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Aerobic, Resistance, Combined, and High-Intensity Interval Training for HbA1c Reduction in Adults with Type 2 Diabetes Mellitus: A Systematic Review and Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - Self-funded. Supported by University of Hail College of Pharmacy academic resources. No pharmaceutical industry, commercial, or external funding was received for this review.

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2026 and was last updated on 23 June 2026.

INTRODUCTION

Review question / Objective In adults aged 18 years or older with confirmed type 2 diabetes mellitus, what is the comparative effectiveness of aerobic training, resistance training, combined (aerobic plus resistance) training, and high-intensity interval training (HIIT) — compared with each other and with no-exercise control — for reducing glycated haemoglobin (HbA1c, %) from baseline, and how is this effectiveness modified by baseline HbA1c, diabetes medication status, supervision, intervention duration, age group, and weekly exercise volume?

Rationale Type 2 diabetes mellitus affects over 537 million adults globally and imposes immense individual and health-system burden; HbA1c reduction is the primary therapeutic target for preventing micro- and macrovascular complications. Structured exercise training — aerobic (AT), resistance (RT), combined (CT), and high-intensity interval training (HIIT) — is a well-established non-pharmacological intervention endorsed in all major clinical guidelines. Eight existing network meta-analyses and more than twenty pairwise meta-analyses have addressed exercise modality comparisons for HbA1c in T2DM. The most recent and largest (Garcia et al., Diabetes Res Clin Pract 2025; 158 RCTs, 17,059 participants) ranked HIIT first (SUCRA 82%). However, four critical gaps justify an updated, registered NMA: (1) most existing NMAs lack CINeMA or GRADE certainty ratings, leaving their rankings unvalidated; (2) the HIIT-versus-combined training and HIIT-versus-resistance training direct-comparison nodes have fewer than five trials each, with 2023–2026 trials not yet captured in any published NMA available to populate them; (3) no existing NMA simultaneously stratifies findings by baseline HbA1c, medication status, and supervised-versus-unsupervised delivery; and (4) HIIT protocol heterogeneity has not been addressed through a pre-specified definition-based sensitivity analysis. This NMA addresses all

four gaps within a registered, PRISMA-P-compliant protocol with CINeMA certainty ratings and seven pre-specified subgroup analyses, to deliver clinically actionable, certainty-rated comparative evidence for exercise prescription in T2DM.

Condition being studied Type 2 diabetes mellitus and its glycaemic management through structured exercise training.

METHODS

Search strategy Seven databases will be searched from inception through 01 July 2026: MEDLINE/PubMed, Embase (Ovid or direct), Cochrane CENTRAL, Web of Science Core Collection, SPORTDiscus (EBSCOhost), CINAHL (EBSCOhost), and Scopus. Search terms combine MeSH/Emtree controlled vocabulary and free text covering: type 2 diabetes mellitus, T2DM, HbA1c, glycated haemoglobin, aerobic exercise, aerobic training, resistance exercise, resistance training, strength training, combined exercise, combined training, HIIT, high-intensity interval training, interval training, exercise training, physical activity. Supplementary searches: ClinicalTrials.gov and WHO ICTRP (grey literature); reference lists of all included studies and five landmark NMAs; forward citation tracking via Google Scholar. No language restriction at the search stage. Planned search date: 01 July 2026.

Participant or population Adults aged 18 years or older with a confirmed diagnosis of type 2 diabetes mellitus established by recognised criteria (American Diabetes Association, World Health Organization, or equivalent national guidelines). Studies enrolling exclusively individuals with type 1 diabetes, gestational diabetes, or monogenic diabetes will be excluded. Mixed-population studies will be included if T2DM participants are separately reported or constitute at least 80% of the sample.

Intervention Any structured exercise training programme lasting at least eight weeks, delivered in one of four modalities: (1) aerobic training (AT) — continuous moderate-to-vigorous aerobic exercise (walking, jogging, cycling, swimming); (2) resistance training (RT) — structured progressive resistance exercise using free weights, machines, bands, or bodyweight; (3) combined training (CT) — programmes incorporating both aerobic and resistance components; (4) high-intensity interval training (HIIT) — structured alternating high-intensity effort bouts (typically >80% HRmax) with recovery periods. Other modalities (yoga, tai chi) will be extracted but placed in a sensitivity-only node.

Comparator No exercise control (usual care, sedentary control, wait-list, or physical activity advice only), or an alternative exercise modality (head-to-head comparisons forming the network). Studies with only active non-exercise comparators will be placed in a separate sensitivity analysis.

Study designs to be included Randomised controlled trials (individually randomised and cluster-RCTs) and controlled non-randomised trials with a concurrent comparator group. Minimum intervention duration: 8 weeks. Excluded: uncontrolled before-after studies, cross-sectional studies, narrative reviews, editorials, conference abstracts without extractable data, case reports, and retracted publications.

Eligibility criteria Inclusion: adults ≥18 years with confirmed T2DM; structured exercise intervention ≥8 weeks (AT, RT, CT, HIIT, or other); HbA1c change from baseline reported or calculable; RCT or controlled non-randomised trial with concurrent control; minimum 10 participants per arm.Exclusion: type 1, gestational, or monogenic diabetes exclusively; paediatric-only samples; intervention duration <8 weeks; no HbA1c outcome; uncontrolled designs; narrative reviews, editorials, conference abstracts without primary data; duplicate publications (most complete version retained); retracted studies.

Information sources MEDLINE/PubMed, Embase, Cochrane CENTRAL, Web of Science Core Collection, SPORTDiscus, CINAHL, Scopus (plus ClinicalTrials.gov and WHO ICTRP for grey literature).

Main outcome(s) Change in glycated haemoglobin HbA1c (%) from baseline to end of intervention, expressed as mean difference (MD in percentage points) between exercise and comparator groups. Where HbA1c is reported in mmol/mol, conversion will be applied using the IFCC-NGSP equation.

Additional outcome(s) Fasting blood glucose (mmol/L), fasting insulin (mU/L), HOMA-IR (insulin resistance index), body weight (kg), body mass index (kg/m²), waist circumference (cm), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), and VO2max (mL/kg/min).

Data management Two reviewers (ASA and BAA) will independently screen titles/abstracts and full texts using Rayyan. Data will be extracted into a

pre-piloted standardised form capturing study identifiers, design, setting, country, population characteristics (age, sex, diabetes duration, baseline HbA1c, BMI, medication status), intervention modality, protocol parameters (intensity, frequency, session duration, total weeks, supervision, weekly volume), comparator, primary and secondary outcome values (mean ± SD at baseline and endpoint), follow-up duration, in-trial medication changes, funding source, and declared conflicts of interest. Retraction status will be verified against the Retraction Watch database and Crossref before extraction. Authors of studies with missing key data will be contacted by email up to two times over a four-week period.

Quality assessment / Risk of bias analysis Risk of bias will be assessed independently by two reviewers (ASA and BAA) using design-appropriate tools: Cochrane Risk of Bias tool version 2 (RoB 2) for randomised controlled trials — assessing five domains (randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of reported result) — and ROBINS-I for non-randomised controlled trials. CINeMA (Confidence in Network Meta-Analysis) will be applied to rate certainty across six GRADE-adapted domains for all pairwise comparisons derived from the network. Disagreements will be resolved by consensus; persistent disagreements by third-party adjudication.

Strategy of data synthesis A frequentist random-effects network meta-analysis will be conducted using the netmeta R package under the graph-theoretical approach, estimating all pairwise comparisons within a common heterogeneity model. Results will be expressed as mean differences (MD) with 95% confidence intervals. SUCRA values and P-scores will rank modalities. A Bayesian NMA (gemtc/JAGS) will be run as a sensitivity analysis. Inconsistency will be evaluated globally (design-by-treatment interaction model) and locally (node-splitting). Seven pre-specified subgroup analyses (baseline HbA1c, medication status, supervision, duration, age, weekly volume, study design) and six sensitivity analyses (restriction by RoB, in-trial medication changes, RCTs only, HIIT definition, minimum sample size, leave-one-out) will be conducted. CINeMA certainty ratings will be applied to all network comparisons.

Subgroup analysis Seven pre-specified subgroups for the primary outcome (HbA1c change): (1) baseline HbA1c (<7.5% vs ≥7.5% to 210 min/wk); (7) study design (RCTs only / all eligible designs).

Sensitivity analysis Six sensitivity analyses: (1) restriction to studies at low or some-concerns risk of bias (RoB 2) or low-to-moderate risk (ROBINS-I); (2) exclusion of studies reporting in-trial medication changes; (3) restriction to randomised controlled trials only; (4) restriction to trials with minimum 20 participants per arm and 8-week duration; (5) HIIT protocol sensitivity — restriction to standard HIIT definition (>80% HRmax), excluding walk-interval protocols; (6) leave-one-out analysis for each major trial influencing the primary estimate.

Language restriction No language restriction at the screening stage. Non-English full texts will be translated using certified translation services or collaborator assistance where feasible.

Country(ies) involved Saudi Arabia.

Other relevant information Endocrinology; Clinical Pharmacy; Exercise Physiology; Sports Medicine; Diabetology

Keywords type 2 diabetes; T2DM; HbA1c; glycated haemoglobin; aerobic training; combined training; HIIT; high-intensity interval training; exercise modalities; glycaemic.

Dissemination plans Peer-reviewed publication in a high-impact diabetes, sports medicine, or clinical pharmacy journal (target: Diabetes Care, Diabetologia, Sports Medicine, British Journal of Sports Medicine, or equivalent); open-access preferred. Findings will also be presented at relevant national and international scientific meetings.

Contributions of each author

Author 1 - Abdulrahman Alanazi - Conceived and designed the study, drafted the protocol, will lead data extraction and synthesis, and drafted the manuscript and final manuscript submission.
Email: aas2@hotmail.com
Author 2 - Basmah Alanazi - Contributed to the development of the selection criteria, will assist with data extraction and risk of bias assessment, and validity.
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