6.5.399

16. Son WM, Sung KD, Bharath LP, Choi KJ, Park SY. Combined exercise training reduces blood pressure, arterial stiffness, and insulin resistance in obese prehypertensive adolescent girls. *Clin Exp Hypertens*. 2017;39(6):546-552. doi:10.1080/10641963.2017.1288742

17. Lauer RM, Clarke WR, Mahoney LT, Witt J. Childhood predictors for high adult blood pressure: the Muscatine Study. *Pediatr Clin North Am*. 1993;40(1):23-40. doi:10.1016/S0031-3955(16)38478-4

18. Lauer RM, Clarke WR. Childhood risk factors for high adult blood pressure: the Muscatine Study. *Pediatrics*. 1989;84(4):633-641.

19. Fixler DE, Laird WP. Validity of mass blood pressure screening in children. *Pediatrics*. 1983;72(4):459-463.

20. Stergiou GS, Nasothimiou E, Giovas P, Kapoyiannis A, Vazeou A. Diagnosis of hypertension in children and adolescents based on home versus ambulatory blood pressure monitoring. *J Hypertens*.

2008;26(8):1556-1562. doi:10.1097/HJH.0b013e328301c411

21. Stenn PG, Noce A, Buck C. A study of the labelling phenomenon in school children with elevated blood pressure. *Clin Invest Med*. 1981;4(3-4):179-181.

22. Gregoski MJ, Barnes VA, Tingen MS, Harshfield GA, Treiber FA. Breathing awareness meditation and LifeSkills Training programs influence upon ambulatory blood pressure and sodium excretion among African American adolescents. *J Adolesc Health*. 2011;48(1):59-64. doi:10.1016/j.jadohealth.2010.05.019

23. Hamdani G, Flynn JT, Becker RC, et al. Prediction of ambulatory hypertension based on clinic blood pressure percentile in adolescents. *Hypertension*. 2018;72(4):955-961. doi:10.1161/HYPERTENSIONAHA.118.11530

24. Gillman MW, Cook NR, Rosner B, et al. Identifying children at high risk for the development of essential hypertension. *J Pediatr*. 1993;122(6):837-846. doi:10.1016/S0022-3476(09)90005-1

25. Beckett LA, Rosner B, Roche AF, Guo S. Serial changes in blood pressure from adolescence into adulthood. *Am J Epidemiol*. 1992;135(10):1166-1177. doi:10.1093/oxfordjournals.aje.a116217

26. Sun SS, Grave GD, Siervogel RM, Pickoff AA, Arslanian SS, Daniels SR. Systolic blood pressure in childhood predicts hypertension and metabolic syndrome later in life. *Pediatrics*. 2007;119(2):237-246. doi:10.1542/peds.2006-2543

27. Bao W, Threefoot SA, Srinivasan SR, Berenson GS. Essential hypertension predicted by tracking of elevated blood pressure from childhood to adulthood: the Bogalusa Heart Study. *Am J Hypertens*. 1995;8(7):657-665. doi:10.1016/0895-7061(95)00116-7

28. Hoq S, Chen W, Srinivasan SR, Berenson GS. Childhood blood pressure predicts adult microalbuminuria in African Americans, but not in whites: the Bogalusa Heart Study. *Am J Hypertens*. 2002;15(12):1036-1041. doi:10.1016/S0895-7061(02)03066-2

29. Li S, Chen W, Srinivasan SR, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study. *JAMA*. 2003;290(17):2271-2276. doi:10.1001/jama.290.17.2271

30. Shear CL, Burke GL, Freedman DS, Webber LS, Berenson GS. Designation of children with high blood pressure—considerations on percentile cut points and subsequent high blood pressure: the Bogalusa Heart Study. *Am J Epidemiol*. 1987;125(1):73-84. doi:10.1093/oxfordjournals.aje.a114513

31. Xi B, Zhang T, Li S, et al. Can pediatric hypertension criteria be simplified? a prediction analysis of subclinical cardiovascular outcomes from the Bogalusa Heart Study. *Hypertension*. 2017;69(4):691-696. doi:10.1161/HYPERTENSIONAHA.116.08782

32. Raitakari OT, Juonala M, Kähönen M, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA*. 2003;290(17):2277-2283. doi:10.1001/jama.290.17.2277

33. Juhola J, Magnussen CG, Viikari JSA, et al. Tracking of serum lipid levels, blood pressure, and body mass index from childhood to adulthood: the Cardiovascular Risk in Young Finns Study. *J Pediatr*. 2011;159(4):584-590. doi:10.1016/j.jpeds.2011.03.021

34. Juonala M, Viikari JSA, Hutri-Kähönen N, et al. The 21-year follow-up of the Cardiovascular Risk in Young Finns Study: risk factor levels, secular trends and east-west difference. *J Intern Med*. 2004;255(4):457-468. doi:10.1111/j.1365-2796.2004.01308.x

35. Juhola J, Oikonen M, Magnussen CG, et al. Childhood physical, environmental, and genetic predictors of adult hypertension: the Cardiovascular Risk in Young Finns Study. *Circulation*. 2012;126(4):402-409. doi:10.1161/CIRCULATIONAHA.111.085977

36. Oikonen M, Nuotio J, Magnussen CG, et al. Repeated blood pressure measurements in childhood in prediction of hypertension in adulthood. *Hypertension*. 2016;67(1):41-47. doi:10.1161/HYPERTENSIONAHA.115.06395

37. Aatola H, Koivistoinen T, Tuominen H, et al. Influence of child and adult elevated blood pressure on adult arterial stiffness: the Cardiovascular Risk in Young Finns Study. *Hypertension*. 2017;70(3):531-536. doi:10.1161/HYPERTENSIONAHA.117.09444

38. Theodore RF, Broadbent J, Nagin D, et al. Childhood to early-midlife systolic blood pressure trajectories: early-life predictors, effect modifiers, and adult cardiovascular outcomes. *Hypertension*. 2015;66(6):1108-1115. doi:10.1161/HYPERTENSIONAHA.115.05831

39. Juhola J, Magnussen CG, Berenson GS, et al. Combined effects of child and adult elevated blood pressure on subclinical atherosclerosis: the International Childhood Cardiovascular Cohort Consortium. *Circulation*. 2013;128(3):217-224. doi:10.1161/CIRCULATIONAHA.113.001614

40. Du T, Fernandez C, Barshop R, Chen W, Urbina EM, Bazzano LA. 2017 pediatric hypertension guidelines improve prediction of adult cardiovascular outcomes. *Hypertension*. 2019;73(6):1217-1223. doi:10.1161/HYPERTENSIONAHA.118.12469

41. Koskinen J, Juonala M, Dwyer T, et al. Utility of different blood pressure measurement components in childhood to predict adult carotid intima-media thickness. *Hypertension*. 2019;73(2):335-341. doi:10.1161/HYPERTENSIONAHA.118.12225

42. Batisky DL, Sorof JM, Sugg J, et al; Toprol-XL Pediatric Hypertension Investigators. Efficacy and safety of extended release metoprolol succinate in hypertensive children 6 to 16 years of age: a clinical trial experience. *J Pediatr*. 2007;150(2):134-139. doi:10.1016/j.jpeds.2006.09.034

43. Trachtman H, Hainer JW, Sugg J, Teng R, Sorof JM, Radcliffe J; Candesartan in Children With Hypertension (CINCH) Investigators. Efficacy, safety, and pharmacokinetics of candesartan cilexetil in hypertensive children aged 6 to 17 years. *J Clin Hypertens (Greenwich)*. 2008;10(10):743-750. doi:10.1111/j.1751-7176.2008.00022.x

44. Trachtman H, Frank R, Mahan JD, et al. Clinical trial of extended-release felodipine in pediatric essential hypertension. *Pediatr Nephrol*. 2003;18(6):548-553. doi:10.1007/s00467-003-1134-0

45. Wells TG, Portman R, Norman P, Haertter S, Davidai G, Fei Wang. Safety, efficacy, and pharmacokinetics of telmisartan in pediatric patients with hypertension. *Clin Pediatr (Phila)*. 2010;49(10):938-946. doi:10.1177/0009922810363609

46. Sorof JM, Cargo P, Graepel J, et al. β-blocker/thiazide combination for treatment of hypertensive children: a randomized double-blind, placebo-controlled trial. *Pediatr Nephrol*. 2002;17(5):345-350. doi:10.1007/s00467-002-0851-0

47. Li JS, Berezny K, Kilaru R, et al. Is the extrapolated adult dose of fosinopril safe and effective in treating hypertensive children? *Hypertension*. 2004;44(3):289-293. doi:10.1161/01.HYP.0000138069.68413.f0

48. Wells T, Frame V, Soffer B, et al; Enalapril Pediatric Hypertension Collaborative Study Group. A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of enalapril for children with hypertension. *J Clin Pharmacol*. 2002;42(8):870-880. doi:10.1177/009127002401102786

49. Soffer B, Zhang Z, Miller K, Vogt BA, Shahinfar S. A double-blind, placebo-controlled, dose-response study of the effectiveness and safety of lisinopril for children with hypertension. *Am J Hypertens*. 2003;16(10):795-800. doi:10.1016/S0895-7061(03)00900-2

50. Shahinfar S, Cano F, Soffer BA, et al. A double-blind, dose-response study of losartan in hypertensive children. *Am J Hypertens*. 2005;18(2, pt 1):183-190. doi:10.1016/j.amjhyper.2004.09.009

51. Hazan L, Hernández Rodriguez OA, Bhorat AE, Miyazaki K, Tao B, Heyrman R; Assessment of Efficacy and Safety of Olmesartan in Pediatric Hypertension Study Group. A double-blind, dose-response study of the efficacy and safety of olmesartan medoxomil in children and adolescents with hypertension. *Hypertension*. 2010;55(6):1323-1330. doi:10.1161/HYPERTENSIONAHA.109.147702

52. Li JS, Flynn JT, Portman R, et al. The efficacy and safety of the novel aldosterone antagonist eplerenone in children with hypertension: a randomized, double-blind, dose-response study. *J Pediatr*. 2010;157(2):282-287. doi:10.1016/j.jpeds.2010.02.042

53. Wells T, Blumer J, Meyers KEC, et al; Valsartan Pediatric Hypertension Study Group. Effectiveness and safety of valsartan in children aged 6 to 16 years with hypertension. *J Clin Hypertens (Greenwich)*. 2011;13(5):357-365. doi:10.1111/j.1751-7176.2011.00432.x

54. Flynn JT, Newburger JW, Daniels SR, et al; PATH-1 Investigators. A randomized, placebo-controlled trial of amlodipine in children with hypertension. *J Pediatr*. 2004;145(3):353-359. doi:10.1016/j.jpeds.2004.04.009

55. Berenson GS, Voors AW, Webber LS, et al. A model of intervention for prevention of early essential hypertension in the 1980s. *Hypertension*. 1983;5(1):41-54. doi:10.1161/01.HYP.5.1.41

56. Couch SC, Saelens BE, Levin L, Dart K, Falciglia G, Daniels SR. The efficacy of a clinic-based behavioral nutrition intervention emphasizing a DASH-type diet for adolescents with elevated blood pressure. *J Pediatr*. 2008;152(4):494-501. doi:10.1016/j.jpeds.2007.09.022

57. Howe PRC, Cobiac L, Smith RM. Lack of effect of short-term changes in sodium intake on blood pressure in adolescent schoolchildren. *J Hypertens*. 1991;9(2):181-186. doi:10.1097/00004872-199102000-00014

58. Sinaiko AR, Gomez-Marin O, Prineas RJ. Effect of low sodium diet or potassium supplementation on adolescent blood pressure. *Hypertension*. 1993; 21(6, pt 2):989-994. doi:10.1161/01.hyp.21.6.989

59. Burrello J, Erhardt EM, Saint-Hilary G, et al. Pharmacological treatment of arterial hypertension in children and adolescents: a network meta-analysis. *Hypertension*. 2018;72(2):306-313. doi:10.1161/HYPERTENSIONAHA.118.10862

60. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics*. 2004;114(2 suppl 4th report):555-576.

61. Dwyer T, Magnussen CG, Schmidt MD, et al. Decline in physical fitness from childhood to adulthood associated with increased obesity and insulin resistance in adults. *Diabetes Care*. 2009;32 (4):683-687. doi:10.2337/dc08-1638

62. Ceponiene I, Klumbiene J, Tamuleviciute-Prasciene E, et al. Associations between risk factors in childhood (12-13 years) and adulthood (48-49 years) and subclinical atherosclerosis: the Kaunas Cardiovascular Risk Cohort Study. *BMC Cardiovasc Disord*. 2015;15(1):89. doi:10.1186/s12872-015-0087-0

63. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/ NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138(17):e426-e483. doi:10.1161/cir.0000000000000597

64. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-520. doi:10.1001/jama.2013.284427

65. Berenson GS, Shear CL, Chiang YK, Webber LS, Voors AW. Combined low-dose medication and primary intervention over a 30-month period for sustained high blood pressure in childhood. *Am J Med Sci*. 1990;299(2):79-86. doi:10.1097/ 00000441-199002000-00001

66. Hanevold C, Waller J, Daniels S, Portman R, Sorof J; International Pediatric Hypertension Association. The effects of obesity, gender, and ethnic group on left ventricular hypertrophy and geometry in hypertensive children: a collaborative study of the International Pediatric Hypertension Association. *Pediatrics*. 2004;113(2):328-333. doi: 10.1542/peds.113.2.328

67. Brady TM, Fivush B, Flynn JT, Parekh R. Ability of blood pressure to predict left ventricular hypertrophy in children with primary hypertension. *J Pediatr*. 2008;152(1):73-78. doi:10.1016/j.jpeds. 2007.05.053

68. Sinaiko AR, Jacobs DR Jr, Woo JG, et al. The International Childhood Cardiovascular Cohort (i3C) Consortium Outcomes Study of childhood cardiovascular risk factors and adult cardiovascular morbidity and mortality: design and recruitment. *Contemp Clin Trials*. 2018;69:55-64. doi:10.1016/j. cct.2018.04.009