INPLASY

Dose-Response Relationship of Normobaric Hypoxia Training on Body Composition and Metabolic Health in Obese Adults: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - Anhui Province Higher Education Institutions Scientific Research Program.

Review Stage at time of this submission - Preliminary searches.

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 2 July 2025 and was last updated on 2 July 2025.

INTRODUCTION

Review question / Objective Review Question/Objective This systematic review and meta-analysis aim to comprehensively investigate the dose-response relationship between normobaric hypoxia training parameters and body composition/metabolic outcomes in adults with obesity. The review seeks to address the following primary research questions: Primary Research Question: What is the dose-response relationship between normobaric hypoxia training parameters (oxygen concentration, duration, frequency) and body composition changes in adults with obesity? Secondary Research Questions: 1.Which hypoxia dose parameters (FiO2 level, session duration, frequency) demonstrate optimal effects on body weight, body mass index, and body composition? 2.How do different exercise modalities (aerobic, resistance, high-intensity interval training) interact with hypoxia dose to influence metabolic outcomes? 3.What is the minimum effective hypoxia dose for clinically meaningful changes in body composition and metabolic health markers? 4.How do intervention duration and total hypoxia exposure time affect treatmentoutcomes?

Condition being studied This review will systematically evaluate the dose-response effects of normobaric hypoxia training on body composition and metabolic health outcomes in adults with obesity. Obesity is defined as a body mass index (BMI) ≥30 kg/m², or ≥25 kg/m² when studies specifically focus on metabolic health outcomes. The review will examine both primary obesity (without underlying medical causes) and obesity-related metabolic conditions including type 2 diabetes, metabolic syndrome, and insulin resistance.

METHODS

Participant or population
Inclusion Criteria:
-Adults aged ≥18 years

-Body Mass Index (BMI) ≥30 kg/m² (obese) OR ≥25 kg/m² (overweight) if the study specifically focuses on metabolic health outcomes
-Generally healthy adults or those with obesity-related metabolic conditions (type 2 diabetes, metabolic syndrome, hypertension, insulin resistance)
-Both male and female participants
-Any setting (laboratory, clinical, community-based)
Exclusion Criteria:
-Age 10 hours training per week or competitive sport participation)
-Pregnancy
-Acute illness or unstable medical conditions at baseline
-Previous altitude acclimatization within 3 months before study commencement (exposure >2,500m)
-Studies exclusively involving clinical populations with severe comorbidities unrelated to obesity (e.g., cancer, severe cardiovascular disease, chronic obstructive pulmonary disease).

Intervention Primary Intervention:
Normobaric hypoxia training, defined as exercise training performed under artificially reduced oxygen conditions (simulated altitude) using normobaric hypoxia systems.
1.Hypoxia Parameters:
-Oxygen Concentration (FiO2): 10-18% (equivalent to approximately 1,500-6,000m simulated altitude)
-Session Duration: ≥20 minutes per session
-Frequency: ≥2 sessions over them study period
-Delivery Method: Normobaric hypoxia chambers, masks, tents, or other validated hypoxia delivery systems
2.Exercise Components:
Any form of structured exercise training (aerobic, resistance, high-intensity interval training, or combined modalities)
Exercise must be performed concurrently with hypoxic exposure
Progressive or standardized exercise protocols
-Minimum Intervention Requirements:
-Total intervention duration ≥2 weeks
-Documented hypoxia parameters (FiO2 level or equivalent altitude simulation)
-Structured exercise protocol with specified intensity, duration, and frequency.

Comparator Control Groups:
The comparator must be exercise training performed under normoxic conditions (FiO2 approximately 21% or sea-level equivalent).
Control Group Requirements:
-Identical exercise protocol to the intervention group
-Same exercise modality, intensity, duration, and frequency
-Same intervention duration
-Same population characteristics
-Performed under normoxic conditions only
-Studies without appropriate normoxic exercise control groups will be excluded.

Study designs to be included Included Study Designs:-Randomized controlled trials (RCTs) only-Parallel-group or crossover designs-Single-blind, double-blind, or open-label trials-Multi-center or single-center studiesMinimum Study Requirements:-Intervention duration ≥2 weeks-Sample size ≥10 participants per group-Adequate randomization procedures-Appropriate control group as defined above Eligibility CriteriaInclusion Criteria:1.Study Design: Randomized controlled trials (parallel or crossover design)2.Population: Adults ≥18 years with BMI ≥25 kg/m² (overweight/obese).

Eligibility criteria Exclusion Criteria:
1.Study Design: Non-randomized studies, observational studies, case reports, case series, reviews, conference abstracts
2.Population: Children/adolescents (<18 years), highly trained athletes, pregnancy, severe comorbidities
3.Intervention: Hypobaric hypoxia (actual altitude), passive hypoxia without exercise, blood flow restriction, FiO2 18%
4.Comparator: No normoxic exercise control group, different exercise protocols between groups
5.Outcomes: Studies not reporting any primary or secondary outcomes of interest
6.Duration: Intervention <2 weeks, acute studies (single session effects only)
7.Publication Date: Studies published before 2014 or after June 30, 2025
8.Data: Insufficient data for analysis, duplicated publications, non-English language.

Information sources This systematic review will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines for search strategy, study selection, data extraction, and result reporting.

Main outcome(s) Primary Outcomes:
1.Body Weight (kg): Absolute change in body weight from baseline to post-intervention
2.Body Mass Index (kg/m²): Change in BMI calculated from weight and height measurements
3.Body Fat Percentage (%): Change in body fat percentage measured by validated methods (DEXA, BodPod, bioelectrical impedance, skinfolds)

4.Fat Mass (kg): Absolute change in fat mass measured by validated body composition methods
5.Waist Circumference (cm): Change in waist circumference as a marker of central adiposity
Hierarchy of Measurement Methods:
For body composition outcomes, measurements will be prioritized based on accuracy and validity:
1.Dual-energy X-ray absorptiometry (DEXA)
2.Air displacement plethysmography (BodPod)
3.Hydrostatic weighing
4.Bioelectrical impedance analysis
5.Skinfold measurements.

Quality assessment / Risk of bias analysis
Assessment Tools:
1.Cochrane Risk of Bias Tool 2.0 (RoB 2) for randomized controlled trials
2.Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for overall evidence quality
Publication Bias Assessment:
6.Funnel plots (when ≥10 studies available)
7.Egger's test for small study effects
8.Assessment of selective outcome reporting.

Strategy of data synthesis Meta-Analysis Approach:
Random-effects meta-analysis using the DerSimonian-Laird method will be the primary analytical approach, accounting for expected heterogeneity between studies.
Effect Size Calculation:
9.Weighted Mean Difference (WMD) for outcomes measured on the same scale
10.Standardized Mean Difference (SMD) for outcomes measured on different scales
11.95% Confidence Intervals for all effect estimates
12.Number Needed to Treat (NNT) for clinically relevant outcomes when appropriate
Heterogeneity Assessment:
13.I^2 statistic: 75% (considerable)
14.τ^2 (tau-squared): Measure of between-study variance
15.Chi-squared test: Statistical significance of heterogeneity (p8 weeks)
d.Population: Overweight vs. obese, with vs. without metabolic comorbidities
e.Session Duration: Short (20-45 min), Medium (46-90 min), Long (>90 min)
f.Training Frequency: Low (2-3 sessions/week), High (≥4 sessions/week)
Statistical Software:
16.Review Manager (RevMan 5.4) for standard meta-analyses and GRADE evidence assessment
17.R statistical software (metafor package) for advanced dose-response modeling and meta-regression analyses

Sensitivity Analyses:
1.Study Quality: Excluding studies with high risk of bias
2.Study Design: Parallel vs. crossover studies
3.Population: Studies with different BMI thresholds
4.Outcome Measurement: Different body composition assessment methods
5.Statistical Model: Fixed-effects vs. random-effects models
6.Outlier Analysis: Excluding studies with extreme results
Clinical Significance Thresholds:
Pre-defined clinically meaningful changes:
-Body weight: ≥3% reduction
-BMI: ≥1 kg/m² reduction
-Body fat: ≥2% reduction
-Waist circumference: ≥5 cm reduction.

Subgroup analysis
Planned Subgroup Analyses:
1.Hypoxia Dose Parameters:
-FiO2 Level: Mild (16-18%), Moderate (14-16%), Severe (10-14%)
-Session Duration: 90 minutes
-Training Frequency: 2-3 sessions/week vs. ≥4 sessions/week
-Intervention Duration: ≤4 weeks, 5-8 weeks, >8 weeks
-Total Hypoxia Exposure: Quartiles of total exposure time
2.Exercise Characteristics:
-Exercise Type: Aerobic only, resistance only, HIIT, combined training
-Exercise Intensity: Low-moderate (<70% HRmax), High (≥70% HRmax)
-Exercise Volume: Low, moderate, high (based on total exercise time)
3.Population Characteristics:
-BMI Category: Overweight (25-29.9 kg/m²) vs. obese (≥30 kg/m²)
-Age Groups: 60 years
-Sex: Male only, female only, mixed populations
-Metabolic Status: Metabolically healthy vs. metabolic comorbidities
-Baseline Fitness: Sedentary vs. recreationally active
4.Study Characteristics:
-Study Duration: Short-term (≤8 weeks) vs. long-term (>8 weeks)
-Sample Size: Small (<30 per group) vs. large (≥30 per group)
-Geographic Region: North America, Europe, Asia, Other
-Publication Year: Before 2015 vs. 2015 and after
5.Methodological Factors:
-Blinding: Single-blind vs. double-blind vs. open-label

-Body Composition Method: DEXA vs. other methods
-Dropout Rate: <10% vs. ≥10%.

Sensitivity analysis
Planned Sensitivity Analyses:
6.Study Quality Assessment:
-Excluding studies with high overall risk of bias
-Excluding studies with high risk in specific domains (randomization, missing data)
-Including only studies with low risk of bias across all domains
3.Statistical Model Choice:
-Fixed-effects vs. random-effects models
-Alternative heterogeneity estimators (restricted maximum likelihood, Paule-Mandel)
-Robust variance estimation methods
4.Population Characteristics:
-Including only obese participants (BMI ≥30 kg/m²)
-Excluding studies with mixed populations (athletes/non-athletes)
-Including only metabolically healthy participants
5.Intervention Characteristics:
-Excluding studies with very short interventions (75%)
-Inconsistent results across subgroups
-Potential outlying studies
-Suspected publication bias
Then corresponding sensitivity analyses will be performed to assess the robustness of findings.

Country(ies) involved China.

Keywords Normobaric hypoxia; simulated altitude; hypoxic training; obesity; body composition; dose-response; meta-analysis; systematic review; exercise training; metabolic health; weight loss.

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