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[Intervention Protocol]

Community and home-based exercise for the prevention and treatment of hypertension

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

The objective of this review is to assess the effects of community and home-based exercise interventions for the prevention and treatment of hypertension.

BACKGROUND

Description of the condition

Hypertension (elevated blood pressure) is a global public health concern, affecting more than one billion people globally (WHO 2013). Hypertension is an important risk factor for non-communicable diseases, particularly cardiovascular, cerebrovascular, and peripheral vascular disease, which are associated with high morbidity and mortality (National Heart Foundation of Australia 2016; WHO 2014). Untreated, hypertension can lead to heart failure, ischaemic and haemorrhagic stroke, chronic kidney disease, retinal haemorrhage, visual impairment, and vascular dementia (WHO 2018a). Diseases arising from hypertension reduce people's functional capacity and quality of life, and reduced functional capacity often results in a concomitant reduction in social and economic activity. Further, the World Health Organization (WHO) estimates that complications of hypertension cause the deaths of 9.4 million people every year, accounting for at least 45% of deaths due to ischaemic heart disease and 51% of deaths due to cerebrovascular disease (WHO 2013).

Hypertension is traditionally measured manually using a sphygmomanometer and stethoscope, or more recently using an automated sphygmomanometer. Blood pressure is liable to change, so a diagnosis of hypertension is made only if blood pressure is demonstrated to be high at repeated measurements. Blood pressure is usually measured as systolic pressure over diastolic pressure, that is the highest measured pressure in arteries when the heart is at the peak of contraction to expel blood from the ventricles (during systole) over the lowest measured pressure when the heart is at maximal relaxation to draw blood in to the ventricles (in diastole).

The WHO defines hypertension as systolic blood pressure of 140 millimetres of mercury (mmHg) or greater, or diastolic blood pressure of 90 mmHg or more (or both) (WHO 2013; WHO 2018a). More detailed classifications of hypertension vary between countries. The current Australian classifications of hypertension are as follows.

- Grade 1 (mild): systolic blood pressure of 140 mmHg to 159 mmHg and/or diastolic blood pressure of 90 mmHg to 99 mmHg
- Grade 2 (moderate): systolic blood pressure of 160 mmHg to 179 mmHg and/or diastolic blood pressure of 100 mmHg to 109 mmHg
- Grade 3 (severe): systolic blood pressure of 180 mmHg or more and/or diastolic blood pressure of 110 mmHg or more
- Isolated systolic hypertension: systolic blood pressure greater than 140 mmHg and diastolic blood pressure less than 90 mmHg (National Heart Foundation of Australia 2016)

Revised American guidelines released in November 2017 lowered the threshold for diagnosis of hypertension to 130/80 mmHg (Whelton 2017), a level that under previous classification criteria would be "borderline" or "pre-hypertensive" (ACSM 2004). The European guidelines are, however, aligned with the WHO criteria (Williams 2018).

Hypertension is considered to be a disease of lifestyle and is at least partly modifiable by increased physical activity (particularly aerobic exercise), smoking reduction or cessation, and reduced dietary intake of salt and alcohol (National Heart Foundation

of Australia 2016). Diseases of lifestyle may be anticipated to be highly prevalent in wealthy countries where food is available in abundance and physical activity is reduced through the use of labour-saving devices. However, high prevailing levels of hypertension are also observed in countries where Western lifestyles (i.e. high-fat, high-protein diets; abundant food; low levels of incidental physical activity) are viewed as favourable and as evidence of increasing wealth. Hypertension is particularly prevalent in the African region (27%), with some variation by country (WHO 2019). In a national South African survey, an estimated 59% of black Africans visiting general practices had hypertension (Connor 2005). However, these data are of limited use to determine actual care need, potential care costs, or burden of disease on the healthcare system because many South Africans report going without medical care due to living in resource-limited communities (Kon 2008).

The WHO 2011 status report on non-communicable diseases included prevalence estimates of hypertension using data gathered in 2008. In several African countries, prevalence was around 40% (Botswana: 40.8%; Namibia: 43.4%; South Africa: 42.4%, though this was slightly higher in men (43.4%) than women (41.4%); Tanzania: 39.2%; Zambia: 40.1%; and Zimbabwe: 39%). Limited healthcare resources, as well as social influences that compromise care seeking and disease tracking (e.g. civil unrest, war), mean that for some countries, prevalence estimates could not be made (e.g. Burkina Faso; Sudan) (WHO 2011). In the most recent WHO 2018 report on non-communicable diseases (WHO 2018a), prevalence estimates for raised blood pressure were revised, showing reduced hypertension prevalence in Africa (Botswana: 23%; Central African Republic: 25%; Kenya: 20%; Namibia: 22%; Niger: 27%; Nigeria: 18%; South Africa: 24%; Tanzania: 21%; Zambia: 20%; Zimbabwe: 20%). These revised data give room to question the validity of the 2008 data in the WHO 2011 report. Regardless of the precise values, there are high prevailing levels of hypertension in Africa.

Description of the intervention

Evidence from high income countries indicates that lifestyle modifications can be employed to reduce hypertension and that in early hypertension (Grade 1 or mild hypertension) such interventions are likely to be adopted with the greatest ease, identifiable benefit, and least risk (ACSM 2004). For example, engaging in regular aerobic physical activity such as brisk walking for at least 30 minutes a day, most days of the week, for a minimum of 150 minutes per week, has the potential to reduce systolic blood pressure by 4 to 9 mmHg (ACSM 2004); and reducing body mass from overweight to a healthy range by means of limited calorie intake and adequate daily physical activity has the potential to reduce systolic blood pressure by 5 to 20 mmHg for every 10 kg body mass reduction (ACSM 2004). A more recent meta-analysis reported that the effect of structured exercise interventions on systolic blood pressure still remain under-studied (Naci 2019).

Although regular physical activity is a recognised, available, affordable approach to manage (reduce) hypertension, levels of inactivity remain very high. The WHO recommends that children and adolescents should do at least 60 minutes of moderate- to vigorous-intensity physical activity daily and that adults aged up to 64 years should do at least 150 minutes of moderate-intensity physical activity, or at least 75 minutes of vigorous-intensity physical activity, throughout the week. In addition, muscle strengthening exercise should be included two days per

week (WHO 2018b). The WHO estimates that globally, one in four adults, and four in five adolescents, are not physically active enough to achieve health benefits (WHO 2018b). "Physical inactivity" is defined by the WHO as not meeting the WHO recommendations for physical activity (WHO 2018a).

South Africa is the country with the highest level of physical inactivity in Africa; 37% of South Africans (48% of women, 26% of men) report undertaking insufficient levels of physical activity. Several other African countries show similar behaviour patterns, but inactivity varies considerably across Africa (Botswana: 20%; Central African Republic: 13%; Kenya: 14%; Namibia: 31%; Niger: 21%; Nigeria: 25%; Tanzania: 6%; Zambia: 20%; Zimbabwe: 25%), with considerable disparity between urban and rural dwellers, and between men and women (WHO 2018a).

Although several studies have investigated physical activity in the African context, most measures have used subjective questionnaires, an approach limited by reporting bias because participants provide answers that conform to socially desirable expectations (Aubert 1998; Prince 2008). Results from an unpublished study at North-West University indicates that people from low-resource communities in the North-West Province of South Africa have limited knowledge about hypertension and the role of regular physical activity as a potential intervention strategy (Makamu 2015).

Current management guidelines for hypertension include a strong recommendation that lifestyle advice is offered to all patients (National Heart Foundation of Australia 2016), whilst considering the diverse context from low- to middle-income countries and high-income countries (Unger 2020). A review undertaken by a South African research team, commissioned by the WHO, identified "what works" by way of community interventions for promoting a healthy diet and physical activity (Anderson 2009). Home and community-based interventions are likely to be more available and affordable for people in resource-limited communities than are supervised and practitioner-led interventions.

How the intervention might work

A selection of factors that give rise to hypertension include atherosclerosis (the build-up of plaque in arteries), insulin resistance, dyslipidemia (abnormal levels of lipids (fats) in the blood), an increase in sympathetic drive, and a decrease in beta cholinergic receptor sensitivity; these factors can be influenced by exercise. Regular exercise at intensities of between 65% and 85% of heart rate reserve is documented to produce physiological adaptations in the vascular system, leading to a reduction in peripheral resistance (ACSM 2004). Vasodilatation (widening of blood vessels) has been observed due to an increase in the formation of nitric oxide (NO); this causes a decrease in peripheral resistance which results in a hypotensive effect (lowering of the blood pressure) that can last up to 22 hours following a single training session (Carpio-Rivera 2016).

Regular aerobic exercise improves blood pressure through central and peripheral vasodilation, reduction in inflammatory markers, reactive hyperaemia (temporary increase in blood flow), reduced body fat, improved control of glucose and lipids (thus regulating insulin resistance and hypertriglyceridemia), reduced stress, and increased relaxation (which leads to decreased sympathetic drive and improved autonomic regulation) (ACSM 2004; National Heart

Foundation of Australia 2016). These physiological benefits may reduce mortality and morbidity as well as reduce hypertension itself (Antonakoudis 2007). Improved physiological functioning may improve health-related quality of life, which may, in turn, improve the economic activity of individuals (Seals 2016).

Why it is important to do this review

Hypertension is a modifiable risk factor for cardiovascular disease. Reduction in hypertension is likely to reduce pathological diseases caused by high blood pressure, which have substantial morbidity and mortality. The WHO summarised the global health concern of hypertension as follows.

"Hypertension is a silent, invisible killer that rarely causes symptoms.... Raised blood pressure is a serious warning sign that significant lifestyle changes are urgently needed. It disproportionately affects populations in low- and middle-income countries where health systems are weak.... Addressing behavioural risk factors, e.g. unhealthy diet, harmful use of alcohol and physical inactivity, can prevent hypertension. ... Integrated non-communicable disease programmes implemented through a primary health care approach are an affordable and sustainable way for countries to tackle hypertension." (WHO 2013)

There are high prevailing levels of hypertension in Africa, concurrent with resource limitations in many communities, which raises sustainability questions regarding long-term drug therapies (Seedat 2012). The ongoing costs of pharmaceuticals may make these interventions prohibitive, particularly if limited to prescription only, which adds the cost of clinical consultations to the costs of the medicines themselves. Further, the use of pharmacotherapy in control of hypertension is open to some conjecture. A 2012 Cochrane Review identified that pharmacotherapy provided no demonstrable benefits in the management of mild hypertension (Diao 2012). Across four included trials there were no demonstrable benefits in mortality or morbidity from pharmacotherapy alone, but 9% of participants discontinued pharmacotherapy due to adverse events. Inconsistencies in findings from interventions with pharmacotherapy indicate that alternative interventions should be considered (Webster 2018)

A recent meta-analysis of 391 randomised controlled trials found that aerobic and strength training exercises are as effective as medication for lowering systolic blood pressure (Naci 2019). Home-based and community-based interventions are likely to be more available and affordable for people with hypertension in resource-limited communities. A 2005 WHO review of best practices to promote physical activity in developing countries included recommendations to raise awareness of the importance and benefits of physical activity, educate the population, conduct local programmes, build capacity, create supportive environments, and give recognition to those who are physically active (Bauman 2005). A further review undertaken by a South African research team, commissioned by the WHO, reviewed "what works" by way of community interventions for promoting a healthy diet and physical activity: community-level interventions were highly regarded, but neither of these larger-scale reviews specifically measured the effects of physical activity to change health outcomes (Anderson 2009). Rather, "what worked" was defined as interventions that were "stickable", that is, interventions that produced compliance. As a first step, these reviews were important; an intervention

cannot possibly be effective if it is not sufficiently undertaken, maintained, or completed. Our Cochrane Review will add to the existing body of knowledge by determining whether community and home-based exercise interventions are effective for reducing a measurable risk factor for serious diseases (i.e. hypertension).

We will collate known data on community and home-based physical activity interventions for the reduction of blood pressure, to determine which interventions are the most effective and safest. This information is important to allow community leaders and individuals in resource-limited environments to make evidence-based choices about interventions and care-seeking for hypertension. If there are insufficient trials or data from which to draw firm conclusions, the review will be used for recommendations to researchers on the design and development of future intervention studies.

We will limit our review to community and home-based exercise interventions only, excluding trials of interventions in specialised laboratories or gymnasium facilities, to ensure that the results are applicable to resource-limited settings such as those found in many African countries. Our review is important because it will inform clinicians as to whether the outcomes of accessible, affordable community and home-based interventions are comparable with less accessible, more expensive, structured, supervised exercise. Further, our review could assist healthcare professionals to design appropriate exercise management plans for hypertensive adults in low-resource communities. This information may also be used in influencing policy to drive the appointment of clinical exercise physiologists in low-resource communities to oversee exercise interventions for health outcomes.

OBJECTIVES

The objective of this review is to assess the effects of community and home-based exercise interventions for the prevention and treatment of hypertension.

METHODS

Criteria for considering studies for this review

Types of studies

We will include all randomised controlled trials (RCTs) which examine the effects of exercise for the prevention or treatment of hypertension. We will include parallel and cross-over trials, and cluster-RCTs, using either non-intervention or active controls.

We will include all trials in which hypertension is defined according to published diagnostic criteria. Trials with vague definitions of hypertension (e.g. 'high blood', 'blood pressure'), without measured diagnostic criteria, will not be considered. Trials which define hypertension according to incomplete or partial diagnostic criteria will be included, and notes will be provided to identify possible weaknesses in selection.

We will seek trials comparing the following.

- Community or home-based exercise (resistance or aerobic) versus no exercise or wait-list control
- Community or home-based exercise versus practitioner-supervised exercise

- Community or home-based exercise versus active control (i.e. pharmacological management or dietary modification)

Studies in which community or home-based exercise is used adjunctive to other therapies, such as pharmacological management or dietary modification, will be included if the effect of the exercise intervention alone can be determined. Studies in which hypertension is part of a broader diagnosis (such as type 2 diabetes or cardiovascular disease) will be included if the effect of interventions on blood pressure are reported.

We will exclude cross-over trials without pre-cross-over data, due to the carry-over effect of exercise interventions and the impossibility of a wash-out period.

Types of participants

We will include trials with adult participants (aged 18 years or more) without regard to race or gender. Studies in children, and studies of hypertension or pre-eclampsia in pregnant women, will be excluded. Treatment trials will include participants with diagnosed hypertension of any severity and duration, treated or not treated with anti-hypertensive medication, assessed in primary care, outpatient, or community settings.

Types of interventions

We will consider trials that employ home-based exercise interventions (e.g. walking, unsupervised gym training, incidental activities) and community-based exercise interventions (e.g. community sport, recreation, and traditional dancing) for the purpose of preventing or reducing blood pressure. Because hypertension is a chronic condition that requires ongoing management, we will not limit studies by duration of intervention.

Types of outcome measures

Outcome measures considered will be consistent with those used across Cochrane Hypertension systematic reviews of interventions. To assess the effects of exercise for the prevention or treatment of hypertension, we will extract data on the following.

- Measurements of blood pressure in both intervention and comparator groups
- Incidence (i.e. new cases) of hypertension in both intervention and comparator groups
- Prevalence (i.e. continuing cases) of hypertension in both intervention and comparator groups

Primary outcomes

- Change in mean systolic and diastolic blood pressure, measured in mmHg
- Change in mean arterial pressure, measured in mmHg
- Adverse events, measured as counts of mortality, or participants reporting any adverse event, or withdrawal due to adverse events

A primary outcome measure of hypertension is a criterion for inclusion; studies that do not include at least one primary outcome measure of hypertension will be excluded.

Secondary outcomes

- The proportion of participants achieving target blood pressure, as defined by each trial's investigators
- Incidence (new cases) of hypertension identified within the period of a trial, measured as counts
- Prevalence (continuing cases) of hypertension identified within the period of a trial, measured as counts
- Change in anti-hypertensive medication use, measured as change in a regular dose
- Change in categorical classification of hypertension, as defined by the investigators of each trial

We will not extract data for the following (however, where possible, we will include notes on these factors as confounders or covariates).

- Cardiovascular risk factors e.g. family history, smoking, alcohol consumption
- Changes in medications known to alter cardiovascular function e.g. anti-retrovirals, glucocorticoids
- Standardised measures of cardiovascular fitness e.g. VO₂ peak (maximal oxygen consumption during incremental exercise that does not plateau), VO₂ max (the point where oxygen uptake no longer increase with an increase in workload)
- Body composition e.g. body mass index (BMI), waist circumference, waist-to-hip ratio
- Blood markers related to cardiovascular physiology
- Use of other medications
- Cardiovascular imaging e.g. Doppler ultrasound, angiography
- Electrocardiogram (ECG) data
- Quality of life

Search methods for identification of studies

Electronic searches

The Cochrane Hypertension Information Specialist will search the following databases, without restrictions on language, publication year, or publication status.

- The Cochrane Hypertension Specialised Register via the Cochrane Register of Studies (CRS-Web)
- The Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies (CRS-Web)
- MEDLINE Ovid (from 1946 onwards), MEDLINE Ovid Epub Ahead of Print, and MEDLINE Ovid In-Process & Other Non-Indexed Citations
- Embase Ovid (from 1974 onwards)
- CINAHL EBSCO (from 1982 onwards)
- SPORTDiscus (from date of inception)
- ClinicalTrials.gov (www.clinicaltrials.gov)
- World Health Organization International Clinical Trials Registry Platform (www.who.it.trialsearch)

The subject strategies for databases will be modelled on the search strategy designed for MEDLINE in [Appendix 1](#). Where appropriate, these will be combined with subject strategy adaptations of the sensitivity- and precision-maximising search strategy designed by Cochrane for identifying RCTs (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2020](#))).

Searching other resources

- The Cochrane Hypertension Information Specialist will search the 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 can 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, CINAHL, ProQuest Dissertations & Theses and Web of Science.
- We will search Epistemonikos for related systematic reviews.
- We will check the bibliographies of included studies and any relevant systematic reviews identified for further references to relevant trials.
- We will contact experts/organisations in the field to obtain additional information on relevant trials.
- We may contact original authors for clarification and further data if trial reports are unclear.
- We will seek unpublished research reports and theses (grey literature) directly from university libraries and other third parties.

Data collection and analysis

All stages of data collection and analysis will be completed by at least two review authors, acting independently. Potential disagreements will be discussed with all review authors and resolved by referring to the original protocol. If consensus cannot be reached between the authors, then disagreements will be referred to a third author for resolution.

Selection of studies

All titles and abstracts identified from electronic databases and other searches will be independently examined by two investigators (MC, SJM). We will use [Covidence](#) for the screening of trials. The full manuscript will be retrieved for each record that has the possibility of meeting the review criteria. Two review authors, acting independently, will assess the eligibility of retrieved studies, according to the inclusion criteria. If consensus cannot be reached between the authors, then disagreements will be referred to a third author for resolution.

Data extraction and management

Data will be extracted from each eligible study by two review authors, independently. All extracted data will be entered into [Covidence](#). Because we anticipate including a large number of studies in this review, as well as studies in languages other than English, all investigators (MC, SJM, SOO, SM) will contribute to data extraction. Any disagreements in data extraction will be discussed with all review authors and resolved by referring to the original protocol.

Two review authors will independently extract the following data from the included trials and enter the data into Review Manager Web ([RevMan Web 2019](#)).

- Trial characteristics, including size, location, and source of funding

- Characteristics of the study population, including age, and characteristics of the clinical presentation (i.e. risk of hypertension, stage of hypertension)
- Characteristics of the therapy in all trial arms, including type and duration of intervention
- Information on the Cochrane 'Risk of bias' domains (as outlined in [Assessment of risk of bias in included studies](#))
- Outcome measures, mean and standard deviation for continuous outcomes, and number of events for dichotomous outcomes (as outlined in [Types of outcome measures](#))

To avoid multiple outcome reporting in the review, we will apply the following rules to extract data.

- We will extract data from the last time point in each trial. Where possible, we will also extract data from earlier time points to allow data pooling with trials of shorter duration.
- Where outcomes were reported at several time points, we will extract the measure at the end of the intervention as the main outcome. Studies of similar duration will be analysed using the end-of-intervention data only. We will also extract data at interim time points only when there is the opportunity to pool these data with trials of shorter durations, and we will clearly identify these data as being non-end-point data.
- Where trial authors report both final values and change from baseline values for the same outcome, we will extract final values.
- Where trial authors report data analysis based on the intention-to-treat (ITT) sample and another sample (e.g. per-protocol, as-treated), we will extract ITT-analysed data.
- For cross-over trials, data will be extracted only up to the point of cross-over, given the potential for carry-over effects of interventions to bias results following cross-over.

Adverse events will be measured as the number of participants experiencing any adverse event, who withdrew or dropped out because of adverse events, and who experienced any serious adverse events. Serious adverse events are defined as events resulting in in-patient hospitalisation, prolongation of hospitalisation, persistent or significant disability, congenital abnormality or birth defect of offspring, life-threatening events, or death.

If additional data are required, we will contact the trial authors to obtain these data. If study authors are unavailable, or the data are not provided, we will impute data where possible. Where data are imputed or calculated (e.g. standard deviations calculated from standard errors, P values, or confidence intervals; last measures carried forward; results imputed from graphs; or from the standard deviations in other trials) we will report these adjustments in the characteristics of included studies.

Assessment of risk of bias in included studies

Two review authors, acting independently, will use the Cochrane 'Risk of bias' tool to assess the risk of bias of each included trial against the following key criteria: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias ([Higgins 2017](#)). For each study, each of these criteria will be explicitly judged to be at low risk of bias, unclear risk of bias (due to lack of information

or uncertainty over the potential for bias), or high risk of bias. Potential disagreements in assessment will be discussed with all review authors and resolved by referring to the original protocol.

We will also use the 'Risk of bias' tool to assess attrition bias by looking at the completeness of outcome data for each main outcome, including the number of dropouts or withdrawals in each group and whether dropout rates were reported and included in the analysis. 'Risk of bias' judgements will be used to inform the analysis and interpretation of results. We will include notes on risk of bias in the narrative descriptions of each included trial. If any trial is judged to be at high risk of bias across all categories, we will downgrade the certainty of evidence from that trial in our analysis.

Measures of treatment effect

When possible, the analyses will be based on ITT data (outcomes provided for every randomised participant) from the individual trials. For each trial, we will present outcome data as point estimates, with mean and standard deviation for continuous outcomes, and risk ratio (RR) with corresponding 95% confidence intervals (CIs) for dichotomous outcomes.

Where possible, for continuous outcomes, we will extract data as change-from-baseline rather than absolute scores at the end of treatment. Pooled effects of treatment will be presented as mean differences (MDs) and 95% CIs. If multiple trials used different scales to measure the same outcome or concept, we will calculate the treatment effect as standardised mean difference (SMD). Outcomes pooled using SMD will be re-expressed as MD by multiplying the SMD by a representative control-group baseline standard deviation from one trial using a familiar instrument.

Although hypertension is an independent predictor of cardiovascular disease risk, and lowering blood pressure reduces cardiovascular events and all-cause mortality, effective treatment targets have been subject to frequent change and debate ([National Heart Foundation of Australia 2016](#)). Treatment effect sizes in this review will be discussed with reference to treatment targets in hypertension rather than any agreed minimum clinically important difference.

Unit of analysis issues

Where a study is defined as a cross-over trial, data will be extracted only up to the point of cross-over, given the potential for carry-over effects of these particular interventions to bias the treatment effect following cross-over.

Dealing with missing data

Data missing from published studies will be sought directly from the trial authors. Details of author responses, as well as data conversion and imputation, will be explained in the 'Characteristics of included studies' and associated tables.

If data cannot be provided, then we will impute missing data using the 'last observation carried forward' method. For dichotomous outcomes, we will use the number randomised as the denominator, making the assumption that any participants missing at the end of treatment did not have a positive outcome. For continuous outcomes with no standard deviation reported, we will calculate standard deviations, where possible, from standard errors (SEM), P values, or CIs. If no measures of variance are reported, standard deviation cannot not be calculated, and only a small proportion

of studies in the meta-analysis have missing data, we will impute standard deviations from other studies in the same meta-analysis, using the average of the other standard deviations available provided.

Assessment of heterogeneity

We will assess included trials for clinical homogeneity in terms of participants, interventions, and comparators. For studies judged as clinically homogenous, we will quantify the possible magnitude of inconsistency (heterogeneity) across studies using the I^2 statistic, with a guide to interpretation as follows: 0% to 40% might not be important; 30% to 60% might represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% represents considerable heterogeneity (Deeks 2011). Where the I^2 value is greater than 50%, we will not pool studies for meta-analysis and we will narratively describe the findings instead.

Assessment of reporting biases

As one method to examine the possibility of publication bias, we will construct funnel plots if at least 10 studies are available for the meta-analysis of a primary outcome. Asymmetric funnels plots are not necessarily caused by publication bias, but the omission of negative trials indicates the possibility of a "file drawer effect" (Rosenthal 1979). We will also assess the presence of small-study bias in the overall meta-analysis by checking if the random-effects model estimate of the intervention effect is more beneficial than the estimate using the fixed-effect model.

Data synthesis

Descriptive results will be reported for all included studies. We will pool data from clinically homogenous trials (i.e. those with the same interventions, doses, comparators, and outcomes). Data will be synthesised according to expected pair-wise comparisons of exercise versus no exercise, home or community exercise versus supervised exercise, exercise adjunctive to pharmacotherapy versus pharmacotherapy alone, and home or community exercise versus another active control (e.g. dietary modification, smoking cessation). Where we cannot combine data, we will summarise effect estimates and 95% CIs of each trial narratively.

Subgroup analysis and investigation of heterogeneity

If there are sufficient data, we will conduct subgroup analyses for all outcomes according to gender (i.e. male, female, transgender). Because we are particularly concerned about the prevention and treatment of hypertension in low-resource communities, we will, where possible, group studies according to equity parameters (e.g. low-, middle-, or high-income country).

If moderate to substantial heterogeneity is present in any pooled studies, we will investigate the possibility of subgrouping by type and length of intervention in order to explain the heterogeneity.

Sensitivity analysis

Typically, sensitivity analyses would be conducted to investigate the robustness of the intervention effects on subjective outcomes (e.g. quality of life), relative to allocation concealment and participant blinding. In exercise intervention trials, participant blinding is almost impossible (i.e. participants know whether they are exercising or not), examiner blinding may be difficult (i.e. examiners may observe exercise training effects in participants and be able to deduce the groups to which they were allocated), and allocation concealment is unlikely to reduce these study limitations. We will consider other sensitivity analyses if there are substantial differences in trial design and quality within a meta-analysis. Further, low quality trials that meet inclusion criteria will be included in analyses, but due to poor trial design, we may downgrade our confidence in the results of these trials.

Summary of findings and assessment of the certainty of the evidence

At least two review authors will assess the certainty of the supporting evidence behind each estimate of treatment effect, using the GRADE approach (Schunemann 2011). This will take into account the methodological quality, directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias. We will present key findings of the review, including a summary of the amount of data, the magnitude of the effect size and the overall certainty of the evidence. GRADEPro GDT software will be utilised to prepare 'Summary of findings' tables (GRADEpro GDT). We have preselected the following important outcomes for inclusion in the 'Summary of findings' tables.

- Change in mean systolic blood pressure
- Change in mean diastolic blood pressure
- Change in mean arterial pressure
- The proportion of participants achieving target blood pressure
- Adverse events

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APPENDICES

Appendix 1. MEDLINE search strategy

- 1 exp exercise/
- 2 exp exercise therapy/
- 3 exp sports/
- 4 exp exercise movement techniques/
- 5 exp walking/ or exp running/
- 6 exp dancing/
- 7 gardening/

- 8 physical exertion/
9 (exercis\$ adj25 (activit\$ or bout? or community\$ or home\$ or intervention\$ or program\$ or regimen\$ or training\$)).tw,kf.
- 10 (aerobic exercis\$ or aerobics or bicycl\$ or cardio or cycling or dance or dancing or elliptical or football or gardening or isometric\$ or jogging or physical enduranc\$ or physical exert\$ or recreation\$ or resistance exercis\$ or resistance train\$ or running or soccer or sport? or swim or swimming or tai chi or tai ji or tennis or treadmill\$ or walking or weight lifting or weightlifting or work out? or workout? or yoga).tw,kf.
- 11 ((aerobic? or conditioning or muscl\$ or physical or resistance or strength or training or weight\$) adj2 activ\$).tw,kf.
- 12 ((aerobic? or conditioning or fitness or muscl\$ or physical or resistance or strength or training or weight\$) adj2 program\$).tw,kf.
- 13 ((aerobic? or conditioning or fitness or muscl\$ or physical or resistance or strength or training or weight\$) adj2 regimen\$).tw,kf.
- 14 ((aerobic? or fitness or physical or resistance or strength or weight\$) adj2 training\$).tw,kf.
- 15 or/1-14
- 16 hypertension/
17 essential hypertension/
18 hypertens\$.tw,kf.
- 19 ((elevated or high) adj2 blood pressur\$).tw,kf.
- 20 or/16-19
- 21 randomized controlled trial.pt.
- 22 pragmatic clinical trial.pt.
- 23 controlled clinical trial.pt.
- 24 randomi?ed.ab.
- 25 placebo.ab.
- 26 clinical trials as topic/
27 randomly.ab.
- 28 trial.ti.
- 29 or/21-28
- 30 animals/ not (humans/ and animals/)
- 31 29 not 30
- 32 15 and 20 and 31

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CONTRIBUTIONS OF AUTHORS

Melanie Cameron contributed to each stage of the protocol, including conceiving the protocol, designing the protocol, planning the search strategy, designing data extraction methods, planning data management and analysis, writing, proof-reading, editing the protocol, and responding to critique from reviewers.

Sarah Johanna Moss contributed to each stage of the protocol, including conceiving the protocol, designing the protocol, planning the search strategy, designing data extraction methods, planning data management and analysis, writing, proof-reading, editing the protocol, and responding to critique from reviewers.

Sweetness Makamu-Beteck contributed to conceiving the protocol and writing, proof-reading, and editing the protocol.

Sunday Onagbiye contributed to conceiving the protocol and writing, proof-reading, and editing the protocol.

DECLARATIONS OF INTEREST

Melanie Cameron: nothing to declare

Sarah Johanna Moss: nothing to declare

Sweetness Makamu-Beteck: nothing to declare

Sunday Onagbiye: nothing to declare

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