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# **Screening strategies for hypertension (Review)**

Schmidt BM, Durao S, Toews I, Bavuma CM, Hohlfeld A, Nury E, Meerpohl JJ, Kredo T

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# TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	3
Figure 1	4
OBJECTIVES	5
METHODS	5
Figure 2	7
RESULTS	9
DISCUSSION	10
AUTHORS' CONCLUSIONS	10
ACKNOWLEDGEMENTS	11
REFERENCES	12
CHARACTERISTICS OF STUDIES	15
ADDITIONAL TABLES	20
APPENDICES	20
WHAT'S NEW	23
HISTORY	23
CONTRIBUTIONS OF AUTHORS	23
DECLARATIONS OF INTEREST	23
SOURCES OF SUPPORT	24
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	24
INDEX TERMS	24



# [Intervention Review]

# Screening strategies for hypertension

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# ABSTRACT

#### Background

Hypertension is a major public health challenge affecting more than one billion people worldwide; it disproportionately affects populations in low- and middle-income countries (LMICs), where health systems are generally weak. The increasing prevalence of hypertension is associated with population growth, ageing, genetic factors, and behavioural risk factors, such as excessive salt and fat consumption, physical inactivity, being overweight and obese, harmful alcohol consumption, and poor management of stress. Over the long term, hypertension leads to risk for cardiovascular events, such as heart disease, stroke, kidney failure, disability, and premature mortality.

Cardiovascular events can be preventable when high-risk populations are targeted, for example, through population-wide screening strategies. When available resources are limited, taking a total risk approach whereby several risk factors of hypertension are taken into consideration (e.g. age, gender, lifestyle factors, diabetes, blood cholesterol) can enable more accurate targeting of high-risk groups. Targeting of high-risk groups can help reduce costs in that resources are not spent on the entire population.

Early detection in the form of screening for hypertension (and associated risk factors) can help identify high-risk groups, which can result in timely treatment and management of risk factors. Ultimately, early detection can help reduce morbidity and mortality linked to it and can help contain health-related costs, for example, those associated with hospitalisation due to severe illness and poorly managed risk factors and comorbidities.

# Objectives

To assess the effectiveness of different screening strategies for hypertension (mass, targeted, or opportunistic) to reduce morbidity and mortality associated with hypertension.

#### Search methods

An Information Specialist searched the Cochrane Register of Studies (CRS-Web), the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, Latin American Caribbean Health Sciences Literature (LILACS) Bireme, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) without language, publication year, or publication status restrictions. The searches were conducted from inception until 9 April 2020.

# Selection criteria

Randomised controlled trials (RCTs) and non-RCTs (NRCTs), that is, controlled before and after (CBA), interrupted time series (ITS), and prospective analytic cohort studies of healthy adolescents, adults, and elderly people participating in mass, targeted, or opportunistic screening of hypertension.

Screening strategies for hypertension (Review)



#### Data collection and analysis

Screening of all retrieved studies was done in Covidence. A team of reviewers, in pairs, independently assessed titles and abstracts of identified studies and acquired full texts for studies that were potentially eligible. Studies were deemed to be eligible for full-text screening if two review authors agreed, or if consensus was reached through discussion with a third review author. It was planned that at least two review authors would independently extract data from included studies, assess risk of bias using pre-specified Cochrane criteria, and conduct a meta-analysis of sufficiently similar studies or present a narrative synthesis of the results.

#### **Main results**

We screened 9335 titles and abstracts. We identified 54 potentially eligible studies for full-text screening. However, no studies met the eligibility criteria.

#### **Authors' conclusions**

There is an implicit assumption that early detection of hypertension through screening can reduce the burden of morbidity and mortality, but this assumption has not been tested in rigorous research studies. High-quality evidence from RCTs or programmatic evidence from NRCTs on the effectiveness and costs or harms of different screening strategies for hypertension (mass, targeted, or opportunistic) to reduce hypertension-related morbidity and mortality is lacking.

# PLAIN LANGUAGE SUMMARY

#### Screening strategies for hypertension

#### **Review question**

What effects do the different ways of screening for hypertension (mass, targeted, or opportunistic) have in decreasing illness and death?

### Background

Hypertension is a long-term non-communicable disease (NCD), also known as high, raised, or elevated blood pressure. Blood pressure is expressed by two measurements (systolic (SBP) and diastolic (DBP) pressures), which are the maximum and minimum pressures. High blood pressure is generally diagnosed when resting blood pressure is persistently at SBP  $\geq$  130/140 millimetres mercury (mmHg) or at DBP  $\geq$  80/90 mmHg for adults.

Even though blood pressure in the arteries is continuously raised, in many cases, high blood pressure does not cause symptoms. Nonetheless, hypertension can increase the risk for heart failure, stroke, vision loss, and chronic kidney disease, and so on, in the long term. People who have unhealthy diets, consume harmful amounts of alcohol and/or tobacco, and are physically inactive are at higher risk of hypertension.

Early detection, adequate treatment, and good control of high blood pressure can lower the risk of complications associated with hypertension. Although early detection through screening of hypertension has the potential to contain health-related costs, reducing the burden of hypertension will to some extent involve addressing behavioural and socioeconomic risk factors (such as income, occupation, and level of education). Therefore, it is unclear whether early detection of mild hypertension can positively impact health-related costs in the long term and improve health outcomes by reducing the need for hospitalisation and management of hypertension-related complications, which can be severe.

# **Review methods**

We searched various electronic databases on this topic until 9 April 2020. We searched for studies written in any language, whether published or not. We planned to include studies that compared one type of screening strategy for hypertension versus no screening strategy, that is, mass screening versus no screening, targeted screening versus no screening, and opportunistic screening versus no screening. We were interested in studies in which participants were healthy adolescents, adults, and elderly people, and in which researchers measured clinical outcomes, health system outcomes, and adverse events.

#### **Key results**

We found no studies that met the criteria described above.

# **Quality of the evidence**

High-certainty evidence that can tell us whether mass, targeted, or opportunistic screening strategies are effective for reducing illness and death associated with hypertension is lacking.

Screening strategies for hypertension (Review)



# BACKGROUND

# **Description of the condition**

Hypertension, also known as high, raised, or elevated blood pressure, is a long-term non-communicable medical condition wherein the blood pressure in the arteries is persistently elevated (Guwatudde 2015). Blood pressure can be expressed as two measurements: systolic blood pressure (SBP) and diastolic blood pressure (DBP), which are the maximum and minimum pressures. Table 1 compares previous - WHO 2013 - versus current thresholds for high blood pressure (ACCF 2018; Carey 2018; Whelton 2018).

Hypertension is a major public health problem and is the most common cardiovascular disorder, affecting approximately one billion people globally. It remains, since the early 2000s, the single leading contributor to the global burden of morbidity and mortality (Guwatudde 2015). In sub-Saharan Africa, an estimated 10 to 20 million people out of approximately 650 million people may have hypertension (Lloyd-Sherlock 2014). This high prevalence of hypertension is attributed to population growth (migration from rural to urban areas), changes in dietary habits (resulting in being overweight or obese), ageing of the population, and social stress (Guwatudde 2015; WHO 2013). A large proportion of the population with hypertension remains undiagnosed, untreated, or inadequately treated, with subsequent complications contributing to the rising burden of cardiovascular disease (AtakIte 2015).

Over the long term, hypertension is a major risk factor for cardiovascular events, such as heart disease, stroke, and kidney failure, as well as disability and premature mortality (WHO 2013). Factors that increase the risk of hypertension include genetic and lifestyle factors, such as excessive salt and fat consumption, physical inactivity, harmful alcohol consumption, and poor management of stress (WHO 2013). Growing evidence shows that younger people, such as adolescents, are also at risk of hypertension because of these unhealthy lifestyle factors (Cheung 2017; Kar 2015).

# **Description of the intervention**

Screening programmes for hypertension could help reduce morbidity and mortality linked to it (Legorreta 2015; WHO 2013).

Screening is generally defined as the detection of unknown disease among apparently healthy individuals through tests or examinations conducted to identify those at increased risk for the condition (Screening Subcommittee 2008).

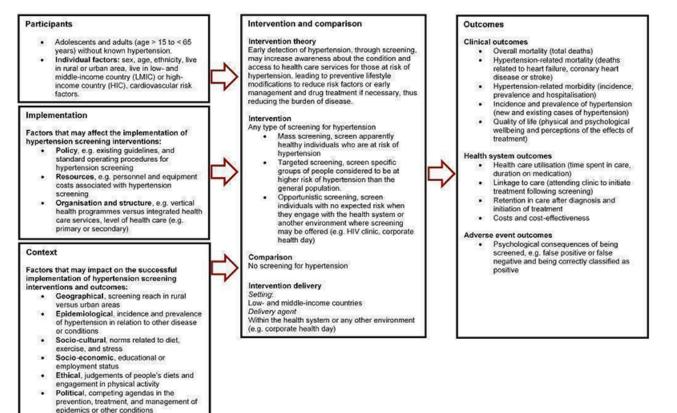
Various devices (electronic, mercury, and aneroid) can be used to measure blood pressure (WHO 2013). Two blood pressure measurements should be recorded daily for several days. These measurements should be taken at least a minute apart, ideally in the morning and again in the evening, while the person is seated. For accuracy, measurements taken on the first day are discarded, and an average is taken of all remaining measurements to confirm the diagnosis of hypertension (WHO 2013). It is common practice that diagnosis of hypertension is confirmed if the resting blood pressure is persistently at SBP  $\geq$  130/140 millimetres mercury (mmHg) or DBP  $\geq$  80/90 mmHg (ACCF 2018; WHO 2013). This Cochrane Review focused primarily on screening strategies for hypertension and not on the thresholds used for diagnosis.

Key components of screening programmes for hypertension include not only equipment and trained health professionals, but also patient education and informed consent, as well as good relationships between health professions (which are beneficial for referral processes between different healthcare facilities or services) (WHO 2013). These components make screening for hypertension (across an entire population) a costly intervention because of the lengthy time needed to diagnosis and the human and financial resources required.

#### How the intervention might work

The logic model in Figure 1 outlines how hypertension screening may reduce the burden of disease in terms of participant, intervention, implementation, and contextual factors (Rohwer 2017). Early detection of hypertension through screening could increase awareness for those at risk of hypertension, and thus lead to preventative action or early management, which may ultimately curb the societal and economic burden of the disease (Ataklte 2015).

## Figure 1. Screening for hypertension



Early detection of hypertension through screening can provide benefits for those identified as hypertensive. Treatment can be especially beneficial for people with moderate to severe hypertension, that is, people with resting blood pressure of greater than 160 over 100 mmHg (Musini 2017; Musini 2019). However, treatment has not proved beneficial for people with mild hypertension (Diao 2012).

On the contrary, screening (including for hypertension) can also lead to harmful consequences for those being screened. For example, patients can sometimes be misdiagnosed as hypertensive when subsequent blood pressure readings are limited over several months. This can result in non-hypertensive individuals being unnecessarily exposed to treatments and their potential side effects. For the workforce, attending the required number of screening sessions can lead to increased absenteeism from work. Employees may increasingly stay away from work once they are aware that they are potentially hypertensive, and if diagnosed as hypertensive, low adherence to treatment may result in sickness and increased absenteeism (Haynes 1978). Additionally, screening for hypertension can be harmful in settings where the harms of treatment outweigh the benefits.

# Why it is important to do this review

Interventions to prevent or manage hypertension should be effective, feasible, affordable, and sustainable. Vertical programmes that focus solely on hypertension are therefore not widely recommended (WHO 2013). Early detection of hypertension may be a feasible and affordable intervention, especially when screening for hypertension is offered as a point-of-care or integrated service. However, it is unclear whether or when early detection of hypertension may be an effective intervention, specifically because hypertension is associated with behavioural and socioeconomic risk factors (Bernabé-Ortiz 2017). Therefore, early detection of mild hypertension may not significantly impact health-related costs in the long term nor improve health outcomes. Additionally, lifestyle factors associated with hypertension (e.g. changes in diet, physical activity patterns) can generally be attributed to urbanisation in resource-limited countries. Therefore, preventing hypertension may involve other stakeholders (e.g. policy-makers) and may extend beyond screening by health professionals (Hunter-Adams 2017; WHO 2013).

Because it is unclear whether screening for hypertension leads to healthier behaviours and better control of blood pressure levels, it is important to learn from studies that have assessed the impact of screening on hypertension outcomes. A 2014 systematic review informed the US Preventive Services Task Force update of its recommendation on screening for high blood pressure in adults (Piper 2014). The review focused on the role of confirming hypertension diagnoses, re-screening intervals, ambulatory blood pressure monitoring, and home blood pressure monitoring. Evidence from the systematic review does not provide guidance on different screening strategies.

A recent overview of systematic reviews on diabetes and hypertension screening programmes found that a systematic review is needed to assess the effectiveness and impact of various screening interventions (Durao 2014). Thus, this Cochrane Review aimed to address this gap in the literature, with specific focus

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on evidence from resource-limited countries, where behavioural and socioeconomic risk factors for hypertension are similar to the broader problems of urban areas in these countries. It aimed to clarify whether screening for hypertension, in all age groups, helps contain health-related costs and improve outcomes related to hypertension and associated life-threatening complications.

# OBJECTIVES

To assess the effectiveness of different screening strategies for hypertension (mass, targeted, or opportunistic) to reduce morbidity and mortality associated with hypertension.

### METHODS

#### Criteria for considering studies for this review

#### **Types of studies**

We planned to include randomised trials, non-randomised trials, controlled before and after (CBA) studies, interrupted time series (ITS), and prospective analytic cohort studies (Cochrane EPOC 2017a). Given the programmatic nature of screening for hypertension, we did not expect to find many randomised controlled trials (RCTs), and so we also planned to include nonrandomised studies (NRSs). RCTs are experimental studies in which people are randomly allocated to one of two or more groups receiving an intervention or control treatment or no treatment. A CBA study is an NRS in which outcomes are measured before and after treatment, both in a group that receives the treatment and in another comparison group. An ITS study is an NRS that measures an outcome at multiple time points before and after an intervention (the 'interruption'). The design attempts to detect whether the intervention has had an effect greater than any underlying trend over time. To be eligible, ITS studies should be controlled and they must have at least three data points before and after a clearly defined intervention in terms of content and timing (Cochrane EPOC 2017a). Prospective analytic cohort studies were also eligible when participants were already exposed or unexposed to an intervention but had not developed the outcome of interest at the start of the study; participants are followed forward in time, after which outcomes are measured. To be eligible, cohort studies needed to have at least two study arms, so they could provide a comparison of the exposure of interest.

We planned to include studies regardless of their language or publication status.

#### **Types of participants**

Healthy adolescents (15 to 24 years old), adults (25 to 64 years old), and elderly people (over 65 years old) without known hypertension. We were also interested in studies in which participants presented with risk factors for hypertension.

#### Types of interventions

Studies on mass, targeted, or opportunistic hypertension screening compared to no screening with participant follow-up of at least one year were eligible.

Mass screening involves screening apparently healthy populations regardless of the presence of risk factors (at public places, e.g. markets). Targeted screening involves screening specific groups of people who are considered to be at higher risk of hypertension than the general population. Opportunistic screening involves screening individuals engaging with the health system or in another environment in which screening may be offered (e.g. HIV clinic, corporate health day).

#### Types of outcome measures

#### **Primary outcomes**

#### **Clinical outcomes**

1. Overall mortality (total deaths)

2. Hypertension-related mortality (death related to heart failure, coronary heart disease, stroke, or end-stage kidney disease)

3. Hypertension-related morbidity (incidence, prevalence, and hospitalisation due to stroke, coronary heart disease, heart failure, or end-stage renal disease)

4. Incidence and prevalence of hypertension (ratio of detected hypertension to expected prevalence of hypertension)

5. Quality of life (physical and psychological well-being and perceptions of the effects of treatment)

#### Secondary outcomes

#### Health system outcomes

6. Healthcare utilisation (time spent in care, duration on medication)

7. Linkage to care (attending clinic to initiate treatment following screening)

8. Retention in care after diagnosis and initiation of treatment

9. Costs and cost-effectiveness (as described in the included studies, or in related sub-studies)

#### Adverse events of being screened

10. Psychological consequences of being screened (e.g. false positive or false negative, being correctly classified as positive (new diagnosis))

# Search methods for identification of studies

#### **Electronic searches**

The Cochrane Hypertension Information Specialist searched the following databases without language, publication year, or publication status restrictions until 9 April 2020.

- 1. Cochrane Hypertension Specialised Register via the Cochrane Register of Studies (CRS-Web).
- 2. Cochrane Central Register of Controlled Trials (CENTRAL), in the Cochrane Library, via the Cochrane Register of Studies (CRS-Web).
- 3. MEDLINE Ovid (from 1946 onwards), MEDLINE Ovid Epub Ahead of Print, and MEDLINE Ovid In-Process & Other Non-Indexed Citations.
- 4. Embase Ovid (from 1974 onwards).
- 5. Latin American Caribbean Health Sciences Literature (LILACS) Bireme (from 1982 onwards).
- 6. ClinicalTrials.gov (www.clinicaltrials.gov).
- 7. World Health Organization International Clinical Trials Registry Platform (www.who.it.trialsearch).

The subject strategies for databases were modelled on the search strategy designed for MEDLINE (Appendix 1). When appropriate, these were combined with subject strategy adaptations of the

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sensitivity- and precision-maximising search strategy designed by Cochrane for identifying RCTs (as described in Box 6.4.c of Higgins 2011). We based the search terms for non-randomised trials on the EPOC search filter for Ovid MEDLINE (Cochrane EPOC 2017b), and we provide the full search strategies for the listed databases in Appendix 1.

#### Searching other resources

The Information Specialist searched the Cochrane Hypertension Specialised Register segment (which includes searches of MEDLINE, Embase, the Cochrane Library, and Epistemonikos for systematic reviews) to retrieve published systematic reviews related to this review title, so that we could scan their reference lists to identify additional relevant trials. The Specialised Register also includes searches of the Allied and Complementary Medicine Database (AMED), CAB Abstracts & Global Health, Cumulative Index to Nursing and Allied Health Literature (CINAHL), ProQuest Dissertations & Theses, and Web of Science. We also contacted experts in this research field to identify relevant studies.

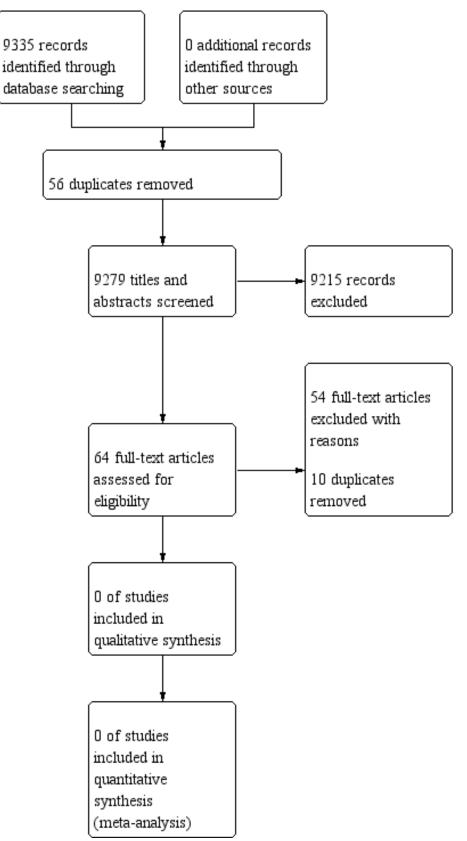
# Data collection and analysis

#### **Selection of studies**

Pairs of review authors (BS, AH, EN, RM, IT, CB, and TK) independently screened all titles or abstracts, or both, of all records retrieved, to determine their eligibility for full-text screening. We retrieved the full texts of potentially eligible or unclear studies, which were assessed for inclusion independently by pairs of review authors (BS, AH, EN, RM, TK). We solved disagreements by rechecking the full-text article or by consulting a third review author, or both. We present the study selection process in a PRISMA flow diagram (Figure 2), and we list all studies excluded after full-text assessment along with reasons for their exclusion in the Characteristics of excluded studies table (Liberati 2009).



# Figure 2. PRISMA diagram of eligible studies





#### Data extraction and management

We planned to pilot the data extraction form on two included studies to ensure that information is captured in a standardised manner. It was intended that two review authors would independently extract study data related to participant, intervention, comparison, and outcome (PICO) characteristics using the standard data extraction form. Any missing information was going to be noted with a plan to contact the author of the primary study. Any disagreements would have been resolved through discussion or by consultation with a third review author.

#### Assessment of risk of bias in included studies

We were going to use the 'Risk of bias' assessment tool modified by the Cochrane Effective Practice and Organisation of Care (EPOC) Group (Cochrane EPOC 2017a). It is widely used and validated for systematic reviews including a wide range of study designs. We planned that two review authors would independently assess the risk of bias in included studies and resolve any disagreements through discussion or by consultation with a third review author. Individual studies would have been classified as having 'low', 'unclear', or 'high' risk of bias. Low risk of bias is plausible bias that is unlikely to alter results, unclear risk of bias is plausible bias that raises some doubt about the results, and high risk of bias is plausible bias that seriously weakens confidence in results. We will follow the recommendations of Cochrane EPOC to score NRCTs as 'high' risk of bias (Cochrane EPOC 2017a).

We planned to apply the following criteria to the 'Risk of bias' assessments of RCTs and NRCTs.

- 1. Was the allocation sequence adequately generated? (RCTs)
- 2. Was the allocation adequately concealed? (RCTs)
- 3. Were baseline outcome measurements similar? (all)
- 4. Were baseline characteristics similar? (all)
- 5. Were incomplete outcome data adequately addressed? (RCTs)
- 6. Was knowledge of the allocated intervention adequately prevented during the study? (RCTs)
- 7. Was the study adequately protected against contamination? (RCTs)
- 8. Was the study free from selective outcome reporting? (RCTs)
- 9. Was the study free from other risks of bias? (all)

We planned to apply the following criteria to the 'Risk of bias' assessments of ITS.

- 1. Was the intervention independent of other changes?
- 2. Was the shape of the intervention effect pre-specified?
- 3. Was the intervention unlikely to affect data collection?
- 4. Was knowledge of the allocated interventions adequately prevented during the study?
- 5. Were incomplete outcome data adequately addressed?
- 6. Was the study free from selective outcome reporting?
- 7. Was the study free from other risks of bias?

## Measures of treatment effect

We planned to present dichotomous outcomes as risk ratios, and continuous outcomes as mean differences with standard deviations between the change in intervention and control groups if outcomes were measured in the same way across all studies. In Cochrane Database of Systematic Reviews

the case that included studies measured continuous outcomes in different ways, we were going to calculate the standardised mean differences between intervention and control groups. We planned to present time-to-event outcomes as hazard ratios, and to present 95% confidence intervals (CIs) for all outcomes.

## Unit of analysis issues

We planned to consider the level at which randomisation occurred (e.g. in cluster-randomised trials, groups of individuals may be randomised together to the same intervention). When repeated measurements were taken, there may be multiple observations for the same outcome (Higgins 2011). In the case that more than one comparison was available from the same study, we were going to combine groups into a single pair-wise comparison. If included cluster-randomised trials had not appropriately adjusted for the clustering of participants in their analysis, then we were going to re-analyse them. The design effect (of cluster-randomised trials) may lead to inflated effect sizes of the intervention, so we had planned to calculate the design effect, which involves an estimation of an intracluster correlation (ICC). We planned to impute estimates of the ICC value using estimates from other included studies that reported ICCs, or using external estimates from empirical research. Also, we planned to examine the impact of clustering by performing sensitivity analyses.

#### Dealing with missing data

When necessary, we were going to contact the authors of included studies to ask for data related to study methods, attrition rates, and outcomes that were unclear or missing. For example, we were going to request information on the number of participants screened, randomly assigned participants, intention-to-treat (ITT), as-treated or per-protocol samples, dropouts, losses to follow-up, or withdrawals. If the study authors did not provide estimates for the entire study sample (e.g. they provide estimates only for each sex group), then we would have calculated these using available information, including imputing data, when appropriate. We would have reported all missing outcome data on the data extraction form and the 'Risk of bias' table, and we would have assessed the impact of including in the sensitivity analysis studies with missing data.

#### Assessment of heterogeneity

We planned to assess heterogeneity and variability amongst studies in relation to participant, intervention, comparison, and outcome information, as well as context and type of screening and its implementation. If we had conducted a meta-analysis, we would have assessed heterogeneity by visually inspecting overlap of CIs and by using statistical methods (i.e. Chi<sup>2</sup> test and I<sup>2</sup> statistic values). If the Chi<sup>2</sup> test had a small P value (P < 0.1) and the I<sup>2</sup> statistic was 60% or above, we would have concluded that heterogeneity is moderate or substantial (Higgins 2011). We planned to explore reasons for heterogeneity through subgroup analyses.

#### Assessment of reporting biases

We planned to assess the likelihood of reporting bias for each outcome if a sufficient number of studies (more than 10) were included in a meta-analysis. We would have used a funnel plot to visually check for asymmetry associated with small-study effects and publication bias. Through sensitivity analysis, we would have assessed how these factors affect the results and conclusions of the meta-analysis.

Screening strategies for hypertension (Review)



# **Data synthesis**

We planned to conduct a meta-analysis if the included studies were sufficiently homogenous, and if at least two studies of the same design assess the same intervention, comparison, and outcome. Outcomes should have occurred at clinically relevant time points after hypertension screening, to be analysed (e.g. death within three months of screening may not be clinically relevant). If the characteristics of included studies were excessively heterogeneous, we would have pooled results but would have presented only a narrative synthesis of the results, potentially grouping findings by context measures.

#### Subgroup analysis and investigation of heterogeneity

We would have considered subgroup analyses according to the following.

- 1. Sex: female or male.
- 2. Age: adolescents (15 to 24 years old), adults (25 to 64 years old), and elderly people (over 65 years old).
- 3. Ethnicity: white, black, Asian, or other.
- Setting: rural versus urban; low- and middle-income countries versus high-income countries (which we would have defined according to the World Bank's country classifications by income level (World Bank 2018)).
- 5. Screening tools: electronic, mercury, or aneroid.
- 6. Cardiovascular risk factors: overweight or obesity, physical inactivity, dietary factors (e.g. sodium or salt intake), and comorbid condition.

# Sensitivity analysis

We planned to conduct sensitivity analyses to explore the influence of various factors, when applicable, on the effect size. We would have stratified analyses per publication status and level of risk of bias to determine whether studies with high risk of bias skew the results.

# Summary of findings and assessment of the certainty of the evidence

We planned to assess the certainty of the overall evidence for each outcome according to the GRADE approach (Guyatt 2008). GRADE is a methodology for rating the certainty of evidence and grading the strength of recommendations in systematic reviews. It includes five criteria for downgrading the certainty of evidence: risk of bias, inconsistency, imprecision, publication bias, and indirectness; and three criteria for upgrading the certainty of evidence: large effect, dose response, and residual confounding opposing the observed effect. We will report the certainty of evidence as either 'high', 'moderate', 'low', or 'very low'. High certainty means that further research is very unlikely to change our confidence in the estimate of effect; moderate certainty means that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low certainty means that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; and very low certainty means that we are very uncertain about the estimate.

We aimed to report GRADE assessments in 'Summary of findings' table(s). The 'Summary of findings' table(s) would have included the number of participants and studies included for each outcome,

a summary of intervention effect, and a measure of the certainty of evidence against GRADE criteria. We would have presented results for the following outcomes: overall morality, hypertensionrelated mortality, hypertension-related morbidity, incidence and prevalence of hypertension, quality of life, health care utilisation and linkage to care. These are listed as 1 to 7 in the 'Types of outcome measures' section. The seven main outcomes to be presented prioritise clinically important outcomes, followed by adverse effect and health system outcomes. Given the complex nature of the interventions being studied, pre-specification of the outcomes was challenging (Cochrane EPOC 2017a).

# RESULTS

#### **Description of studies**

None of the retrieved studies met the inclusion criteria. This 'empty' review (no studies were included) will follow the guidelines provided by Cochrane on reporting empty reviews and results from excluded studies. For the discussion, this review will draw on some studies that assessed the effectiveness of screening strategies for hypertension but did not meet the inclusion criteria.

## **Results of the search**

The electronic databases search yielded 9335 records, which were exported into Covidence 2019; 56 duplicates were removed. As is presented in Figure 2, 9279 titles and/or abstracts were screened, from which 64 studies were identified as eligible for full-text screening. Of these 64, 10 additional duplicates were removed, 54 studies were excluded, no studies are awaiting classification, and no relevant ongoing studies were found. We did not find any studies for inclusion into this review.

# **Included studies**

No studies (RCTs and NRS) met the inclusion criteria.

### **Excluded studies**

Of the 54 excluded studies, 44 did not have a study design eligible for this review (such as cohort studies with no control arm and cross-sectional studies); two studies included participants already diagnosed with hypertension; and eight studies did not report on our interventions of interest (i.e. mass, targeted, or opportunistic screening). Detailed reasons for exclusion of individual studies are provided in the Characteristics of excluded studies table.

#### **Risk of bias in included studies**

No studies met the inclusion criteria for this review.

#### Allocation

N/A.

Blinding

N/A.

#### Incomplete outcome data

N/A.

# Selective reporting

N/A.

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# Other potential sources of bias

N/A.

# **Effects of interventions**

No studies met the inclusion criteria for this review.

# DISCUSSION

## Summary of main results

We did not identify any studies that were eligible for inclusion in the review, nor ongoing studies, making this an 'empty' review. About half of the excluded studies (29 of 54) were conducted during the 1970s and 1980s and could potentially have been included in a 2014 systematic review to update the US Preventive Services Task Force recommendation (Whelton 2018). That review, however, focused on the role of confirming hypertension diagnoses, rescreening intervals, ambulatory blood pressure monitoring, and home blood pressure monitoring instead of different types of screening strategies. We are confident that all relevant literature was identified, given the wide range of appropriate databases that we searched and the double screening of all titles or abstracts and full texts.

The discussion is based on evidence from two studies that did not meet the inclusion criteria of this review but addressed a similar research question related to screening for hypertension. One study conducted in the United States of America (USA) in 2015 aimed to identify the prevalence and characteristics of patients identified with high blood pressure and the proportion of falsepositives after an initial elevated blood pressure reading during non-primary care visits compared with primary care visits (Handler 2015). This study was excluded because it was a cohort study without a control arm, and there was no analysis comparing screening with no screening of hypertension. The results of 111,996 patients (82.7% in primary care and 17.3% in non-primary care) suggest that expanding screening for hypertension to non-primary care settings may improve the detection of hypertension. Although study authors identified non-primary care as an opportunity to identify individuals with increased blood pressure, they were also concerned about false-positives. Falsely identifying patients as hypertensive will increase the absolute number of patients who require follow-up but do not have hypertension. This could lead to wasted time and resources for both patients and the healthcare system in making additional but unnecessary screenings (Handler 2015).

A study conducted in Finland in 1999 assessed a programme for both hypertension screening and hypertension treatment and adherence. We excluded this study from our systematic review because of the absence of a control group (Takala 1983). People aged 40 to 64 years living in a southwestern municipality of Finland were invited to attend screening for hypertension (mass screening). Those identified as hypertensive were divided into two groups: one group received a letter notifying them that they had elevated blood pressure, and the other group received additional written information about hypertension and the importance of receiving treatment. Trial authors report that receiving written information explaining the nature of hypertension and stressing the importance of its treatment, in addition to the notification letter, did not lead to a significant increase in seeking treatment (Handler 2015). The first study suggests that offering screening across both primary and non-primary healthcare settings may improve the detection of hypertension, and the second study suggests that there may be no improvement in treatment-seeking amongst those who are screened, diagnosed, and given encouragement. These studies did not look at different screening strategies for hypertension, but the first study suggests that wider screening of hypertension across healthcare services can improve detection. It is however unclear what the additional costs or harms for screening people in nonprimary care were compared to the benefits of, for example, getting more people on anti-hypertensive treatment.

#### **Overall completeness and applicability of evidence**

N/A.

#### **Quality of the evidence**

N/A.

#### Potential biases in the review process

N/A.

# Agreements and disagreements with other studies or reviews

N/A.

# AUTHORS' CONCLUSIONS

#### Implications for practice

The latest recommendation related to screening for hypertension was issued by the US Preventive Services Task Force in 2015 (Whelton 2018). The USPSTF recommends screening for high blood pressure in adults aged 18 years or older. However, this recommendation does not provide details on different types of screening strategies for hypertension.

Evidence suggests that screening for hypertension regardless of the type of screening strategy used can reduce morbidity and mortality associated with hypertension. This is based on the notion that early detection can lead hypertensive individuals to seek treatment and positively change lifestyle-related behaviours. However, falsely diagnosing individuals as hypertensive can have adverse psychological effects on them, and unnecessary screening can lead to wasted resources for patients and the healthcare system.

Currently, evidence to support any specific type of screening strategy for hypertension is lacking. Pragmatically, on the one hand, governments should be cautious in rolling out mass (population-wide) screening programmes that are costly, without evidence that screening will lead to treatment-seeking, treatment adherence, and changed lifestyle behaviours. On the other hand, governments may continue to offer screening to those individuals who are at greater risk than the general population, or to individuals who are already engaging with integrated healthcare services.

#### Implications for research

Well-conducted experimental and observational studies are needed to assess the effectiveness of different screening strategies for hypertension (mass, targeted, or opportunistic) to reduce

Screening strategies for hypertension (Review)

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morbidity and mortality associated with hypertension. Knowing which screening strategy is most effective could help decisionmakers, including policy-makers and practitioners, especially in resource-limited settings, in prioritising how screening for hypertension should be offered.

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Study	Reason for exclusion	
Abernethy 1974	This study reports on hypertension screening for men and women aged 30 to 69 years throughout Australia. Results show the response of the community, the general pattern of blood pressure, and complications in the screened population. There was no control group; therefore this study was ex- cluded from this review	

Screening strategies for hypertension (Review)

Cochrane Library

Study	Reason for exclusion	
Bruneau 2017	This study aimed to implement and test a cardiovascular assessment screening programme. The intervention described in the study (a cardiovascular screening checklist) is not eligible for inclusion in this review	
Cretens 1978	This study reported on a hypertension screening programme that followed up on children who were previously identified with elevated blood pressure. Children are not eligible for this review; therefore this study was excluded from this review	
Cromwell 2005	This study evaluated an underlying disorder that is called secondary hypertension, to assess for co- morbidities (such as obesity) and to assess for end-organ damage. It was excluded because of the wrong study design (there was no control group) and the wrong intervention (screening for hyper- tension was not the intervention of interest)	
DeSales 2015	This study aimed to identify the prevalence and characteristics of patients identified with high blood pressure in non-primary care compared with primary care visits. There was no control group, and the intervention described in this study is not eligible for inclusion in this review	
Grancio 1979	This article presents concepts and principles of community control to professional nurses work- ing and living in communities where efforts directed at prevention and control of chronic health problems (such as hypertension) are appropriate. It is not an empirical study; therefore it uses the wrong study design and was excluded from the review	
Handler 2015	This study aimed to identify the prevalence and characteristics of patients identified with high blood pressure in non-primary care compared to primary care visits. It was excluded from this review because of the wrong study design and the wrong intervention	
Haynes 1978	This study confirmed that labelling patients as hypertensive can result in increased absenteeism from work. There is no control group; therefore this study was excluded from this review	
Hoegh 2014	This study evaluated the cost-effectiveness of a combined screening programme for the following conditions: abdominal aortic aneurysm, peripheral arterial disease, carotid plaque, hypertension, arrhythmia, and type 2 diabetes. There is no control group, and the intervention is not of interest to this review; therefore this study was excluded from this review	
Hong 2011	This study investigated the impact of a national mass screening programme on health service util- isation and medical expenses. There is no control group; therefore this study was excluded from this review	
Hypertension Detection & Fol- low-up Program 1978	The Hypertension Detection and Follow-up Program (HDFP) occurred over a 5-year period and addressed the following questions: (1) Will successful community hypertension intervention pro- grammes have an impact on death and disability rates in the community? (2) Can hypertensives, detected in general populations, be brought under pharmacologic management? (3) Do the bene- fits of therapy exceed undesirable side effects and costs in the subgroup with mild hypertension? (4) Is antihypertensive therapy effective in young adults and in females, and equally effective in blacks and whites? (5) Can morbidity and mortality from coronary artery disease be decreased by antihypertensive therapy? This study was excluded from this review because it did not have a con- trol group	
Jastrup 1986	This study did not have a control group	
John 2010	This study was conducted in India to assess whether primary care health workers (Health Aides), similar in training and educational qualifications to the Village Health Nurse, can be sufficiently trained to measure blood pressure without substantially increasing workload. Screening for hyper-tension was not the intervention of interest; therefore this study was excluded from this review	

Study	Reason for exclusion	
Kaufman 1993	This study summarised existing data on the epidemiology of hypertension in Africa and outlined important known risk factors. Both the study design and the intervention in this study were not eli-gible for inclusion into this review	
Kortge 1976	The Hypertension Screening and Awareness Project had 3 objectives: (1) to collect data on blood pressure measurements in the community; (2) to provide educational information for the screened population; and (3) to screen the population of south-central Kansas for undetected hypertension. There was no control group; therefore this study was excluded from this review	
Kulbertus 1978	This cross-sectional study reports on hypertension screening that was conducted in mobile units generally used for detection of tuberculosis and chest diseases. This study was excluded because it used the wrong study design and did not provide follow-up of at least 1 year	
Lauridsen 1979	This cohort study reports on a screening programme for workers in Copenhagen. However, there was no control group; therefore this study was excluded from this review	
Leshchinskii 1986	This study assessed early detection of arterial hypertension and ischaemic heart disease in mass screening at the polyclinics of large industrial enterprises. There was no control group; therefore this study was excluded from this review	
LugoDeOrtellado 2007	This study evaluated the effectiveness of a programme of Pharmaceutical Care in Paraguay in a controlled prospective study directed at hypertensive patients in community pharmacies. The intervention described in the study was not eligible for inclusion in this review	
Marin-Rives 2015	This study assessed the value of having pharmacists measuring blood pressure to detect hyperten- sion in adults without a previous diagnosis and/or antihypertensive treatment. There was no con- trol group; therefore this study was excluded from this review	
McAlister 1980	This study assessed whether an information management system can help family doctors in treat- ing high blood pressure more effectively. The intervention described in the study was not eligible for inclusion in this review	
Mendy 2014	The aim of the "Barbers Reaching Out to Help Educate on Routine Screenings" (BROTHERS) initia- tive was provided for barbers to routinely screen adult black men in the Mississippi Delta region, thereby increasing awareness of high blood pressure, and to refer clients with high blood pressure to a healthcare provider. There was no control group; therefore this study was excluded from this review	
Miall 1982	This paper summarised the relevant epidemiological background, evidence from trials concerning the value of treatment for mild hypertension, and technical aspects of mounting screening or case- finding programmes. This is not an empirical study; therefore it used the wrong study design to be included in this review	
Miller 1976	This study evaluated the Franklin County High Blood Pressure Program (FCHHBP), which is a popu- lation-wide network of community blood pressure centres. There was no control group; therefore this study was excluded from this review	
Mohan 2018	This paper describes the design and methods of "UDAY" - a comprehensive diabetes and hyperten- sion prevention and management programme in India. Pre- and post-treatment evaluations were conducted, but there was no control group, so this study was excluded from this review	
Moser 1977	The Task Force I of the USA National High Blood Pressure Education Program, National Heart, Lung and Blood Institute, was charged with providing practical recommendations for (1) identifying that segment of the total population with high blood pressure, (2) detecting those who could be expect- ed to benefit from antihypertensive therapy, and (3) proposing appropriate therapeutic regimens. The report provides 6 general recommendations for detection, evaluation, and treatment of high	

Screening strategies for hypertension (Review)

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Study	Reason for exclusion	
	blood pressure in adults. This is not an empirical study; therefore it used the wrong study design to be included in this review	
Musicha 2016	This study evaluated the uptake of referral for clinical assessment and retention in care following a large rural and urban population screening programme (for hypertension and diabetes) in Malawi. Two cross-sectional studies were carried out, so this study was excluded from the review for wrong study design	
Niessen 2014	The aim of this study was to define and subsequently validate blood pressure cut-off values to ei- ther confirm or reject the diagnosis of hypertension after 1 or 2 duplicate home blood pressure measurements in persons at low and high cardiovascular risk. The intervention described in this study (i.e. home blood pressure measurements) is not eligible for inclusion in this review	
Nugent 1980	This study reported on screening for hypertension, referral of hypertensive patients to local physi- cians for management, and re-screening of those identified as hypertensive. There was no control group; therefore this study was excluded from this review	
O'Connell 1985	This study reported on screening for hypertension and follow-up in the workplace. There was no control group; therefore this study was excluded from this review	
O'Sullivan 1979	This study recorded the blood pressure measurements of non-pregnant patients between the ages of 20 and 60 years who presented at the Blackburn Clinic. It was excluded from this review because it did not include a control group	
Petrovitch 1991	This study reports on the recruitment strategies used in the Systolic Hypertension in the Elderly Program. The intervention described in the study (i.e. recruitment of older individuals) is not eligi- ble for inclusion in this review	
Prat Gonzalez 2011	This study evaluated the effectiveness of an intervention to increase youth participation in the Health Prevention and Promotion Activities Programme (PAPPS). The intervention described in the study (letter and phone invitation) is not eligible for inclusion in this review	
Prins 1980	This cross-sectional study reported on people with hypertension and their willingness to have it checked. This study was excluded because it used the wrong study design; there was no control group and follow-up of at least 1 year was not provided	
Radice 1984	The aim of this cross-sectional study was to assess the efficacy of screening for arterial hyperten- sion in an adult population. The study authors concluded that there was no efficacy in screening for arterial hypertension; however, this study was excluded from this review because it used the wrong study design; there was no control group and follow-up of at least 1 year was not provided	
Ramsay 1997	This paper provided a critique of the Hypertension Detection and Follow-up Program. It is not an empirical study; therefore it used the wrong study design	
Risse 2015	This study evaluated the feasibility and effectiveness of a high blood pressure screening strate- gy for unknown or insufficiently treated hypertensive patients with Self-Blood Pressure Measure- ments (SBPM) in barbershops. There was no control group; therefore this study was excluded from this review	
Schnohr 1975	This study reported on a 'heart-week' intervention whereby people attending supermarkets in Copenhagen were invited to have their blood pressure checked. Data were collected cross-section- ally; follow-up of at least 1 year was not provided, and no control group was included; therefore this study was excluded from this review	
Secrest 1994	This paper is a commentary by the National Institutes of Health, which is primarily responsible for collecting and disseminating information on detection and treatment of hypertension. This article is not an empirical study; therefore it used the wrong study design to be included in this review	

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tudy Reason for exclusion	
Shah 2013	This cross-sectional study reported on the prevalence of type 2 diabetes mellitus and hypertension and the influence of possible risk factors. This study was excluded because it used the wrong study design, there was no control group, and follow-up of at least 1 year was not provided
Soricelli 1975	The aims of this study were to determine the productive results of hypertension detection in pri- vate dental offices, to expand screening facilities for hypertension, and to encourage dentists to in- clude blood pressure screening as part of their physical examination of patients. This study was ex- cluded because it included no control group
Stamler 1978	This article is a commentary titled, "Where do we go in hypertension screening?"; it used the wrong study design so was excluded from this review
Takala 1983	This study reported on the Sakyla-Koylio project, which involved multi-phasic screening at the health centre level. There was no control group; therefore this study was excluded from this review
Taylor 1990	This cross-sectional study aimed to identify hypertensive patients engaging with general practice, who were then linked to treatment. It was not eligible for inclusion in this review because it used the wrong study design
van der Feen 1980	This paper reports on a hypertension screening programme that a physician introduced in his prac- tice in The Netherlands, specifically for men and women aged 31 to 60. There was no control group; therefore this study is not eligible for inclusion in this review
van der Graaf 2013	This study aimed to identify predictors of future cardiovascular events. It was excluded from this review because it included the wrong participants (i.e. hypertensive patients)
Velez 1983	This study tested 2 methods of referral for follow-up evaluation of patients with high blood pres- sure detected in the walk-in screening clinic of a Veterans Administration Medical Center (VAMC) during a 6-week period in June and July 1979. There was no control group, and the intervention be- ing studied is not eligible for this review
Verdesca 1974	This paper is a commentary on hypertension screening and follow-up. It is not an empirical study; therefore it was excluded from this review
Weinberger 1977	This article explores the approaches used to overcome the hypertension burden in the United States of America. It is a commentary and therefore used the wrong study design
Werba 2017	This study determined the efficacy and cost-effectiveness (i.e. change in cardiovascular risk factors and lifestyle vs costs) of ProSALUTE, a new organisational model of primary cardiovascular prevention. The intervention described in this study is not eligible for inclusion in this review
Whelton 2018	This paper presents a guideline for prevention, detection, evaluation, and management of high blood pressure in adults in the United States of America. It is not an empirical study; therefore it was excluded from this review
Wieliczky 1987	This cross-sectional study reported on blood pressure screening for all employees at Mercerville Nursing Center from August 1983 to July 1984. This study was excluded because it used the wrong study design, there was no control group, and follow-up of at least 1 year was not provided
Wilber 1972	This study evaluated various methods of screening for elevated blood pressure. There was no con- trol group, and the intervention described in this study was not eligible for this review
Xi'an Jiaotong University 2016	This study investigated the effects of interaction between environmental factors and genetic factors on long-term blood pressure based on 2 established cohorts, including "the cohort of Hanzhong adolescent hypertension study" and "the cohort of Mei county adult salt-sensitive hypertension study". There was no control group, and the intervention being studied was not eligible for this review

Screening strategies for hypertension (Review)

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# ADDITIONAL TABLES

# Table 1. Thresholds for hypertension screening

BP category	SBP (mmHg)	DBP (mmHg)
Previous guidelines (WHO 20	13)	
High	≥ 140 and	≥ 90
Current guidelines ( ACCF 202	18; Carey 2018; Whelton 2018)	
Normal	< 120 and	< 80
Elevated	120 to 129 and	< 80
Hypertension	Stage 1: 130 to 139 or	80 to 89
	Stage 2: ≥ 140 or	≥ 90
Hypertensive crisis	> 180 and/or	> 120

BP: blood pressure. DBP: diastolic blood pressure. mmHg: millimetres mercury. SBP: systolic blood pressure.

## APPENDICES

# **Appendix 1. Search strategies**

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to April 06, 2020>

# Search Date: 7 April 2020

1 mass screening/ 2 early diagnosis/ 3 (screen? or screened or screening?).tw,kf. 4 (early adj3 (detect\$ or diagnos\$ or intervent\$)).tw,kf. 5 detect\$.ti. 6 or/1-5 7 hypertension/di, pc 8 essential hypertension/di, pc 9 (hypertens\$ or prehypertens\$).ti,kf. 10 ((elevat\$ or increas\$ or lower or high or rais\$ or rising) adj2 (arterial pressure or blood pressure or diastolic pressure or systolic pressure)).tw,kf. 11 ((elevat\$ or increas\$ or lower or high or rais\$ or rising) adj2 (bp or dbp or hbp or sbp)).tw,kf. 12 or/7-11 13 randomized controlled trial.pt. 14 pragmatic clinical trial.pt. 15 controlled clinical trial.pt. 16 randomi\$.ab. 17 placebo.ab. 18 clinical trials as topic/ 19 randomly.ab. 20 trial.ti.

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21 multicenter study.pt. 22 non-randomized controlled trials as topic/ 23 interrupted time series analysis/ 24 controlled before-after studies/ 25 groups.ab. 26 (multicenter or multi center or multicentre or multi centre).ti. 27 intervention?.ti. 28 (effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment\$ or quasi experiment\$ or evaluat\$ or time series or time point? or repeated measur\$).tw. 29 exp cohort studies/ 30 (cohort adj2 (analys\$ or design? or stud\$)).tw,kf. 31 epidemiologic methods/ 32 limit 31 to yr=1971-1988 33 or/13-30,32 34 animals/ not (humans/ and animals/) 35 33 not 34 36 6 and 12 and 35

Database: Cochrane Hypertension Specialised Register via Cochrane Register of Studies (CRS-Web)

#### Search Date: 8 April 2020

#1 MESH DESCRIPTOR Mass Screening AND INSEGMENT
#2 MESH DESCRIPTOR Early Diagnosis AND INSEGMENT
#3 (screen\* OR screened OR screening\*) AND INSEGMENT
#4 (early NEAR3 (detect\* OR diagnos\* OR intervent\*)) AND INSEGMENT
#5 detect\*:TI AND INSEGMENT
#6 (#1 OR #2 OR #3 OR #4 OR #5) AND INSEGMENT
#7 RCT:DE AND INSEGMENT
#8 Review:ODE AND INSEGMENT
#9 (#7 OR #8) AND INSEGMENT
#10 #6 AND #9 AND INSEGMENT
#11 \* AND INSEGMENT AND 01/11/2018\_TO\_08/04/2020:CRSCREATED
#12 #11 AND #10

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\_\_\_\_\_

#### Database: Cochrane Central Register of Controlled Trials (Issue 3, 2020) via Cochrane Register of Studies (CRS-Web)

#### Search Date: 8 April 2020

#1 MESH DESCRIPTOR Mass Screening AND CENTRAL: TARGET #2 MESH DESCRIPTOR Early Diagnosis AND CENTRAL: TARGET #3 (screen\* OR screened OR screening\*) AND CENTRAL:TARGET #4 (early NEAR3 (detect\* OR diagnos\* OR intervent\*)) AND CENTRAL: TARGET #5 detect\*:TI AND CENTRAL:TARGET #6 #1 OR #2 OR #3 OR #4 OR #5 AND CENTRAL: TARGET #7 MESH DESCRIPTOR Hypertension WITH QUALIFIER DI PC AND CENTRAL:TARGET #8 MESH DESCRIPTOR Essential Hypertension AND CENTRAL: TARGET #9 (hypertens\* OR prehypertens\*):TI AND CENTRAL:TARGET #10 ((elevat\* OR increas\* OR lower OR high OR rais\* OR rising) NEAR2 (arterial pressure OR blood pressure OR diastolic pressure OR systolic pressure)) AND CENTRAL: TARGET #11 ((elevat\* OR increas\* OR lower OR high OR rais\* OR rising) NEAR2 (bp OR dbp OR hbp OR sbp)) AND CENTRAL:TARGET #12 #7 OR #8 OR #9 OR #10 OR #11 AND CENTRAL: TARGET #13 #6 AND #12 AND CENTRAL:TARGET #14 \* AND 01/11/2018\_TO\_08/04/2020:CRSINCENTRAL AND CENTRAL:TARGET #15 #14 AND #13

# Database: Embase <1974 to 2020 April 03>

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## Search 7 April 2020

- 1 \*mass screening/
- 2 \*early diagnosis/
- 3 (screen? or screened or screening?).ti.
- 4 (screen? or screened or screening?).ab. /freq=2
- 5 (early adj3 (detect\$ or diagnos\$ or intervent\$)).tw.

\_\_\_\_\_

- 6 or/1-5
- 7 hypertension/di, pc
- 8 (hypertens\$ or prehypertens\$).ti.

9 ((elevat\$ or increas\$ or lower or high or rais\$ or rising) adj2 (arterial pressure or blood pressure or diastolic pressure or systolic pressure)).tw.

- 10 ((elevat\$ or increas\$ or lower or high or rais\$ or rising) adj2 (bp or dbp or hbp or sbp)).tw.
- 11 or/7-10
- 12 randomized controlled trial/
- 13 crossover procedure/
- 14 double-blind procedure/
- 15 (randomi?ed or randomly).tw.
- 16 (crossover\$ or cross-over\$).tw.
- 17 placebo.ab.
- 18 (doubl\$ adj blind\$).tw.
- 19 assign\$.ab.
- 20 allocat\$.ab.
- 21 time series analysis/
- 22 groups.ab.
- 23 (multicenter or multi center or multicentre or multi centre).ti.
- 24 intervention?.ti.

25 (effect? or impact? or controlled or control group? or (before adj5 after) or (pre adj5 post) or ((pretest or pre test) and (posttest or post test)) or quasiexperiment\$ or quasi experiment\$ or evaluat\$ or time series or time point? or repeated measur\$).tw.

- 26 exp cohort analysis/
- 27 (cohort adj2 (analys\$ or design? or stud\$)).tw.
- 28 exp longitudinal study/
- 29 exp prospective study/
- 30 or/12-29
- 31 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
- 32 30 not 31
- 33 6 and 11 and 32

\_\_\_\_\_

## Database: LILACS Bireme Search Date: 9 April 2020

(tw:("early diagnosis" OR "early detection" OR screening)) AND (tw:("high blood pressure" OR hypertension OR prehypertension)) AND (instance:"regional") AND ( db:("LILACS") AND type\_of\_study:("clinical\_trials" OR "cohort" OR "systematic\_reviews") AND limit: ("humans"))

Database: ClinicalTrials.gov Search Date: 9 April 2020

Condition or disease: Hypertension

Intervention/treatment: "early diagnosis" OR "early detection" OR screening

\_\_\_\_\_

\_\_\_\_\_

Database: WHO International Clinical Trials Registry Platform (ICTRP) Search Date: 29 November 2018

Title: high blood pressure OR hypertension OR prehypertension

Screening strategies for hypertension (Review)



Intervention: "early diagnosis" OR "early detection" OR screening Recruitment status: ALL

# OR

Condition: healthy OR hypertension OR prehypertension Intervention: "early diagnosis" OR "early detection" OR screening Recruitment status: ALL

OR

Title: "early diagnosis" OR "early detection" OR screening Condition: healthy OR hypertension OR prehypertension Recruitment status: ALL

\_\_\_\_\_

# WHAT'S NEW

Date	Event	Description
21 May 2020	Amended	Minor amendment: corrected image type for Figure 1

# HISTORY

Protocol first published: Issue 11, 2018 Review first published: Issue 5, 2020

Date	Event	Description
16 January 2019	Amended	Amended to include correct citation for the other published ver- sion of this protocol in <i>BMJ Open</i>

# CONTRIBUTIONS OF AUTHORS

All review authors read and approved the final manuscript.

# DECLARATIONS OF INTEREST

BS: nothing to declare.

SD: nothing to declare.

IT: nothing to declare.

CMB: nothing to declare.

AH: nothing to declare.

EN: nothing to declare.

JJM: nothing to declare.

TK: nothing to declare.



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salary support

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# DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There were no differences in the conduct of this review and the protocol.

# INDEX TERMS

# Medical Subject Headings (MeSH)

Early Diagnosis; Hypertension [\*diagnosis]; Mass Screening

# **MeSH check words**

Humans