

## 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

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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 <u>population screening</u> and supports implementation of screening programmes. Conditions are reviewed against <u>evidence review criteria</u> according to the UK NSC's <u>evidence review process</u>.

Read a complete list of UK NSC recommendations.

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## 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 nonpharmacological 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 nonpharmacological 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<sup>\*</sup> 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 metaanalysis. 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

<sup>\*</sup> 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, antihypertensive 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 carotidfemoral 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 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 90<sup>th</sup> 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  $\geq$ 95<sup>th</sup> percentile for sex and height percentiles for patients aged less than 13 years and by a blood pressure of  $\geq$ 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 nonpharmacological 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, nonpharmacological 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  $15 \pm 1$  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 |  | Emba    | ase search adverse outcomes |  |         |
|---------------------------------|--|---------|-----------------------------|--|---------|
| 1                               | *hypertension/ or *prehypertension/  | 178267  | 1                           | *hypertension/ or<br>*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<br>schoolchild* or boys or girls or<br>pediatric* or paediatric* or adolescen*<br>or teen* or youth? or young<br>people).ti,ab. | 1180447 | 6                           | (adolescent/ or child/) and (child*<br>or schoolchild* or boys or girls or<br>pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti,ab. | 1544999 |
| 7                               | (child* or schoolchild* or boys or girls<br>or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti.                                   | 1176885 | 7                           | (child* or schoolchild* or boys or<br>girls or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>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<br>injur* or failure)).ti,ab.   | 49906   | 10                          | organ injury/  | 8960    |
| 11                              | hypertrophy, left ventricular/ or<br>hypertrophy, right ventricular/   | 16443   | 11                          | ((organ or organs) adj3 (damag* or injur* or failure)).ti,ab.  | 78070   |
| 12                              | ((heart or cardi* or ventric*) adj3<br>hypertroph*).ti,ab.   | 55259   | 12                          | exp heart ventricle hypertrophy/   | 70376   |
| 13                              | arteriosclerosis/  | 56680   | 13                          | ((heart or cardi* or ventric*) adj3<br>hypertroph*).ti,ab.   | 80403   |
| 14                              | exp atherosclerosis/   | 48421   | 14                          | arterial wall thickness/   | 23113   |
| 15                              | (atheroscleros?s or arterioscleros?s<br>or (arterial adj3 (thickness or<br>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<br>arterioscleros?s or (arterial adj3<br>(thickness or diameter? or<br>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*<br>or damag* or injur* or<br>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<br>(chang* or damag* or injur* or<br>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*<br>or deteriorat* or defect* or impair* or<br>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<br>(chang* or deteriorat* or defect* or<br>impair* or assess*)).ti,ab.   | 175170   |
| 26 | heart diseases/ or exp myocardial<br>ischemia/   | 511988  | 26 | *cardiovascular disease/  | 101025   |
| 27 | (((cardiovascular or cardio-vascular<br>or coronary or heart or myocardi* or<br>cardi* or isch?mic or cerebrovascular<br>or cerebro-vascular) adj (disease? or<br>disorder? or health)) or cvd or<br>chd).ti,ab. | 430767  | 27 | *cerebrovascular disease/ or exp<br>brain infarction/ or exp<br>cerebrovascular accident/   | 330300   |
| 28 | ((cardiovascular or cardio-vascular or<br>coronary or heart or myocardi* or<br>cardi* or isch?mic or cerebrovascular<br>or cerebro-vascular) adj risk).ti,ab.  | 87417   | 28 | exp ischemic heart disease/   | 704565   |
| 29 | (myocardi* adj (infarct* or<br>isch?emi*)).ti,ab.  | 231903  | 29 | (((cardiovascular or cardio-<br>vascular or coronary or heart or<br>myocardi* or cardi* or isch?mic or<br>cerebrovascular or cerebro-<br>vascular) adj (disease? or<br>disorder? or health)) or cvd or<br>chd).ti,ab. | 613254   |
| 30 | angina.ti,ab.  | 54331   | 30 | ((cardiovascular or cardio-vascular<br>or coronary or heart or myocardi*<br>or cardi* or isch?mic or<br>cerebrovascular or cerebro-<br>vascular) adj risk).ti,ab.   | 138682   |
| 31 | acute coronary syndrome.ti,ab.   | 24088   | 31 | (myocardi* adj (infarct* or<br>isch?emi*)).ti,ab.   | 328506   |
| 32 | ((adverse or longterm or long-term)<br>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<br>or 17 or 18 or 19 or 20 or 21 or 22 or<br>23 or 24 or 25 or 26 or 27 or 28 or 29<br>or 30 or 31 or 32 or 33  | 2046383 | 34 | ((adverse or longterm or long-<br>term) adj3 outcome?).ti,ab.   | 236599   |
| 35 | 9 and 34   | 3054    | 35 | outcome?.ti.  | 589464   |
| 36 | limit 35 to (meta analysis or<br>"systematic review" or "reviews<br>(maximizes specificity)")  | 63      | 36 | 10 or 11 or 12 or 13 or 14 or 15 or<br>16 or 17 or 18 or 19 or 20 or 21 or<br>22 or 23 or 24 or 25 or 26 or 27 or<br>28 or 29 or 30 or 31 or 32 or 33 or<br>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<br>"systematic review" or "reviews<br>(maximizes specificity)")   | 97       |
| 39 | 36 or 38   | 2568    | 39 | (conference* or editorial or letter or<br>note or review).pt. or case<br>report.ti,ab.  | 10884583 |

| 40  | limit 39 to (english language and<br>vr="2017 -Current")  | 764     | 40                      | 37 not 39  | 2549    |  |
|-----|---|---------|-------------------------|--|---------|--|
|     |   |         | 41                      | 38 or 40   | 2625    |  |
|     |   |         | 42                      | limit 41 to (english language and  | 776     |  |
|     |   |         |                         | yr="2017 -Current")  |         |  |
| Med | dline search therapies  |         | Embase search therapies |  |         |  |
| 1   | *hypertension/ or *prehypertension/   | 178267  | 1                       | *hypertension/ or<br>*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<br>schoolchild* or boys or girls or<br>pediatric* or paediatric* or adolescen*<br>or teen* or youth? or young<br>people).ti,ab.  | 1180447 | 6                       | (adolescent/ or child/) and (child*<br>or schoolchild* or boys or girls or<br>pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti,ab.   | 1544999 |  |
| 7   | (child* or schoolchild* or boys or girls<br>or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti.  | 1176885 | 7                       | (child* or schoolchild* or boys or<br>girls or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>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-<br>hypertensive* or pharmacolog* or<br>therap* or treatment? or<br>intervention?).ti.  | 2721150 |  |
| 11  | (antihypertensive* or anti-<br>hypertensive* or pharmacolog* or<br>therap* or treatment? or<br>intervention?).ti.   | 2244351 | 11                      | ((antihypertensive* or anti-<br>hypertensive* or pharmacolog*)<br>adj3 (therap* or treatment? or<br>intervention?)).ti,ab.   | 137399  |  |
| 12  | ((antihypertensive* or anti-<br>hypertensive* or pharmacolog*) adj3<br>(therap* or treatment? or<br>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*<br>or nutrition* or exercise* or physical<br>activity or salt or sodium or lifestyle or<br>life-style) adj3 (therap* or treatment?<br>or intervention? or program* or<br>modif*)).ti,ab. | 173787  | 17                      | sodium restriction/  | 9671    |  |
| 18  | ((weight loss or weight reduction or<br>weight management) adj3<br>(intervention? or program*)).ti,ab.  | 8746    | 18                      | ((nonpharma* or non-pharma* or<br>diet* or nutrition* or exercise* or<br>physical activity or salt or sodium<br>or lifestyle or life-style) adj3<br>(therap* or treatment? or<br>intervention? or program* or<br>modif*)).ti,ab. | 236431  |  |
| 19  | ((sodium or salt) adj2 reduc*).ti,ab.   | 8351    | 19                      | ((weight loss or weight reduction<br>or weight management) adj3<br>(intervention? or program*)).ti,ab.   | 12692   |  |
| 20  | 10 or 11 or 12 or 13 or 14 or 15 or 16<br>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<br>15 or 16 or 17 or 18 or 19 or 20   | 3703142 |
|-----|--|---------|------|--|---------|
| 22  | limit 21 to (meta analysis or<br>"systematic review" or "reviews<br>(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<br>"systematic review" or "reviews<br>(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<br>or note or review).pt. or case<br>report.ti,ab.  | 1.1E+07 |
| 26  | 22 or 25   | 1047    | 26   | 24 not 25  | 524     |
| 27  | limit 26 to (english language and<br>yr="2017 -Current")   | 179     | 27   | 23 or 26   | 579     |
|     |  |         | 28   | limit 27 to (english language and<br>yr="2017 -Current")   | 165     |
| Med | dline search screening   |         | Emba | ase search screening   |         |
| 1   | *hypertension/ or *prehypertension/  | 178267  | 1    | *hypertension/ or<br>*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<br>schoolchild* or boys or girls or<br>pediatric* or paediatric* or adolescen*<br>or teen* or youth? or young<br>people).ti.ab. | 1180447 | 6    | (adolescent/ or child/) and (child*<br>or schoolchild* or boys or girls or<br>pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti.ab. | 1544999 |
| 7   | (child* or schoolchild* or boys or girls<br>or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti.                                   | 1176885 | 7    | (child* or schoolchild* or boys or<br>girls or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people).ti.                                   | 1399582 |
| 8   | 6 or 7   | 1495277 | 8    | 6 or 7   | 1883396 |
| 9   | Mass Screening/  | 110031  | 9    | exp screening/ or exp screening<br>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<br>(screen* or test* or measur* or<br>monitor*)).ti,ab.   | 89380   |
| 13  | ((blood pressure or bp) adj5 (screen*<br>or test* or measur* or monitor*)).ti,ab.  | 58209   | 13   | ((hypertens* or prehypertens* or<br>pre-hypertens*) adj5 (screen* or<br>test* or measur* or monitor*)).ti,ab.  | 22116   |
| 14  | ((hypertens* or prehypertens* or pre-<br>hypertens*) adj5 (screen* or test* or<br>measur* or monitor*)).ti,ab.   | 14672   | 14   | ((oscillomet* or auscultat*) adj3<br>(device? or machine?)).ti,ab.   | 1549    |
| 15  | ((oscillomet* or auscultat*) adj3<br>(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/<br>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*<br>or npv or ppv or accura* or<br>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<br>"systematic review" or "reviews<br>(maximizes specificity)")  | 63      | 23 | limit 22 to (meta analysis or<br>"systematic review" or "reviews<br>(maximizes specificity)")   | 81       |
| 24 | ((child* or schoolchild* or boys or girls<br>or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people) and (blood pressure or<br>bp or hypertens* or prehypertens* or<br>pre-hypertens*) and (screen* or<br>diagnos* or test*)).ti. | 517     | 24 | ((child* or schoolchild* or boys or<br>girls or pediatric* or paediatric* or<br>adolescen* or teen* or youth? or<br>young people) and (blood<br>pressure or bp or hypertens* or<br>prehypertens* or pre-hypertens*)<br>and (screen* or diagnos* or<br>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<br>note or review).pt. or case<br>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<br>yr="2017 -Current")   | 384     | 30 | limit 29 to (english language and<br>yr="2017 -Current")  | 367      |

| Coch | rane 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  |
|      | (child* OR schoolchild* OR boys OR girls OR pediatric* OR paediatric* OR adolescen* |
| #5   | 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
  - o 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
  - o retinal vascular changes
  - end organ damage (such as ventricular hypertrophy and thickening of the carotid vessel wall)
  - o cognitive changes
  - o 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)
  - o non-pharmacological interventions (diet, exercise etc)
  - o combination of the above
- comparator: clinically diagnosis followed by:
  - pharmacological interventions (antihypertensive medications which are currently approved for use in children and young people)
  - o non-pharmacological interventions (diet, exercise etc)
  - o combination of the above
- outcomes:
  - o blood pressure normalisation
  - o retinal vascular changes
  - end organ damage (such as ventricular hypertrophy and thickening of the carotid vessel wall)
  - o cognitive changes
  - o cardiovascular disease
  - o 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 <i>et al.</i> (2020) [6]   |
| BACKGROUND              |   |
| Study type              | Systematic review   |
| Objectives              | To update the evidence on screening and treatment of hypertension<br>in childhood and adolescence for the US Preventive Services Task<br>Force  |
| Components of the study | For the key question on the association between high blood<br>pressure in children and adolescents and adverse outcomes in<br>adults:<br>Population – children and adolescents with elevated blood pressure   |
|                         | Intervention – N/A<br>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<br>reported:<br>end organ damage (carotid intima-media thickness,<br>left ventricular hypertrophy)<br>cardiovascular disease  |
|                         | Outcomes specified by the commissioning document that are<br>not reported include cognitive changes and retinal vascular<br>changes<br>[full-text checked]  |

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

| TITLE                   |   |
|-------------------------|---|
| Citation                | Goulas <i>et al.</i> (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                | 1   |
| 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            |
|                         |   |
| Conclusions             | I he authors concluded that left ventricular hypertrophy is         |
|                         | associated with hypertension with similar associations using        |
|                         | the different guidelines  |

| TITLE      |  |
|------------|--|
| Citation   | Schuh <i>et al.</i> (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,<br>obese or had signs of arterial hypertension<br>Intervention – N/A<br>Comparator – healthy children<br>Study design – observational studies and baseline descriptions of<br>RCTs that measured ophthalmological alterations<br>Search date – May 2017<br>[full-text checked] |
|-------------------------|--|
| OUTCOMES                |  |
| Outcomes reported       | Outcomes specified by the commissioning document that are<br>reported:<br>• retinal vascular changes<br>Outcomes specified by the commissioning document that are<br>not reported include end organ damage, cognitive changes  |
| Canalysiana             | and cardiovascular disease   |
| Conclusions             | hypertension show associations with ophthalmological alterations, especially with retinal vessel diameter  |

| TITLE                   | T  |
|-------------------------|--|
| Citation                | Yang <i>et al.</i> (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<br>not reported include cognitive changes and retinal vascular<br>changes  |
|-------------|--|
| Conclusions | The authors concluded that elevated blood pressure in<br>childhood or adolescence was significantly associated with<br>high carotid intima-media thickness, left ventricular<br>hypertrophy, high pulse wave velocity in adults. The authors<br>also reported evidence of associations with cardiovascular<br>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:  |
|                         | <ul> <li>end organ damage (left ventricular diastolic</li> </ul>     |
|                         | 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<br>Intervention – N/A<br>Comparator – N/A  |
|-------------------------|--|
| OUTCOMES                |  |
| Outcomes reported       | Outcomes specified by the commissioning document that are<br>reported:<br>• end organ damage (left ventricular hypertrophy)<br>Outcomes specified by the commissioning document that are<br>not reported include cognitive changes, retinal vascular<br>changes and cardiovascular disease |
| Conclusions             | The authors concluded that significant reclassification of<br>hypertension occurs when adult norms are applied to patients aged<br>13 to 17 years. Hypertension was significantly associated with left<br>ventricular hypertrophy when using adult blood pressure norms                    |

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

| TITLE                   |   |
|-------------------------|---|
| Citation                | Kupferman <i>et al.</i> (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:   |
|                         | <ul> <li>cognitive changes (executive function)</li> </ul>          |
|                         |   |

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

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

| TITLE      |                                  |
|------------|----------------------------------|
| Citation   | Truong <i>et al.</i> (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:   |
|                         | <ul> <li>end organ damage (left ventricular hypertrophy)</li> </ul> |
|                         |   |
|                         | 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 <i>et al.</i> (2020) [6]  |
| BACKGROUND              |  |
| Study type              | Systematic review  |
| Objectives              | To update the evidence on screening and treatment of hypertension<br>in childhood and adolescence for the US Preventive Services Task<br>Force   |
| Components of the study | For the key question on the diagnostic accuracy of screening tests<br>for high blood pressure in children and adolescents:<br>Population – asymptomatic children and adolescents<br>Index test – studies reporting diagnostic test accuracy of blood<br>pressure measurements<br>Reference standard – confirmed clinical diagnosis (after diagnostic<br>workup) of abnormal blood pressure<br>Search date – September 2019, with surveillance for relevant<br>studies up to October 2020 |

| OUTCOMES          |   |
|-------------------|---|
| Outcomes reported | Outcomes specified by the commissioning document that are<br>reported:<br>• sensitivity<br>• specificity  |
|                   | not reported include positive predictive value, negative<br>predictive value, positive likelihood ratio and negative<br>likelihood ratio  |
| Conclusions       | The authors concluded that the evidence is inconclusive<br>about whether the diagnostic accuracy of blood pressure<br>measurements is adequate for screening asymptomatic<br>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<br>office blood pressure, auscultated or manual office blood<br>pressure and 24-hour ambulatory blood pressure and to<br>explore the ability of automated office blood pressure and<br>manual office blood pressure to correctly identify daytime<br>ambulatory hypertension in children |
| Components of the study | Population – children evaluated at a hypertension clinic<br>Index test – automated office blood pressure assessed by an<br>oscillometric device and auscultated or manual office blood<br>pressure<br>Reference standard – 24-hour ambulatory blood pressure<br>monitoring   |
| OUTCOMES                |  |
| Outcomes reported       | Outcomes specified by the commissioning document that are<br>reported:<br>• sensitivity<br>• specificity<br>Outcomes specified by the commissioning document that are<br>not reported include positive predictive value, negative<br>predictive value, positive likelihood ratio and negative<br>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 <i>et al.</i> (2020) [6]  |  |
| BACKGROUND              |  |  |
| Study type              | Systematic review  |  |
| Objectives              | To update the evidence on screening and treatment of hypertension<br>in childhood and adolescence for the US Preventive Services Task<br>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<br>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, distant     |
|---|
| 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

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#### Question 1 (Association with risk of adverse outcomes)

- 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.
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#### **Question 2 (Screening tests)**

- 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.
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#### **Question 3 (Treatment)**

- 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.
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#### **Question 4 (Screening)**

 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.