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Corresponding author:
Tongwu Yu

18101351378@163.com

Author Affiliation:
Anhui Communcaitions Vocational & Technical College.

Effects of high-intensity interval training on blood pressure, arterial stiffness, and endothelial function in adults with pre-hypertension and unmedicated stage 1 hypertension: a protocol for an umbrella review and hybrid meta-meta-analysis

Wang, S; Yu, TW.

ADMINISTRATIVE INFORMATION

Support - This review is conducted without external funding from any government agency, pharmaceutical company, device manufacturer, or commercial sponsor. All costs are met by the authors through institutional resources. The absence of commercial funding eliminates financial conflicts of interest pertaining to high-intensity interval training and the vascular outcomes under review. Should funding be secured after initial registration, this item will be updated and full disclosure of the funding source provided.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - All authors declare that they have no financial or non-financial conflicts of interest that could influence the conduct or conclusions of this review. No author has received payment, honoraria, or research funding from manufacturers of exercise equipment. No author has a personal, academic, or institutional interest in promoting or discouraging high-intensity interval training as a clinical intervention. No author holds a prior publication record that creates a directional bias in the assessment of included systematic reviews. These declarations will be updated if circumstances change during the conduct of the review..

INPLASY registration number: INPLASY202650057

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 May 2026 and was last updated on 10 May 2026.

INTRODUCTION

Review question / Objective In adults with pre-hypertension (resting systolic blood pressure 120 to 139 mmHg) or unmedicated stage 1 hypertension (resting systolic blood pressure 140 to 159 mmHg), does high-intensity interval training, compared with moderate-intensity continuous training or non-exercise sedentary control as reported in included systematic reviews with meta-analysis, produce clinically meaningful reductions in blood pressure, arterial stiffness, and endothelial function outcomes?
The review question is structured using the PICO framework adapted for umbrella reviews, where the unit of analysis is the systematic review rather than the primary study.

Rationale Cardiovascular disease attributable to elevated blood pressure constitutes one of the most consequential and modifiable public health burdens globally. Adults with pre-hypertension and unmedicated stage 1 hypertension occupy a

clinically critical stratum: blood pressure is already elevated to a degree associated with progressive vascular damage and increased cardiovascular risk, yet pharmacological intervention is not yet indicated or has been deferred in favour of lifestyle modification. For this population, exercise-based strategies represent the primary modifiable clinical lever, and their evidence base has accumulated substantially over the preceding decade.
High-intensity interval training has generated a large body of systematic reviews across cardiovascular and metabolic conditions. Umbrella reviews synthesising this evidence have been published for healthy adults, older adults, individuals with type 2 diabetes mellitus, and children and adolescents.

Condition being studied This review addresses two related cardiovascular conditions defined by blood pressure elevation below the threshold for routine pharmacological intervention. Pre-hypertension is defined as a resting systolic blood pressure of 120 to 139 mmHg or a resting diastolic blood pressure of 80 to 89 mmHg in the absence of antihypertensive medication, consistent with JNC 7 and related cardiovascular society criteria. Unmedicated stage 1 hypertension is defined as a resting systolic blood pressure of 140 to 159 mmHg or a resting diastolic blood pressure of 90 to 99 mmHg in the absence of antihypertensive pharmacotherapy. Both conditions are associated with progressive arterial stiffening, endothelial dysfunction, and increased lifetime cardiovascular risk. The co-occurrence of these conditions within a single review is justified by the contiguous clinical profile of both populations, which share the same evidence-based rationale for lifestyle modification through structured exercise.

METHODS

Search strategy Complete search strings for all five primary databases are provided below, written exactly as they would be entered into each database interface. All strings combine two blocks using AND: Block 1 captures review methodology terms (systematic review, meta-analysis, pooled analysis, umbrella review) and Block 2 captures topic-specific terms. Two additional mandatory sources (Cochrane Database of Systematic Reviews and the INPLASY register) are specified under Item 17. The strings would be improved in the final papers.
Database 1: PubMed / MEDLINE
((("systematic review"[ti] OR "meta-analysis"[ti] OR "pooled analysis"[ti] OR "umbrella review"[ti] OR "systematic review"[tiab] OR "meta-analysis"[tiab] OR "Meta-Analysis"[pt] OR "systematic[sb])) AND (("high-intensity interval training"[tiab] OR "HIIT"[tiab] OR "high intensity interval training"[tiab] OR "interval training"[tiab] OR "sprint interval training"[tiab] OR "SIT"[tiab] OR "high-intensity exercise"[tiab] OR "intermittent exercise"[tiab] OR "interval exerci.

Participant or population Eligible population: adults aged 18 years and older who, at the time of enrolment in the primary studies included in eligible systematic reviews, met the clinical definition of pre-hypertension or unmedicated stage 1 hypertension as follows:
Category Blood Pressure Criteria and Medication Status
Pre-hypertension Resting systolic blood pressure 120 to 139 mmHg OR resting diastolic blood pressure 80 to 89 mmHg; no antihypertensive pharmacotherapy; classification consistent with JNC 7 or equivalent cardiovascular society criteria.
Unmedicated stage 1 hypertension Resting systolic blood pressure 140 to 159 mmHg OR resting diastolic blood pressure 90 to 99 mmHg; confirmed absence of antihypertensive pharmacotherapy at enrolment; classification consistent with JNC 7, ESC, or ESH criteria.
Medication status Included systematic reviews must either explicitly state that participants were not receiving antihypertensive medication, or define the eligible population in terms that necessarily exclude medicated individuals (e.g., untreated hypertension, lifestyle modification cohort).
Mixed population handling Systematic reviews including a mixed population are eligible where results are reported stratified by blood pressure category, or where more than 70% of total enrolment falls within the eligible blood pressure range. In the latter case, the review is included and flagged for sensitivity analysis.
Age Adults 18 years and older with no upper age restriction.
Sex No restriction. Sex distribution is recorded at the review level; subgroup analyses by sex are pre-specified.
Comorbidities Reviews exclusively recruiting participants with concurrent clinical diagnoses are excluded unless stratum-specific results for the eligible population are reported separately.
Ineligible populations Participants with stage 2 or stage 3 hypertension (systolic blood pressure at or above 160 mmHg) without stratified reporting; participants receiving antihypertensive pharmacotherapy; children and adolescents under 18 years; pregnant women; participants with secondary hypertension.

Intervention The intervention of interest is high-intensity interval training in any format delivered to the eligible population. No restriction is imposed on any FITT parameter (frequency, intensity, time, type) at the review level; variation in FITT parameters is characterised during data extraction and examined as a potential source of heterogeneity across review findings.
Eligible formats include: sprint interval training with maximal or near-maximal effort work intervals; aerobic high-intensity interval training at 80% or above of maximal oxygen uptake or heart rate maximum; cycling-based, running-based, rowing-based, and other ergometer-based interval protocols; and resistance-based high-intensity interval protocols. The defining feature is structured alternation between high-intensity and recovery phases. Continuous exercise at a single intensity does not qualify regardless of absolute intensity.
HIIT parameters extracted from each included review: work interval duration; rest or recovery interval duration; work to rest ratio; intensity specification; total session duration; weekly session frequency; and total programme duration in weeks.

Comparator Moderate-intensity continuous training: structured continuous aerobic exercise at 40% to 59% of maximal oxygen uptake or 50% to 69% of heart rate maximum, sustained without structured recovery intervals. This comparator enables quantification of the incremental benefit of HIIT over the established exercise standard for blood pressure management.
Non-exercise sedentary control: a condition in which participants maintain habitual sedentary behaviour or receive no structured exercise, including waitlist controls, usual care controls defined as no structured exercise, and health education controls.
Other active comparators reported in eligible reviews (resistance training, combined training, other modalities) are eligible for extraction and qualitative synthesis but are not included in the primary quantitative meta-meta-analysis, which is restricted to comparisons against moderate-intensity continuous training or sedentary control.

Study designs to be included Only systematic reviews that conducted meta-analysis (quantitative pooling of primary study effect estimates producing a pooled effect estimate with confidence interval) are eligible as included studies. Standalone systematic reviews without meta-analysis are not eligible for the primary analysis.Justification: the research question is specifically formulated to address quantitative effect estimates and their credibility classification; this requires that included reviews provide pooled estimates that can be appraised and selectively re-pooled. The credibility classification framework applie.

Eligibility criteria All criteria are pre-specified and will not be modified after the formal search begins.
Inclusion Criteria
Criterion Specification
1)Study design Systematic review with meta-analysis. Must include a systematic search of at least two electronic databases, pre-specified inclusion and exclusion criteria, and a quantitative pooling procedure producing a pooled effect estimate with confidence interval for at least one eligible outcome.
2)Population Addresses adults with pre-hypertension, stage 1 hypertension, or an equivalent clinically elevated blood pressure category (systolic blood pressure 120 to 159 mmHg) as the primary or a clearly stratified secondary population, as specified in Item 12.
3)Intervention Includes at least one high-intensity interval training protocol as a distinct and extractable study arm.
4)Comparator Includes at least one eligible comparator (moderate-intensity continuous training or non-exercise sedentary control) against which HIIT outcomes are compared in the pooled analysis.
5)Outcome Reports a pooled effect estimate for at least one eligible vascular outcome: blood pressure (systolic or diastolic; clinic or ambulatory); arterial stiffness (pulse wave velocity, augmentation index, or central systolic blood pressure); or endothelial function (flow-mediated dilation, reactive hyperaemia index, or plasma nitric oxide concentration).
6)Effect measure Pooled effect estimate reported as a mean difference in mmHg (blood pressure), a mean difference or standardised mean difference with 95% confidence interval (arterial stiffness and endothelial function), or an equivalent continuous measure permitting extraction and conversion.
7)Publication status Published in a peer-reviewed journal. Conference abstracts and preprints are not eligible.
8)Language English language publications only.

Exclusion Criteria
Criterion Specification
1)Not a systematic review Narrative reviews, scoping reviews, expert consensus statements, and clinical practice documents are excluded; they do not apply a systematic search and formal inclusion criteria.

2)No meta-analysis Systematic reviews that did not conduct quantitative pooling are excluded from the primary analysis and documented in the PRISMA flow diagram.
3)Wrong population Reviews exclusively addressing stage 2 or stage 3 hypertension, medicated hypertension, normotensive adults, or paediatric populations without stratified data for the eligible stratum.
4)Wrong intervention Reviews that do not include a high-intensity interval training arm as a distinct and extractable intervention.
5)Wrong outcome Reviews reporting exclusively non-vascular outcomes without any eligible haemodynamic or vascular outcome.
6)Superseded Where a review has been formally updated by the same author group, only the most recent update is included; the original is documented as superseded.
7)Protocol only Registered protocols without a corresponding published review.
8)Insufficient methodological detail Reviews lacking sufficient methodological description to permit quality appraisal of all relevant domains.

Information sources Source Rationale and Search Approach
PubMed / MEDLINE Primary biomedical database. Searched using the full string in Item 11, including the PubMed systematic review filter (systematic[sb]).
Scopus Broad interdisciplinary coverage with strong indexing of exercise science journals. Title-abstract-keyword search.
Web of Science Core Collection Document type filter (Review Article) applied. Captures systematic reviews and meta-analyses not indexed in MEDLINE.
SPORTDiscus (via EBSCOhost) Specialist sports and exercise science database.
CENTRAL (Cochrane Central Register of Controlled Trials) Searched to ensure comprehensive coverage. Records identified as primary trials are excluded at screening.
Cochrane Database of Systematic Reviews (CDSR) Principal repository for Cochrane systematic reviews. Searched separately from CENTRAL. All Cochrane reviews on the topic are eligible for inclusion regardless of appearance in other databases.
INPLASY Searched for registered but not yet published systematic review protocols.

Main outcome(s) Primary outcome: blood pressure, encompassing systolic and diastolic components, assessed at rest. Effect measure: mean difference in millimetres of mercury with 95% confidence interval (frequentist) or 95% credible interval (Bayesian meta-meta-analysis).
Blood pressure measurement instrument preference: 24-hour ambulatory blood pressure monitoring is the preferred instrument and is the primary source of effect estimates for quantitative synthesis. Resting clinic blood pressure is extracted for all eligible reviews and used in the primary quantitative synthesis only where ambulatory data are unavailable. A sensitivity analysis restricted to reviews using ambulatory monitoring exclusively is pre-specified under Item 24.
Justification for mean difference as the effect measure: blood pressure is measured on a common metric (millimetres of mercury) across all eligible reviews; mean difference preserves clinical interpretability and permits direct comparison with established minimally important clinical difference.

Additional outcome(s) Secondary outcomes: arterial stiffness and endothelial function. These outcomes are designated secondary because the volume and homogeneity of the available systematic review pool is expected to be insufficient to satisfy the feasibility thresholds for quantitative re-pooling. Both secondary outcomes receive structured qualitative synthesis as the primary analytical approach.
Justification for standardised mean difference as the effect measure for arterial stiffness and endothelial function: unlike blood pressure, these outcomes are measured on non-equivalent scales across included reviews. Standardised mean difference (Hedges' g) permits comparison across reviews using different measurement instruments. Mean difference is not appropriate where scale equivalence cannot be assumed.
Secondary Outcome Domain Specific Outcomes Extracted
Arterial stiffness Carotid-femoral pulse wave velocity (metres per second); brachial-ankle pulse wave velocity (metres per second); augmentation index (percentage); central systol.

Data management Function System
Deduplication, title and abstract screening; full-text screening Eppi Reviewer 4. All records from each database are merged into a single library. Automated deduplication is performed followed by manual verification. Screening forms are configured separately for each stage. At title and abstract stage, fields capture: inclusion decision and primary reason for exclusion. At full-text stage, fields capture: inclusion decision, exclusion reason code mapped to the criteria in Item 16, and reviewer identifier. Two reviewers screen independently; disagreements are resolved

through discussion with a third reviewer as arbitrator.
Data extraction Microsoft Excel. A structured extraction form with one tab per data category, drop-down menus for categorical variables, and conditional formatting to flag missing critical items. Two reviewers extract independently; discrepancies are resolved through discussion.
Quantitative synthesis R statistical software (version 4.3 or later). Primary package: gemtc for B.

Quality assessment / Risk of bias analysis Item 21: Quality Assessment / Risk of Bias Analysis
The methodological quality of all included systematic reviews is assessed using AMSTAR-2 (A Measurement Tool to Assess Systematic Reviews, version 2). AMSTAR-2 assesses the methodological quality of the systematic review process itself, not the quality of the evidence within the reviews.
AMSTAR-2 has 16 items. Seven are critical items (Items 2, 4, 7, 9, 11, 13, and 15) whose failure has a disproportionate impact on the overall confidence rating. The overall confidence rating is derived from the pattern of critical item weaknesses:
Confidence Rating Derivation Rule
High No critical item weaknesses AND a maximum of one non-critical item weakness.
Moderate No critical item weaknesses AND more than one non-critical item weakness.
Low Exactly one critical item weakness with or without non-critical item weaknesses.
Critically Low Two or more critical item weaknesses regardless of non-critical item performance.

AMSTAR-2 is applied by two independent reviewers for.

Strategy of data synthesis The data synthesis strategy comprises two parallel components: a qualitative synthesis component applied to all included reviews and all outcomes, and a quantitative meta-meta-analysis component restricted to blood pressure outcomes where pre-specified feasibility thresholds are met (minimum of five reviews with extractable pooled estimates; Corrected Covered Area at or below 15%; at least 80% of reviews using the same or convertible effect measure).
Qualitative Synthesis
Qualitative synthesis follows a structured narrative approach applied to all outcomes. For each outcome, findings are organised by tabulating review reference, primary study count, pooled or qualitative finding, direction of effect, GRADE certainty, and AMSTAR-2 confidence rating. Vote counting is used descriptively only to characterise the pattern of findings and is explicitly not used as a basis for conclusions. A direction-and-consistency assessment examines whether findings are directionally consistent, whether higher-quality reviews agr.

Subgroup analysis The following subgroup analyses are pre-specified for the primary outcome (blood pressure) only:
Subgroup Variable Categories and Rationale
Blood pressure category Pre-hypertension versus unmedicated stage 1 hypertension. Primary subgroup of clinical interest for stratification of exercise recommendations.
HIIT format Sprint interval training versus aerobic high-intensity interval training. These formats differ substantially in intensity and physiological mechanism.
Blood pressure measurement instrument Ambulatory blood pressure monitoring versus resting clinic blood pressure. Addresses the commensurability concern identified in Item 9.
Programme duration Short term (up to 8 weeks) versus medium term (9 to 16 weeks) versus long term (above 16 weeks).
Sex Conducted where included reviews report sex-stratified data.

Sensitivity analysis The following sensitivity analyses are pre-specified (only feasible ones will be run):
Sensitivity Analysis Purpose and Method
AMSTAR-2 quality restriction Re-run synthesis restricted to reviews with AMSTAR-2 confidence ratings of moderate or high. If conclusions differ materially from the primary analysis, AMSTAR-2 quality is identified as a driver of findings.
Overlap exclusion For quantitative synthesis: re-run excluding the most overlapping review per comparison. Documents whether overlap drives the pooled estimate.
Ambulatory blood pressure monitoring restriction Re-run quantitative synthesis using only reviews that employed ambulatory monitoring. Addresses the measurement commensurability concern in Item 9.
GRADE-conducted reviews only Re-run restricted to reviews that conducted their own GRADE certainty assessment.
Alternative CCA threshold Where the CCA is within 3 percentage points of the 15% decision boundary, re-run using a 10% threshold and a 20% threshold to document sensitivity of synthesis deci.

Language restriction This review is restricted to English language publications. The restriction is

applied at full-text screening and is justified by the requirement for full-text quality appraisal: all domains require access to.

Country(ies) involved China.

Other relevant information Overlap with existing umbrella reviews: a search of INPLASY and key databases prior to this registration confirmed that no umbrella review specifically addressing the pre-hypertension and unmedicated stage 1 hypertension population stratum has been registered or published for high-intensity interval training and vascular outcomes. Umbrella reviews in adjacent populations exist but do not address the specific clinical stratum defined in this review.
Reporting standards: the manuscript will be prepared in accordance with both the PRISMA 2020 checklist and the PRIOR (Preferred Reporting Items for Overviews of Reviews) checklist. Both checklists will be completed and uploaded as supplementary files at submission.
Open science: the complete extraction dataset, overlap matrix, and R analysis scripts will be deposited in Zenodo prior to manuscript submission. The Zenodo DOI will be reported in the methods section of the manuscript.

Keywords Umbrella review; high-intensity interval training; blood pressure; hypertension; pre-hypertension; arterial stiffness; endothelial function.

Dissemination plans The completed review will be submitted to a peer-reviewed journal specialising in cardiovascular medicine, hypertension research, or exercise science evidence synthesis. Findings will additionally be disseminated through conference presentation at relevant international forums and through a lay summary for clinical practitioner audiences. All analytical materials will be deposited on Zenodo under an open-access licence with no embargo period.

Contributions of each author

Author 1 - Shuo Wang.
Email: 13205344111@163.com
Author 2 - Tongwu Yu.
Email: 18101351378@163.com