UK National Screening Committee

SCREENING FOR PRIMARY HYPERTENSION IN CHILDREN AND YOUNG PEOPLE

An evidence map to outline the volume and type of evidence related to screening for primary hypertension for the UK National Screening Committee

Version: Public Consultation

Author: Solutions for Public Health

Date: February 2022

The UK National Screening Committee secretariat is hosted by the Department of Health and Social Care.

About the UK National Screening Committee (UK NSC)

The UK NSC advises ministers and the NHS in the 4 UK countries about all aspects of population screening and supports implementation of screening programmes. Conditions are reviewed against evidence review criteria according to the UK NSC's evidence review process.

Read a complete list of UK NSC recommendations.

UK National Screening Committee, Southside, 39 Victoria Street, London, SW1H 0EU

www.gov.uk/uknsc

Blog: https://nationalscreening.blog.gov.uk/

For queries relating to this document, please contact: https://view-health-screening-recommendations.service.gov.uk/helpdesk/

© Crown copyright 2016
You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit OGL or email psi@nationalarchives.gsi.gov.uk. Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

Published

Contents

Summary

This document discusses the findings of the evidence map on screening for primary hypertension in children and young people.

Evidence maps are a way of scanning published literature to look at the volume and type of the evidence base in relation to a specific topic. Their purpose is to inform the UK NSC about whether the evidence is sufficient to commission further work on the topic under consideration.

Based on the findings of this evidence map, no further work on screening for primary hypertension in children and young people should be commissioned at the present time. The UK National Screening Committee (UK NSC) will return to screening for primary hypertension in children and young people in 3-years' time.

Introduction and approach

Background & Objectives

The UK National Screening Committee (UK NSC) external reviews (also known as evidence summaries or evidence reviews) are developed in keeping with the UK NSC evidence review process to ensure that each topic is addressed in the most appropriate and proportionate manner. Further information on the evidence review process can be accessed online.

Screening for primary hypertension in children and young people is currently due for an updated external review.

Elevated blood pressure in children and young people is considered to be a serious public health concern worldwide and is believed to be growing due to increasing levels of childhood obesity [1]. There are 2 classifications for hypertension in children and young people, primary and secondary. Primary, or essential, hypertension has no apparent cause but has been linked with numerous factors including obesity, low birth weight, family history, physical activity level, ethnicity and gender. Secondary hypertension is caused by an underlying condition such as kidney disease. Primary hypertension is more common in adolescents and is usually asymptomatic. Secondary hypertension is more common in pre-adolescent children [1,2]. This evidence map considers screening for primary hypertension.

Estimates of the prevalence of primary hypertension in children and young people are complicated by a lack of uniform diagnostic criteria. In adults, a pre-fixed blood pressure threshold is used to diagnose hypertension. However, blood pressure in children and young people is dependent on a number of different variables including age, height, weight and sex. Therefore, variations in the threshold used could lead to over or under diagnosis. Despite these uncertainties there are reports of high prevalence in various populations and it is believed that a significant proportion of children and adolescents with hypertension remain undiagnosed [1].

The clinical sequelae of elevated blood pressure are due to its effect on the vascular system over a long period of time [2]. There is a lack of data on the long-term consequences of persistent hypertension in children and young people. However, there is evidence that hypertension in children and young people can lead to end organ damage such as left ventricular hypertrophy or increased intima-media thickness and hypertension in adulthood [1].

Previous UK NSC reports on hypertension in children and young people have set out some of the challenges in obtaining accurate blood pressure test results [2]. These

include natural variations influenced by age, time of day, anxiety levels or food or drink consumed just prior to the test. Another challenge is that different methods of taking blood pressure can lead to different results. Blood pressure measurements can be taken using auscultatory devices, such as a mercury or aneroid sphygmomanometer, when a child is old enough to co-operate with measurement using these devices or using an oscillometric device that is calibrated for use in a paediatric population. The recommended reference standard to confirm a diagnosis of hypertension in children and adults is ambulatory blood pressure monitoring [3].

Children and young people with primary hypertension are often initially treated with non-pharmacological measures. These could include weight reduction, regular physical activity, dietary and lifestyle modification [1]. Pharmacological interventions may also be offered to children and young people, particularly those with evidence of end organ damage [1].

The aim of screening children and young people for elevated blood pressure is to identify hypertension at an early stage. The intention is that intervention would potentially decrease the rate of progression of hypertension from childhood to adulthood and reduce the clinical consequences of hypertension in adulthood [1].

Current national and international screening policies

In 2020, the U.S. Preventive Services Task Force (USPSTF) updated its 2013 recommendation on screening for high blood pressure in children and adolescents aged 3 to 18 years. Unlike their 2013 recommendation, the scope of the 2020 USPSTF recommendation included both primary and secondary hypertension. Evidence on the benefits and harms of screening, test accuracy, the effectiveness of treatment and the association between hypertension and markers of cardiovascular disease in childhood and adulthood was reviewed. The USPSTF concluded that the evidence to support screening for high blood pressure in children and adolescents is insufficient and that the balance of benefits and harms could not be determined [4].

Clinical practice guidelines for the detection and management of high blood pressure in children and adolescents include the 2017 guidance from the American Academy of Pediatrics [3]. This recommended:

- measuring blood pressure annually in children and adolescents ≥ 3 years of age
- checking blood pressure at every healthcare encounter for children and adolescents ≥ 3 years of age if they are obese, are taking medications known to increase blood pressure, have renal disease, a history of aortic arch obstruction or coarctation or diabetes

The European Society of Hypertension produced 2016 guidance on the management of high blood pressure in children and adolescents [5]. This recommends that blood

pressure should be measured in children from the age of 3 years with re-evaluation of children considered to have normal blood pressure every 2 years and those with high-normal blood pressure re-evaluated annually.

The UK NSC does not currently recommend screening for primary hypertension in children and young people aged 3 to 18 years of age. The Committee based this recommendation on the evidence provided by the 2018 UK NSC review carried out by Solutions for Public Health briefly described below.

Previous UK NSC review on screening for primary hypertension in children and young people

The 2018 UK NSC review [2] looked for evidence published between 2010 and October 2017, focusing on gaps identified by a previous UK NSC review in 2010. The 2018 review searched for evidence on the prevalence of primary hypertension in children and young people (3 to 8 years of age) in the UK, the association between primary hypertension in children and young people and the risk of adverse outcomes, the diagnostic accuracy of screening tests for primary hypertension in children and young people and the effectiveness of pharmacological, non-pharmacological or combination interventions for treating primary hypertension in children and young people and preventing hypertension in adults. The 2018 review also searched for evidence on screening strategies for hypertension in children and young people, the optimal age to initiate screening, the optimal time intervals to repeat screening and who should do the screening.

The 2018 review concluded that although there was reasonable evidence to suggest that the prevalence of elevated blood pressure in children and young people was likely to be increasing in the UK, it was uncertain what the prevalence was. There was also good quality evidence that high blood pressure is an independent factor associated with target organ damage in children and adolescents. However, the 2018 review also concluded that whilst hypertension may be identified using current standard techniques in a clinical setting, from the perspective of population screening, these methods would result in many children being identified with elevated blood pressure who did not have hypertension. In relation to intervention, the 2018 review found that some types of non-pharmacological interventions showed some reduction in blood pressure, but it was not clear if this would result in any clinically meaningful change and whether this could be maintained over the long-term. Evidence on the effectiveness of pharmacological interventions and combination interventions in children and young people with primary hypertension was limited and of low quality and there was no evidence that pharmacological, non-pharmacological or combination interventions initiated in childhood were effective in reducing hypertension in adulthood. The 2018 review did not identify any studies demonstrating effective blood pressure screening strategies in children and adolescents or any evidence that addressed the questions of the optimal

age to initiate a population-based screening programme, optimum time intervals or who should carry out the screening test [2].

Aims of the evidence map

Evidence maps are rapid evidence products which aim to gauge the volume and type of evidence relating to a specific topic.

This evidence map has been developed to assess whether a more sustained review on screening for primary hypertension in children and young people should be commissioned and to evaluate the volume and type of evidence on key issues related to screening for primary hypertension in children and young people.

The aim was to address the following questions:

1. What is the association between primary hypertension in children and young people and the risk of adverse outcomes?
2. What is the diagnostic accuracy of screening tests for primary hypertension in children and young people?
3. What is the effectiveness of pharmacological and non-pharmacological and/or combination interventions for preventing hypertension in children and young people and its effectiveness in preventing long-term effect?
4. Is there an effective screening strategy for primary hypertension in children and young people to prevent hypertensive disorders in later life?

The population of interest in this evidence map is children and young people aged 3 to 18 years old. The findings of this evidence map will provide the basis for discussion to support decision making on whether there is sufficient evidence to justify commissioning a more sustained review of the evidence on primary hypertension in children and young people. The aim of this document is to present the information necessary for the UK NSC to decide this.

Search methods and results

The searches were conducted on 12 October 2021 on 3 databases: Medline, Embase and the Cochrane Library. The search period was restricted to October 2017 – October 2021. The search date was determined by the search period for the previous UK NSC review.

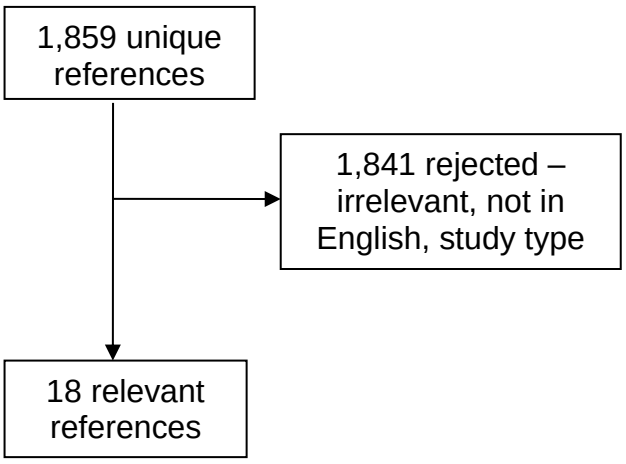
The detailed search strategies, including exclusion and inclusion criteria are available in Appendix 1. The searches returned a total of 1,859 unique references across the 4 questions which were initially sifted by an information scientist for potential relevance. One reviewer assessed 276 titles and abstracts for further appraisal and possible inclusion in the evidence map. Eighteen references were included in the final evidence map: 15 references in question 1, 2 in question 2, one in question 3 and none in question 4.

All references were reviewed at abstract level, though in some cases full texts were reviewed to clarify uncertainty. A formal quality appraisal of the evidence was not required, given the remit of the evidence map.

Abstract reporting tables are available in Appendix 2.

A flow diagram summarising the number of studies included and excluded is presented in Figure 1.

Figure 1: Summary of included and excluded publications



Summary of findings

Question 1: What is the association between primary hypertension in children and young people and the risk of adverse outcomes?

The 2018 UK NSC review concluded that there was good quality evidence that high blood pressure is an independent factor associated with target organ damage in children and adolescents [2]. This was based on studies showing that for left ventricular mass, carotid intima-media thickness and retinal vasculature, target organ damage was independently associated with systolic blood pressure in children.

Fifteen studies published since October 2017 met the inclusion criteria for this question. The inclusion and exclusion criteria are summarised in Appendix 1. The included studies are briefly described below, and further information is provided in the abstract reporting tables in Appendix 2.

The adverse outcomes of interest for this question are end organ damage, cognitive changes, retinal vascular changes and cardiovascular disease (see Appendix 1). Therefore, studies reporting these outcomes were prioritised for inclusion. Studies reporting measures of association such as odds ratio and risk ratio between primary hypertension and the risk of adverse outcomes were also prioritised. However, it was not always possible to determine if the studies reported a measure of association or confirm that the population all had, or mostly had, primary hypertension within the confines of an evidence map.

As recent systematic reviews addressing the key question for the outcomes of end organ damage and cardiovascular disease were identified, only more recently published primary studies have been included in this evidence map. However, all studies exploring an association between primary hypertension in children and young people and cognitive changes and retinal vascular changes were considered for inclusion as no recent systematic reviews were identified for these outcomes.

The search for this evidence map also identified studies exploring the association between high blood pressure in children and young people and high blood pressure or hypertension in adults. These studies are not formally included in the evidence map but are summarised briefly at the end of this section.

The association between hypertension in children and young people and risk of adverse outcomes

Four systematic reviews on the association between hypertension in children and young people and the risk of adverse outcomes were identified and included.

The USPSTF produced a systematic review on screening for hypertension in children and adolescents which included studies published up to October 2020 [6]. This systematic review included a question about the association between high blood pressure in children and adolescents and outcomes in adults. The authors reported a statistically significant association between abnormal childhood blood pressure and carotid intima-media thickness (reported in 6 studies), left ventricular hypertrophy (reported in 2 studies) and cardiovascular disease (reported in 1 study) in adults. These conclusions were based on the 7 studies that were included in the systematic review for these outcomes, 3 of which were published in 2017 or later.

Two systematic reviews with meta-analysis assessing the association between elevated blood pressure in childhood and end organ damage were identified [7, 8]. Goulas *et al.* (2021) [7] investigated the impact of using different guidelines to diagnose hypertension in children and the overall risk of left ventricular hypertension. The meta-analysis included 3 observational studies. The date of the search was not reported in the study abstract or full text. However, all the included studies were published between 2018 and 2020. In the meta-analysis the association between hypertension and left ventricular hypertension was similar for the different guidelines. For the 2017 American Academy of Pediatrics' thresholds for diagnosing hypertension in children and adolescents, the odds ratio for association with left ventricular hypertension was 3.89 (95%CI 1.68 to 8.99). For the Fourth Report* and the 2016 European Society of Hypertension thresholds the odds ratio was 3.19 (95%CI 1.14 to 8.88). Yang *et al.* (2020) [8] included 19 prospective cohort studies published up to August 2019, 12 of which were included in the meta-analysis. Seven of these 12 studies were published in 2017 or later. The authors reported that elevated blood pressure in childhood or adolescence was significantly associated with high carotid intima-media thickness (2 studies, n = 4,152, odds ratio 1.60 (95% CI 1.29 to 2.00)), left ventricular hypertrophy (2 studies, n = 3,019, odds ratio 1.40 (95% CI 1.20 to 1.64)) and high pulse wave velocity (3 studies, n = 3,725, odds ratio 1.83 (95% CI 1.39 to 2.40)) in adulthood. The authors also reported evidence of an association between elevated blood pressure in childhood and cardiovascular disease and mortality in adulthood from 4 studies included in the systematic review that were not suitable for meta-analysis.

A 2017 systematic review was identified that explored the association between body adiposity and hypertension in children and adolescents and ophthalmological alternations in comparison to healthy children [9]. This review included observational studies published up to May 2017. Therefore this review does not include any new studies published since October 2017. The authors reported a positive association between body adiposity and retinal venular dilation, and signs of arterial hypertension

* A 2004 guideline on paediatric hypertension

and retinal arteriolar narrowing. The data were not suitable for meta-analysis due to the heterogeneity between studies.

Five studies on end organ damage and/or cardiovascular outcomes were also included in this evidence map:

- Abdul-Raheem *et al.* (2021) [10] assessed left ventricular function in 83 children and adolescents aged 5 to 21 years who were being evaluated for overweight/obesity and elevated blood pressure. The authors found that elevated diastolic blood pressure was associated with left ventricular diastolic dysfunction after adjustment for age, sex, race, blood pressure medication and body mass index (odds ratio 1.95, 95%CI 1.15 to 3.32)
- Campbell *et al.* (2021) [11] re-evaluated the records of 272 adolescents aged 13 to 17 years who had previously been assessed for hypertension using paediatric guidelines against adult blood pressure norms and assessed the association with left ventricular hypertension. The authors stated that the use of adult norms resulted in significant reclassification of hypertension. The odds ratio for a patient with hypertension having left ventricular hypertension was 8.75 (95%CI 2.1 to 36.4) using the 2005 American Heart Association adult norms and 4.94 (95%CI 1.0 to 24.3) using the 2018 European Society of Hypertension adult norms
- Kaplinski *et al.* (2021) [12] explored the association between paediatric hypertension and adverse cardiovascular outcomes in 212 patients evaluated for hypertension with an interquartile age range of 13 to 18 years. Univariate analysis showed that left ventricular mass index was higher in hypertensive, obese and African American patients. However, only obesity was associated with left ventricular mass index on multivariate analysis (odds ratio 2.9, 95%CI 1.4 to 5.8)
- Truong *et al.* (2021) [13] reviewed whether children evaluated for primary hypertension were more likely to have left ventricular hypertrophy. The number and age of children was not specified in the abstract. The authors found that one third of patients who had completed an echocardiogram had left ventricular hypertrophy. However, of the factors assessed (blood pressure severity, anti-hypertensive medication and body mass index), only body mass index was associated with left ventricular hypertrophy cardiac remodelling
- Liu *et al.* (2021) [14] compared cardiovascular structures in 34 children with simple primary hypertension, 11 children with hypertension and co-existing obesity and 32 healthy children. The mean ages of the groups ranged from 10.9 years to 11.8 years. The authors reported statistically significant differences between the children with hypertension and the healthy children for carotid-femoral pulse wave velocity and measures of cardiovascular structure and function such as left atrial diameter, left ventricular mass, relative wall thickness, end-diastolic left ventricular internal diameter, diastolic interventricular septum thickness, diastolic left ventricular posterior wall thickness and root diameter of aorta.

Three studies on cognitive changes were included:

- Chrysaidou *et al.* (2020) [15] assessed the relationship between blood pressure and executive function in 116 children and adolescents referred to an outpatient hypertension clinic. The mean or age range of the children was not reported in the study abstract. The authors found that high night-time systolic blood pressure was associated with poor performance in executive function. The association remained statistically significant after adjustment for body mass index and socioeconomic status
- George *et al.* (2021) [16] examined the association between cardiovascular risk factors in adolescence, young adulthood and midlife with late-life cognition. The study included 764 African Americans aged more than 50 years old who had received health checks earlier in life. Of the 764 adults, 22% had received health checks as an adolescent (aged 12 to 20 years). The authors reported that adolescents with hypertension had lower late-life executive function compared to normotensive adolescents
- Kupferman *et al.* (2018) [17] explored the association between different measures of blood pressure and neurocognitive function in 75 children aged 10 to 18 years with untreated primary hypertension and compared this to 75 matched normotensive controls. The authors reported that office blood pressure was not associated with neurocognitive test scores. However, parameters of ambulatory blood pressure monitoring were statistically significantly associated with neurocognitive test scores with odds ratios ranging from 1.02 to 1.08

Three studies on retinal vascular changes were included:

- Lona *et al.* (2020) [18] screened 391 children aged 6 to 8 years for blood pressure and retinal vessel diameters. At follow up 4 years later, 262 children were re-assessed. The authors reported that children with increased blood pressure at baseline had narrower central retinal arteriolar diameters at follow-up
- Rogowska *et al.* (2021) [19] assessed the relationship between hypertensive target organ damage and vessel density, foveal thickness, thickness of retinal nerve fibre layer, ganglion cell complex and foveal avascular zone in 157 children and adolescents with arterial hypertension. The mean age of the children and adolescents was 14.9 years. The authors reported that hypertensive children with increased carotid intima-media thickness had statistically significantly decreased retinal vessel density and increased foveal avascular zone in comparison to hypertensive patients with normal carotid intima-media thickness. They also reported that subclinical hypertensive arterial injury was associated with a significant decrease in retinal thickness
- Dereli *et al.* (2020) [20] compared subclinical retinal microvascular alterations in 20 children aged 10 to 18 years with hypertension and 20 healthy matched controls. The authors reported that although there was no evidence of

hypertensive retinopathy, the children with hypertension did have statistically significantly greater subthreshold microvascular alterations

The association between hypertension in children and young people and high blood pressure or hypertension in adults

The 2 systematic reviews summarised in this section were not formally included in the evidence map as they do not report an outcome specified for this question.

The USPSTF systematic review on screening for hypertension in children and adolescents concluded that there is a statistically significant association between childhood hypertension and abnormally high blood pressure in adulthood with odds ratios ranging from 1.1 to 4.5, risk ratios ranging from 1.45 to 3.60 and hazard ratios ranging from 2.8 to 3.2 [6]. This conclusion was based on the results of 20 observational studies published up to October 2020.

A 2020 systematic review and meta-analysis also investigated the strength of association between elevated blood pressure in childhood and hypertension in adulthood [21]. This review included 16 longitudinal studies published up to November 2019 with 11 of these studies (n= 39,714) included in the meta-analysis. The authors reported a statistically significant association between elevated blood pressure in children (aged 3 to 18 years) and hypertension in adults (aged 18 to 57 years) with a summary odds ratio of 2.02 (95%CI 1.62 to 2.53).

In summary, 15 papers were included for this question. These included 4 systematic reviews and 11 primary studies on the association between hypertension in children and young people and the risk of adverse outcomes.

The volume and type of evidence identified is sufficient for more detailed consideration in an evidence summary.

Question 2: What is the diagnostic accuracy of screening tests for primary hypertension in children and young people?

The 2018 UK NSC review concluded that hypertension may be identified using current standard techniques in a clinical setting. However the sensitivities, specificities and positive predictive values reported suggested that these methods would result in many children being identified with elevated blood pressure who did not have hypertension and a significant proportion of children who would remain with undetected hypertension [2].

One systematic review and one primary study met the inclusion criteria for this question. The inclusion and exclusion criteria are summarised in Appendix 1. The included studies are briefly described below, and further information is provided in the abstract reporting tables in Appendix 2.

The USPSTF produced a systematic review on screening for hypertension in children and adolescents which included studies published up to October 2020 [6]. One of the questions considered related to the diagnostic accuracy of screening tests for high blood pressure in children and adolescents. The systematic review concluded that the evidence base was inconclusive about whether the diagnostic accuracy of blood pressure measurements is adequate for screening asymptomatic children and adolescents in primary care. This conclusion was based on the single study on diagnostic accuracy included in the systematic review which reported a sensitivity of 0.82 and a specificity of 0.70 for a threshold of systolic blood pressure at the 90th percentile. The index test was 2 office-based blood pressure measurements taken one to 2 weeks apart and the reference standard 26-hour ambulatory blood pressure monitoring [6]. This single study [22] was also identified by the search for this evidence map. It was published in 2018 and included 247 adolescents aged 11 to 19 years who were either healthy volunteers or had been referred for hypertension evaluation [6].

A further study identified by the search for this evidence map was a retrospective case series assessing the ability of automated office blood pressure and manual office blood pressure to identify hypertension in children against a reference standard of 24-hour ambulatory blood pressure monitoring [23]. For automated blood pressure, calculated from the average of 5 readings using an oscillometric device on the right arm, the sensitivity was 51% and the specificity 71%. For manual office blood pressure, calculated from one to 2 readings taken using an auscultatory device by a health professional, the sensitivity was 67% and the specificity 55%. The study included 187 children under 18 years of age evaluated in a hypertension clinic. Office hypertension was defined by a blood pressure ≥95th percentile for sex and height percentiles for patients aged less than 13 years and by a blood pressure of ≥130/80 mm Hg for patients aged 13 years or older.

In summary, limited new evidence was identified on the diagnostic accuracy of screening tests for primary hypertension in children and young people.

The number and type of studies that met the criteria to address this question does not justify commissioning an evidence review at this time as the nature of the evidence available limits what could be expected from an evidence summary in this area.

Question 3: What is the effectiveness of pharmacological and non-pharmacological and/or combination interventions for preventing hypertension in children and young people and its effectiveness in preventing long-term effect?

The 2018 UK NSC review concluded that some types of non-pharmacological interventions showed some reduction in blood pressure, but it was not clear if this would result in any clinically meaningful change that could be maintained over the long-term. Evidence on the effectiveness of pharmacological interventions and combination interventions in children and young people with primary hypertension was limited and of low quality and there was no evidence that pharmacological, non-pharmacological or combination interventions begun in childhood were effective in reducing hypertension in adulthood.

One systematic review met the inclusion criteria for this question. Two additional studies identified by the search were already included in the systematic review and were therefore not separately included in the evidence map. The inclusion and exclusion criteria are summarised in Appendix 1. Studies of interest were those comparing interventions to no intervention or placebo. Populations with screen-detected hypertension were particularly of interest, but populations of clinically-detected hypertension were also eligible. The included study is briefly described below and further information is provided in the abstract reporting tables in Appendix 2.

The USPSTF produced a systematic review on screening for hypertension in children and adolescents which included studies published up to October 2020 [6]. This systematic review included questions about the effectiveness of pharmacological, non-pharmacological and combination interventions for treating high blood pressure in children and adolescents, the harms of treatment, the effectiveness of treatment during childhood to reduce blood pressure and adverse health outcomes in adulthood. Overall the systematic review concluded that there was moderate strength evidence of efficacy and good tolerability for pharmacological interventions from studies that were mostly limited to participants with primary hypertension. However, the authors noted that none of the drugs were evaluated in more than one study and the magnitude of effect varied and was not always significantly different from placebo. For non-pharmacological interventions there was low strength evidence that physical exercise and a dietary approach (DASH) can reduce blood pressure. There was also poor quality evidence that a combination of pharmacological treatment and lifestyle interventions could reduce blood pressure. However, there was low to moderate strength evidence of no effect for a low-sodium diet or progressive muscle relaxation. These conclusions were based on the results of 20 randomised controlled trials (RCTs) on treating high blood pressure in children and adolescents and 7 RCTs that reported harms of treatment. Only 2 of the included studies, one of which was a meta-analysis of RCTs, were published in 2017 or later. It is not clear that any of the studies were conducted in screened populations. The

systematic review did not identify any studies on the effectiveness of treatment during childhood to reduce blood pressure and adverse health outcomes in adulthood [6].

The 2 studies included in the USPSTF systematic review that were published in 2017 or later were also identified by the search for this evidence map [24,25]. The first of these 2 studies was a meta-analysis of pharmacological treatment for hypertension published in 2018 [24] and included 13 RCTs with a total of 2,378 patients with a median age of 12 years and a median follow-up of 35 days. None of these 13 RCTs were published in 2017 or later. The second study was an RCT published in 2017 [25] which included 40 obese pre-hypertensive girls aged 15 ± 1 years old who received 12-weeks of combined resistance and aerobic exercise or no exercise with assessment at baseline and after 12-weeks.

No further studies that compared interventions for hypertension to no treatment or placebo were identified.

In summary, limited new evidence was identified on the effectiveness of pharmacological and non-pharmacological and/or combination interventions for preventing hypertension in children and young people and its effectiveness in preventing long-term effect.

The number and type of studies that met the criteria to address this question does not justify commissioning an evidence review at this time as the nature of the evidence available limits what could be expected from an evidence summary in this area.

Question 4: Is there an effective screening strategy for primary hypertension in children and young people to prevent hypertensive disorders in later life?

Sub-questions:

- what are the optimal ages at which to initiate screening?
- what are optimal time intervals at which to repeat screening?
- who should do the screening; general paediatricians, renal physicians or other?

The 2018 UK NSC review did not identify any studies demonstrating effective blood pressure screening strategies in children and adolescents or any evidence that addressed the questions of the optimal age to initiate a population-based screening programme, optimum time intervals or who should carry out the screening test [2].

No studies met the inclusion criteria for this question. The inclusion and exclusion criteria are summarised in Appendix 1.

The USPSTF systematic review on screening for hypertension in children and adolescents also included a question about whether screening for high blood pressure (persistently elevated blood pressure or hypertension) in children and adolescents delays the onset of or reduces adverse health outcomes related to high blood pressure. No studies were identified by this systematic review in a search for studies published up to October 2020 [6].

No studies were identified that met the inclusion criteria for this question. Therefore, there is insufficient evidence in this key area to justify commissioning an evidence summary.

Conclusions

Since the previous 2018 UK NSC review, limited new evidence was identified on the diagnostic accuracy of screening tests or the effectiveness of pharmacological and/or non-pharmacological interventions for hypertension in children and young people. No studies were identified on screening strategies for primary hypertension in children and young people to prevent hypertensive disorders in later life. New evidence published since the last UK NSC review was identified on the association between primary hypertension in children and young people and the risk of adverse outcomes. However, it is unlikely that a review of the available evidence in this area alone would lead to a change in the UK NSC's position.

With this in mind, commissioning a full, more sustained review of the evidence on screening for primary hypertension in children and young people is not justified at the current time.

Recommendations

On the basis of this evidence map, no further work on screening for primary hypertension in children and young people should be commissioned at the present time and the topic should be reconsidered in 3-years' time.

Appendix 1 — Search strategy for the evidence map

SOURCES SEARCHED: Medline, Embase and Cochrane Library

DATES OF SEARCH: 2017 to 12 October 2021

SEARCH STRATEGIES

Medline search adverse outcomes			**Embase search adverse outcomes**		
1	*hypertension/ or *prehypertension/	178267	1	*hypertension/ or *prehypertension/	207611
2	*blood pressure/	84543	2	*blood pressure/	77712
3	(hypertensi* or pre-hypertensi* or prehypertensi*).ti.	206076	3	(hypertensi* or pre-hypertensi* or prehypertensi*).ti.	258294
4	(blood pressure or bp).ti.	67787	4	(blood pressure or bp).ti.	87311
5	1 or 2 or 3 or 4	326102	5	1 or 2 or 3 or 4	413706
6	(adolescent/ or child/) and (child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti,ab.	1180447	6	(adolescent/ or child/) and (child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti,ab.	1544999
7	(child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti.	1176885	7	(child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti.	1399582
8	6 or 7	1495277	8	6 or 7	1883396
9	5 and 8	12731	9	5 and 8	16653
10	((organ or organs) adj3 (damag* or injur* or failure)).ti,ab.	49906	10	organ injury/	8960
11	hypertrophy, left ventricular/ or hypertrophy, right ventricular/	16443	11	((organ or organs) adj3 (damag* or injur* or failure)).ti,ab.	78070
12	((heart or cardi* or ventric*) adj3 hypertroph*).ti,ab.	55259	12	exp heart ventricle hypertrophy/	70376
13	arteriosclerosis/	56680	13	((heart or cardi* or ventric*) adj3 hypertroph*).ti,ab.	80403
14	exp atherosclerosis/	48421	14	arterial wall thickness/	23113
15	(atheroscleros?s or arterioscleros?s or (arterial adj3 (thickness or diameter? or plaque?))).ti,ab.	133335	15	exp atherosclerosis/	229941
16	(carotid adj3 (wall or plaque? or thickness or diameter?)).ti,ab.	16279	16	(atheroscleros?s or arterioscleros?s or (arterial adj3 (thickness or diameter? or plaque?))).ti,ab.	180046
17	exp Hypertensive Retinopathy/	234	17	(carotid adj3 (wall or plaque? or thickness or diameter?)).ti,ab.	26465
18	(retinopath* or (retina* adj5 (chang* or damag* or injur* or diameter*))).ti,ab.	65872	18	*retina blood vessel/	4910
19	cognition/	109213	19	exp retinopathy/	107945

20	cognitive dysfunction/	25199	20	(retinopath* or (retina* adj5 (chang* or damag* or injur* or diameter*))).ti,ab.	89298
21	cognition disorders/	65460	21	cognition/	253310
22	Neuropsychological Tests/	98251	22	cognitive defect/	181653
23	((cognitive or cognition) adj3 (chang* or deteriorat* or defect* or impair* or assess*)).ti,ab.	114883	23	mild cognitive impairment/	30704
24	*cardiovascular diseases/	114642	24	cognition assessment/	5683
25	*cerebrovascular diseases/ or stroke/	145042	25	((cognitive or cognition) adj3 (chang* or deteriorat* or defect* or impair* or assess*)).ti,ab.	175170
26	heart diseases/ or exp myocardial ischemia/	511988	26	*cardiovascular disease/	101025
27	(((cardiovascular or cardio-vascular or coronary or heart or myocardi* or cardi* or isch?mic or cerebrovascular or cerebro-vascular) adj (disease? or disorder? or health)) or cvd or chd).ti,ab.	430767	27	*cerebrovascular disease/ or exp brain infarction/ or exp cerebrovascular accident/	330300
28	((cardiovascular or cardio-vascular or coronary or heart or myocardi* or cardi* or isch?mic or cerebrovascular or cerebro-vascular) adj risk).ti,ab.	87417	28	exp ischemic heart disease/	704565
29	(myocardi* adj (infarct* or isch?emi*)).ti,ab.	231903	29	(((cardiovascular or cardio-vascular or coronary or heart or myocardi* or cardi* or isch?mic or cerebrovascular or cerebro-vascular) adj (disease? or disorder? or health)) or cvd or chd).ti,ab.	613254
30	angina.ti,ab.	54331	30	((cardiovascular or cardio-vascular or coronary or heart or myocardi* or cardi* or isch?mic or cerebrovascular or cerebro-vascular) adj risk).ti,ab.	138682
31	acute coronary syndrome.ti,ab.	24088	31	(myocardi* adj (infarct* or isch?emi*)).ti,ab.	328506
32	((adverse or longterm or long-term) adj3 outcome?).ti,ab.	149597	32	angina.ti,ab.	75731
33	outcome?.ti.	383028	33	acute coronary syndrome.ti,ab.	45068
34	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33	2046383	34	((adverse or longterm or long-term) adj3 outcome?).ti,ab.	236599
35	9 and 34	3054	35	outcome?.ti.	589464
36	limit 35 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")	63	36	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35	3004029
37	(comment or editorial or letter or review).pt. or case report.ti,ab.	5136806	37	9 and 36	4708
38	35 not 37	2529	38	limit 37 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")	97
39	36 or 38	2568	39	(conference* or editorial or letter or note or review).pt. or case report.ti,ab.	10884583

40	limit 39 to (english language and yr="2017 -Current")	764	40	37 not 39	2549
			41	38 or 40	2625
			42	limit 41 to (english language and yr="2017 -Current")	776
Medline search therapies			**Embase search therapies**		
1	*hypertension/ or *prehypertension/	178267	1	*hypertension/ or *prehypertension/	207611
2	*blood pressure/	84543	2	*blood pressure/	77712
3	(hypertensi* or pre-hypertensi* or prehypertensi*).ti.	206076	3	(hypertensi* or pre-hypertensi* or prehypertensi*).ti.	258294
4	(blood pressure or bp).ti.	67787	4	(blood pressure or bp).ti.	87311
5	1 or 2 or 3 or 4	326102	5	1 or 2 or 3 or 4	413706
6	(adolescent/ or child/) and (child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti,ab.	1180447	6	(adolescent/ or child/) and (child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti,ab.	1544999
7	(child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti.	1176885	7	(child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti.	1399582
8	6 or 7	1495277	8	6 or 7	1883396
9	5 and 8	12731	9	exp *antihypertensive agent/	314838
10	exp Antihypertensive Agents/	263090	10	(antihypertensive* or anti-hypertensive* or pharmacolog* or therap* or treatment? or intervention?).ti.	2721150
11	(antihypertensive* or anti-hypertensive* or pharmacolog* or therap* or treatment? or intervention?).ti.	2244351	11	((antihypertensive* or anti-hypertensive* or pharmacolog*) adj3 (therap* or treatment? or intervention?)).ti,ab.	137399
12	((antihypertensive* or anti-hypertensive* or pharmacolog*) adj3 (therap* or treatment? or intervention?)).ti,ab.	86059	12	exp diet therapy/	370413
13	exp Diet Therapy/	58211	13	exp kinesiotherapy/	86354
14	exp Exercise Therapy/	56656	14	lifestyle modification/	43194
15	Weight Loss/	39435	15	weight loss program/	2690
16	Weight Reduction Programs/	2575	16	weight reduction/	162011
17	((nonpharma* or non-pharma* or diet* or nutrition* or exercise* or physical activity or salt or sodium or lifestyle or life-style) adj3 (therap* or treatment? or intervention? or program* or modif*)).ti,ab.	173787	17	sodium restriction/	9671
18	((weight loss or weight reduction or weight management) adj3 (intervention? or program*)).ti,ab.	8746	18	((nonpharma* or non-pharma* or diet* or nutrition* or exercise* or physical activity or salt or sodium or lifestyle or life-style) adj3 (therap* or treatment? or intervention? or program* or modif*)).ti,ab.	236431
19	((sodium or salt) adj2 reduc*).ti,ab.	8351	19	((weight loss or weight reduction or weight management) adj3 (intervention? or program*)).ti,ab.	12692
20	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19	2728893	20	((sodium or salt) adj2 reduc*).ti,ab.	10108

21	9 and 20	2112	21	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20	3703142
22	limit 21 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")	49	22	5 and 8 and 21	3134
23	limit 21 to "therapy (maximizes sensitivity)"	1413	23	limit 22 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")	76
24	(comment or editorial or letter or review).pt. or case report.ti,ab.	5136806	24	limit 22 to "therapy (maximizes sensitivity)"	920
25	23 not 24	1007	25	(conference* or editorial* or letter or note or review).pt. or case report.ti,ab.	1.1E+07
26	22 or 25	1047	26	24 not 25	524
27	limit 26 to (english language and yr="2017 -Current")	179	27	23 or 26	579
			28	limit 27 to (english language and yr="2017 -Current")	165
Medline search screening			**Embase search screening**		
1	*hypertension/ or *prehypertension/	178267	1	*hypertension/ or *prehypertension/	207611
2	*blood pressure/	84543	2	*blood pressure/	77712
3	(hypertensi* or pre-hypertensi* or prehypertensi*).ti.	206076	3	(hypertensi* or pre-hypertensi* or prehypertensi*).ti.	258294
4	(blood pressure or bp).ti.	67787	4	(blood pressure or bp).ti.	87311
5	1 or 2 or 3 or 4	326102	5	1 or 2 or 3 or 4	413706
6	(adolescent/ or child/) and (child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti,ab.	1180447	6	(adolescent/ or child/) and (child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti,ab.	1544999
7	(child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti.	1176885	7	(child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people).ti.	1399582
8	6 or 7	1495277	8	6 or 7	1883396
9	Mass Screening/	110031	9	exp screening/ or exp screening test/ or diagnostic test/	809971
10	exp blood pressure determination/	41922	10	*blood pressure measurement/	8503
11	Diagnostic Tests, Routine/	13966	11	(screen* or test*).ti.	715153
12	(screen* or test*).ti.	619042	12	((blood pressure or bp) adj5 (screen* or test* or measur* or monitor*)).ti,ab.	89380
13	((blood pressure or bp) adj5 (screen* or test* or measur* or monitor*)).ti,ab.	58209	13	((hypertens* or prehypertens* or pre-hypertens*) adj5 (screen* or test* or measur* or monitor*)).ti,ab.	22116
14	((hypertens* or prehypertens* or pre-hypertens*) adj5 (screen* or test* or measur* or monitor*)).ti,ab.	14672	14	((oscillomet* or auscultat*) adj3 (device? or machine?)).ti,ab.	1549
15	((oscillomet* or auscultat*) adj3 (device? or machine?)).ti,ab.	882	15	9 or 10 or 11 or 12 or 13 or 14	1409331
16	9 or 10 or 11 or 12 or 13 or 14 or 15	762987	16	*diagnosis/ or diagnostic accuracy/ or diagnostic test accuracy study/	438645
17	*diagnosis/	13377	17	sensitivity and specificity/	408160
18	exp "Sensitivity and Specificity"/	619534	18	predictive value/	200322
19	diagnos*.ti.	632193	19	diagnos*.ti.	730376
20	(sensitivity or specificity or predict* or npv or ppv or accura* or valid*).ti,ab.	3830965	20	(sensitivity or specificity or predict* or npv or ppv or accura* or valid*).ti,ab.	4984344

21	17 or 18 or 19 or 20	4537340	21	16 or 17 or 18 or 19 or 20	5699910
22	5 and 8 and 16	4116	22	5 and 8 and 15	5312
23	limit 22 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")	63	23	limit 22 to (meta analysis or "systematic review" or "reviews (maximizes specificity)")	81
24	((child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people) and (blood pressure or bp or hypertens* or prehypertens* or pre-hypertens*) and (screen* or diagnos* or test*)).ti.	517	24	((child* or schoolchild* or boys or girls or pediatric* or paediatric* or adolescen* or teen* or youth? or young people) and (blood pressure or bp or hypertens* or prehypertens* or pre-hypertens*) and (screen* or diagnos* or test*)).ti.	677
25	5 and 8 and 16 and 21	1160	25	5 and 8 and 15 and 21	1637
26	24 or 25	1509	26	24 or 25	2049
27	(comment or editorial or letter or review).pt. or case report.ti,ab.	5136806	27	(conference* or editorial or letter or note or review).pt. or case report.ti,ab.	10884583
28	26 not 27	1288	28	26 not 27	1210
29	23 or 28	1343	29	23 or 28	1282
30	limit 29 to (english language and yr="2017 -Current")	384	30	limit 29 to (english language and yr="2017 -Current")	367

Cochrane search	
#1	MeSH descriptor: [Hypertension] this term only
#2	MeSH descriptor: [Blood Pressure] explode all trees
#3	(hypertens* OR prehypertens* OR pre-hypertens* OR "blood pressure"):ti
#4	#1 or #2 or #3
#5	(child* OR schoolchild* OR boys OR girls OR pediatric* OR paediatric* OR adolescen* OR teen* OR youth* OR "young people"):ti
#6	MeSH descriptor: [Adolescent] explode all trees
#7	MeSH descriptor: [Child] explode all trees
#8	#5 or #6 or #7
#9	#4 and #8

Results by database

Medline	**1327**
Embase	**1308**
Cochrane Library	**487**
Total	**3122**

After the exclusion of duplicates, 1,859 references remained.

Inclusions and exclusions

Publications not in the English language or published prior to October 2017, case reports, conference abstracts, trial protocols and comment/editorials/letters were excluded.

Eligibility for inclusion in the map

Question 1

- population: children and young people (3 to 18 years of age) with primary hypertension
- intervention: N/A
- comparator: young people (3 to 18 years of age) with normal blood pressure or N/A for non-comparative studies
- outcomes: studies reporting measures of association (eg odds ratio, risk ratio):
    - end organ damage (such as ventricular hypertrophy and thickening of the carotid vessel wall)
    - cognitive changes
    - retinal vascular changes
    - cardiovascular disease
- study design: longitudinal cohort epidemiology, case control studies and case series. Although studies that look at UK populations should be prioritised, other studies carried out in Western populations that are analogous to the UK cohort can also be included

Question 2

- population: children and young people (3 to 18 years of age)
- index test: blood pressure measurements using auscultatory or oscillometric devices performed by a health care professional
- reference standard: ambulatory monitoring
- target condition: primary hypertension
- outcomes: measure of predicative validity of screening tests (eg positive and negative predictive values, positive and negative likelihood ratios, sensitivity, specificity)
- study design: randomised controlled trials, observational studies with a comparison group (eg comparative cohort, cross-sectional and case control studies), and systematic reviews. Although studies that look at UK populations should be prioritised, other studies carried out in Western populations that are analogous to the UK cohort can also be included. Case reports, case series, reviews and non-peer reviewed literature should be excluded

Question 3

- population: screen detected or clinically diagnosed children and young people (3 to 18 years of age) with primary hypertension
- intervention:
    - pharmacological interventions
    - non-pharmacological interventions (diet, exercise etc)
    - combination of the above
- comparator: no screening and treatment or no screening and placebo. Clinically diagnosed and no treatment or placebo.

- outcomes:
    - blood pressure
    - retinal vascular changes
    - end organ damage (such as ventricular hypertrophy and thickening of the carotid vessel wall)
    - cognitive changes
    - cardiovascular disease
- study design: randomised controlled trials, observational studies with a comparison group (eg comparative cohort, cross-sectional and case control studies), and systematic reviews. Although studies that look at UK populations should be prioritised, other studies carried out in Western populations that are analogous to the UK cohort can also be included. Case reports, case series, reviews and non-peer reviewed literature should be excluded

Question 4

- population: children and young people (3 to 18 years of age)
- intervention: screening followed by:
    - pharmacological interventions (antihypertensive medications which are currently approved for use in children and young people)
    - non-pharmacological interventions (diet, exercise etc)
    - combination of the above
- comparator: clinically diagnosis followed by:
    - pharmacological interventions (antihypertensive medications which are currently approved for use in children and young people)
    - non-pharmacological interventions (diet, exercise etc)
    - combination of the above
- outcomes:
    - blood pressure normalisation
    - retinal vascular changes
    - end organ damage (such as ventricular hypertrophy and thickening of the carotid vessel wall)
    - cognitive changes
    - cardiovascular disease
    - overdiagnosis and overtreatment
- study design: randomised controlled trials, controlled clinical trials, observational studies with a comparison group (eg comparative cohort, cross-sectional and case control studies), and systematic reviews. Although studies that look at UK populations should be prioritised, other studies carried out in Western populations that are analogous to the UK cohort can also be included. Case reports, case series, reviews and non-peer reviewed literature should be excluded

Appendix 2 – Abstract reporting tables

Question 1 – What is the association between primary hypertension in children and young people and the risk of adverse outcomes?

Systematic reviews

TITLE	
Citation	Gartlehner *et al.* (2020) [6]
BACKGROUND	
Study type	Systematic review
Objectives	To update the evidence on screening and treatment of hypertension in childhood and adolescence for the US Preventive Services Task Force
Components of the study	For the key question on the association between high blood pressure in children and adolescents and adverse outcomes in adults: Population – children and adolescents with elevated blood pressure or hypertension Intervention – N/A Comparator – N/A Study design – longitudinal cohort studies that assess the association of elevated blood pressure during childhood and adult hypertension or other intermediate outcomes during adulthood Search date – September 2019, with surveillance for relevant studies up to October 2020 [full-text checked]
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (carotid intima-media thickness, left ventricular hypertrophy) • cardiovascular disease Outcomes specified by the commissioning document that are not reported include cognitive changes and retinal vascular changes [full-text checked]

Conclusions	The authors concluded that there is a significant association between childhood hypertension and abnormal blood pressure in adults. The authors also reported statistically significant associations between abnormal childhood blood pressure and carotid intima-media thickness, left ventricular hypertrophy and cardiovascular disease in adults. [full-text checked]

TITLE	
Citation	Goulas *et al.* (2021) [7]
BACKGROUND	
Study type	Systematic review and meta-analysis
Objectives	To compare American and European guidelines for the diagnosis of hypertension and the detection of left ventricular hypertrophy in children and adolescents
Components of the study	Population – children and adolescents assessed for hypertension Intervention – N/A Comparator – N/A Study design – observational studies Search date – not stated in abstract or full text [full-text checked]
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage Outcomes specified by the commissioning document that are not reported include cognitive changes, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that left ventricular hypertrophy is associated with hypertension with similar associations using the different guidelines

TITLE	
Citation	Schuh *et al.* (2017) [9]
BACKGROUND	
Study type	Systematic review
Objectives	To estimate the prevalence of ophthalmological alterations in children and adolescents who are overweight and/or have signs of arterial hypertension

Components of the study	Population – children and/or adolescents who were overweight, obese or had signs of arterial hypertension Intervention – N/A Comparator – healthy children Study design – observational studies and baseline descriptions of RCTs that measured ophthalmological alterations Search date – May 2017 [full-text checked]
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • retinal vascular changes Outcomes specified by the commissioning document that are not reported include end organ damage, cognitive changes and cardiovascular disease
Conclusions	The authors concluded that obesity and signs of arterial hypertension show associations with ophthalmological alterations, especially with retinal vessel diameter

TITLE	
Citation	Yang *et al.* (2020) [8]
BACKGROUND	
Study type	Systematic review and meta-analysis
Objectives	To assess the strength of the association between elevated blood pressure in childhood or adolescence and cardiovascular morbidity and mortality in adulthood
Components of the study	Population – children and adolescents with elevated blood pressure Intervention – N/A Comparator – N/A Study design – prospective cohort studies on the association between blood pressure status in childhood or adolescence and intermediate markers or hard outcomes of cardiovascular disease in adults Search date – August 2019
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (carotid intima-media thickness, left ventricular hypertrophy, high pulse wave velocity) • cardiovascular disease

	Outcomes specified by the commissioning document that are not reported include cognitive changes and retinal vascular changes
Conclusions	The authors concluded that elevated blood pressure in childhood or adolescence was significantly associated with high carotid intima-media thickness, left ventricular hypertrophy, high pulse wave velocity in adults. The authors also reported evidence of associations with cardiovascular disease and mortality in adulthood

Individual studies

TITLE	
Citation	Abdul-Raheem *et al.* (2021) [10]
BACKGROUND	
Study type	Case series
Objectives	To assess prevalence of and factors associated with left ventricular diastolic dysfunction in youth with obesity and elevated blood pressure
Components of the study	Population – children and adolescents with overweight/obesity and elevated blood pressure Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (left ventricular diastolic dysfunction) Outcomes specified by the commissioning document that are not reported include cognitive changes, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that elevated diastolic blood pressure was an independent predictor of left ventricular diastolic dysfunction

TITLE	
Citation	Campbell *et al.* (2021) [11]
BACKGROUND	
Study type	Case series
Objectives	To explore the impact of reclassifying hypertension in adolescents aged 13 to 17 years using adult blood pressure norms and the association with left ventricular hypertrophy

Components of the study	Population – adolescents evaluated for hypertension Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (left ventricular hypertrophy) Outcomes specified by the commissioning document that are not reported include cognitive changes, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that significant reclassification of hypertension occurs when adult norms are applied to patients aged 13 to 17 years. Hypertension was significantly associated with left ventricular hypertrophy when using adult blood pressure norms

TITLE	
Citation	Chrysaidou *et al.* (2020) [15]
BACKGROUND	
Study type	Case series
Objectives	To examine the association between hypertension and overweight on executive function in children and adolescents
Components of the study	Population – children and adolescents referred to an outpatient hypertension clinic Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • cognitive changes (executive function) Outcomes specified by the commissioning document that are not reported include end organ damage, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that elevated night-time systolic blood pressure was associated with poor performance in domains of executive function in children and adolescents. The association remained significantly significant after adjustment for body mass index and executive function

TITLE	
Citation	Dereli *et al.* (2020) [20]
BACKGROUND	

Study type	Case control study
Objectives	To compare subclinical retinal microvascular alterations in children with hypertension and healthy matched controls
Components of the study	Population – children and adolescents with hypertension Intervention – N/A Comparator – matched healthy controls
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • retinal vascular changes Outcomes specified by the commissioning document that are not reported include end organ damage, cognitive changes and cardiovascular disease
Conclusions	The authors concluded that although there was no evidence of hypertensive retinopathy, subthreshold microvascular alterations were found in the retinal circulation of children with hypertension

TITLE	
Citation	George *et al.* (2021) [16]
BACKGROUND	
Study type	Longitudinal study
Objectives	To examine cardiovascular risk factors in adolescence, young adulthood and midlife with late-life cognition
Components of the study	Population – African American adults aged ≥50 years who received multiphasic health check-ups during 1964 and 1985 Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • cognitive changes (executive function, verbal episodic memory, semantic memory) Outcomes specified by the commissioning document that are not reported include end organ damage, retinal vascular changes, and cardiovascular disease
Conclusions	The authors concluded that adolescents with hypertension had lower late-life executive function compared to normotensive adolescents

TITLE	
Citation	Kaplinski *et al.* (2021) [12]
BACKGROUND	
Study type	Case series
Objectives	To explore whether children with hypertension would have left ventricular hypertrophy and abnormal left ventricular global longitudinal strain and whether these values would differ by weight, race and hypertension treatment
Components of the study	Population – children and adolescents in a hypertension programme Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (left ventricular hypertrophy) • cardiovascular disease Outcomes specified by the commissioning document that are not reported include cognitive changes and retinal vascular changes
Conclusions	The authors concluded that left ventricular mass index was higher in hypertensive, obese and African American patients. However, in the multivariate analysis, obesity was the only independent risk factor for an abnormal left ventricular mass index

TITLE	
Citation	Kupferman *et al.* (2018) [17]
BACKGROUND	
Study type	Case control study
Objectives	To examine the association between office and ambulatory blood pressure monitoring and neurocognitive test performance in children with primary hypertension
Components of the study	Population – children and adolescents with untreated primary hypertension Intervention – N/A Comparator – matched normotensive controls
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • cognitive changes (executive function)

	Outcomes specified by the commissioning document that are not reported include end organ damage, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that ambulatory blood pressure monitoring was significantly associated with neurocognitive test scores and is superior to office blood pressure in determining neurocognitive test performance in children and adolescents with hypertension

TITLE	
Citation	Liu *et al.* (2021) [14]
BACKGROUND	
Study type	Case control study
Objectives	To examine changes in cardiovascular structure and function in children with primary hypertension compared to healthy controls
Components of the study	Population – children and adolescents with simple primary hypertension or hypertension with co-existing obesity Intervention – N/A Comparator – healthy children
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (cardiac) Outcomes specified by the commissioning document that are not reported include cognitive changes, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that children and adolescents with primary hypertension demonstrate target organ damage in the heart and blood vessels

TITLE	
Citation	Lona *et al.* (2020) [18]
BACKGROUND	
Study type	Longitudinal study
Objectives	To examine the association between retinal vessel diameters and blood pressure in young children
Components of the study	Population – children screened for blood pressure and retinal vessel diameters with repeat testing 4 years later Intervention – N/A Comparator – N/A
OUTCOMES	

Outcomes reported	Outcomes specified by the commissioning document that are reported: • retinal vascular changes Outcomes specified by the commissioning document that are not reported include end organ damage, cognitive changes and cardiovascular disease
Conclusions	The authors concluded that children with increased blood pressure at baseline developed narrower central retinal arteriolar diameters at follow-up

TITLE	
Citation	Rogowska *et al.* (2021) [19]
BACKGROUND	
Study type	Case series
Objectives	To assess the relationship between hypertensive target organ damage and vessel density, foveal thickness, thickness of retinal nerve fibre layer, ganglion cell complex and foveal avascular zone in hypertensive children
Components of the study	Population – children and adolescents with arterial hypertension Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • retinal vascular changes Outcomes specified by the commissioning document that are not reported include end organ damage, cognitive changes, and cardiovascular disease
Conclusions	The authors concluded that hypertensive children with increased carotid intima-media thickness had significantly decreased retinal vessel density and increased foveal avascular zone in comparison to patients with normal carotid intima-media thickness. They also reported that subclinical hypertensive arterial injury was associated with a significant decrease in retinal thickness [full text checked]

TITLE	
Citation	Truong *et al.* (2021) [13]
BACKGROUND	

Study type	Case series
Objectives	To review whether children referred for primary hypertension evaluation were more likely to complete an echocardiogram and more likely to have left ventricular hypertrophy
Components of the study	Population – children and adolescents referred for primary hypertension evaluation Intervention – N/A Comparator – N/A
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • end organ damage (left ventricular hypertrophy) Outcomes specified by the commissioning document that are not reported include cognitive changes, retinal vascular changes and cardiovascular disease
Conclusions	The authors concluded that high body mass index was associated with left ventricular hypertrophy but not blood pressure severity or anti-hypertensive medication

Question 2 – What is the diagnostic accuracy of screening tests for primary hypertension in children and young people?

TITLE	
Citation	Gartlehner *et al.* (2020) [6]
BACKGROUND	
Study type	Systematic review
Objectives	To update the evidence on screening and treatment of hypertension in childhood and adolescence for the US Preventive Services Task Force
Components of the study	For the key question on the diagnostic accuracy of screening tests for high blood pressure in children and adolescents: Population – asymptomatic children and adolescents Index test – studies reporting diagnostic test accuracy of blood pressure measurements Reference standard – confirmed clinical diagnosis (after diagnostic workup) of abnormal blood pressure Search date – September 2019, with surveillance for relevant studies up to October 2020 [full-text checked]

OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • sensitivity • specificity Outcomes specified by the commissioning document that are not reported include positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio
Conclusions	The authors concluded that the evidence is inconclusive about whether the diagnostic accuracy of blood pressure measurements is adequate for screening asymptomatic children and adolescents in primary care

TITLE	
Citation	Hanevold *et al.* (2020) [23]
BACKGROUND	
Study type	Case series
Objectives	To determine the level of agreement between automated office blood pressure, auscultated or manual office blood pressure and 24-hour ambulatory blood pressure and to explore the ability of automated office blood pressure and manual office blood pressure to correctly identify daytime ambulatory hypertension in children
Components of the study	Population – children evaluated at a hypertension clinic Index test – automated office blood pressure assessed by an oscillometric device and auscultated or manual office blood pressure Reference standard – 24-hour ambulatory blood pressure monitoring
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • sensitivity • specificity Outcomes specified by the commissioning document that are not reported include positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio

Conclusions	The authors concluded that neither ambulatory blood pressure nor manual office blood pressure confirm or exclude daytime ambulatory hypertension with confidence

Question 3 – What is the effectiveness of pharmacological and non-pharmacological and/or combination interventions for preventing hypertension in children and young people and its effectiveness in preventing long-term effect?

TITLE	
Citation	Gartlehner *et al.* (2020) [6]
BACKGROUND	
Study type	Systematic review
Objectives	To update the evidence on screening and treatment of hypertension in childhood and adolescence for the US Preventive Services Task Force
Components of the study	For the key questions on the treatment of high blood pressure in children and adolescents: Population – children and adolescents with elevated blood pressure or hypertension Intervention – pharmacological, non-pharmacological and combination interventions Comparator – any Study design – RCTs and large, controlled, observational studies (sample size >1,000) Search date – September 2019, with surveillance for relevant studies up to October 2020 [full-text checked]
OUTCOMES	
Outcomes reported	Outcomes specified by the commissioning document that are reported: • blood pressure Outcomes specified by the commissioning document that are not reported include retinal vascular changes, end organ damage, cognitive changes and cardiovascular disease [full-text checked]
Conclusions	The authors concluded that no studies assessed the effect of treating childhood hypertension on outcomes in adulthood. Evidence from RCTs reported reductions in blood pressure

	with pharmacological interventions, exercise, dietary approaches and a combination of pharmacological treatment and lifestyle interventions

Question 4 – Is there an effective screening strategy for primary hypertension in children and young people to prevent hypertensive disorders in later life?

No studies were included for this question.

References

Introduction

1. UK National Screening Committee. Commissioning document: screening for primary hypertension in children and young people (3 to 18 years of age). 2021.
2. Solutions for Public Health. Screening to prevent adverse outcomes from primary hypertension in children and young people: external review against programme appraisal criteria for the UK National Screening Committee. 2018.
3. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics. 2017;140(3).
4. Force USPST, Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, et al. Screening for high blood pressure in children and adolescents: US Preventive Services Task Force Recommendation Statement. JAMA. 2020;324(18):1878-83.
5. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. Journal of Hypertension. 2016;34(10):1887-1920.

Question 1 (Association with risk of adverse outcomes)

6. Gartlehner G, Vander Schaaf EB, Orr C, Kennedy SM, Clark R, Viswanathan M. Screening for hypertension in children and adolescents: Updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2020;324(18):1884-95.
7. Goulas I, Farmakis I, Doundoulakis I, Antza C, Kollios K, Economou M, et al. Comparison of the 2017 American Academy of Pediatrics with the fourth report and the 2016 European Society of Hypertension guidelines for the diagnosis of hypertension and the detection of left ventricular hypertrophy in children and adolescents: a systematic review and meta-analysis. Journal of Hypertension. 2021;07:07.
8. Yang L, Magnussen CG, Yang L, Bovet P, Xi B. Elevated blood pressure in childhood or adolescence and cardiovascular outcomes in adulthood: A systematic review. Hypertension. 2020;75(4):948-55.
9. Schuh DS, Piccoli AB, Paiani RL, Maciel CR, Pellanda LC, Vilela MA. Ocular signs related to overweight and arterial hypertension in children: A systematic review. The Open Ophthalmology Journal. 2017;11:273-85.
10. Abdul-Raheem JN, Binka E, Roem J, Turer CB, Urbina EM, Brady TM. Left ventricular diastolic dysfunction among youth with obesity and history of elevated blood pressure. Journal of Pediatrics. 2021;235:130-7.
11. Campbell JF, Shah S, Srivaths P, Acosta AA. Reclassification of adolescent hypertension by ambulatory blood pressure monitoring using adult norms and association with left ventricular hypertrophy. Journal of Clinical Hypertension. 2021;23(2):265-71.

12. Kaplinski M, Griffis H, Liu F, Tinker C, Laney NC, Mendoza M, et al. Left ventricular measurements and strain in pediatric patients evaluated for systemic hypertension and the effect of adequate anti-hypertensive treatment. Pediatric Cardiology. 2021;23:23.
13. Truong G, Kamal S, Samuels JA, Bell CS. Prognostic value of ambulatory blood pressure and clinical use of echocardiography to detect left ventricular hypertrophy in children evaluated for primary hypertension. Pediatric Nephrology. 2021;36(4):961-7.
14. Liu W, Hou C, Hou M, Xu QQ, Wang H, Gu PP, et al. Ultrasonography to detect cardiovascular damage in children with essential hypertension. Cardiovascular Ultrasound. 2021;19(1):26.
15. Chrysaidou K, Kotsis V, Chainoglou A, Tzovaras F, Gidaris D, Chatzipapa N, et al. Impact of ambulatory SBP and overweight on executive function performance in children and adolescents. Journal of Hypertension. 2020;38(6):1123-30.
16. George KM, Gilsanz P, Peterson RL, Barnes LL, DeCarli CS, Mayeda ER, et al. Impact of cardiovascular risk factors in adolescence, young adulthood, and midlife on late-life cognition: Study of healthy aging in African Americans. The Journals of Gerontology. 2021;Series A, Biological Sciences and Medical Sciences. 76(9):1692-8.
17. Kupferman JC, Batisky DL, Samuels J, Adams HR, Hooper SR, Wang H, et al. Ambulatory blood pressure monitoring and neurocognitive function in children with primary hypertension. Pediatric Nephrology. 2018;33(10):1765-71.
18. Lona G, Endes K, Kochli S, Infanger D, Zahner L, Hanssen H. Retinal vessel diameters and blood pressure progression in children. Hypertension. 2020;76(2):450-7.
19. Rogowska A, Obrycki L, Kulaga Z, Kowalewska C, Litwin M. Remodeling of retinal microcirculation is associated with subclinical arterial injury in hypertensive children. Hypertension. 2021;77(4):1203-11.
20. Dereli Can G, Korkmaz MF, Can ME. Subclinical retinal microvascular alterations assessed by optical coherence tomography angiography in children with systemic hypertension. Journal of Aapos: American Association for Pediatric Ophthalmology & Strabismus. 2020;24(3):147.e1-.e6.
21. Yang L, Sun J, Zhao M, Liang Y, Bovet P, Xi B. Elevated blood pressure in childhood and hypertension risk in adulthood: a systematic review and meta-analysis. Journal of Hypertension. 2020;38(12):2346-55.

Question 2 (Screening tests)

6. Gartlehner G, Vander Schaaf EB, Orr C, Kennedy SM, Clark R, Viswanathan M. Screening for hypertension in children and adolescents: Updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2020;324(18):1884-95.
22. Hamdani G, Flynn JT, Becker RC, Daniels SR, Falkner B, Hanevold CD, et al. Prediction of ambulatory hypertension based on clinic blood pressure percentile in adolescents. Hypertension. 2018;72(4):955-61.
23. Hanevold CD, Faino AV, Flynn JT. Use of automated office blood pressure measurement in the evaluation of elevated blood pressures in children and adolescents. Journal of Pediatrics. 2020;227:204-11.e6.

Question 3 (Treatment)

6. Gartlehner G, Vander Schaaf EB, Orr C, Kennedy SM, Clark R, Viswanathan M. Screening for hypertension in children and adolescents: Updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2020;324(18):1884-95.
24. Burrello J, Erhardt EM, Saint-Hilary G, Veglio F, Rabbia F, Mulatero P, et al. Pharmacological treatment of arterial hypertension in children and adolescents: A network meta-analysis. Hypertension. 2018;72(2):306-13.
25. 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. Clinical & Experimental Hypertension (New York). 2017;39(6):546-52.

Question 4 (Screening)

6. Gartlehner G, Vander Schaaf EB, Orr C, Kennedy SM, Clark R, Viswanathan M. Screening for hypertension in children and adolescents: Updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2020;324(18):1884-95.