INPLASY

Effect of Exercise Intervention on Regulation of Insulin Signaling Pathway-Related Proteins: A Systematic Review and Meta-analysis

INPLASY202580014
doi: 10.37766/inplasy2025.8.0014
Received: 4 August 2025
Published: 4 August 2025

Li, B; Hu, SY; Zhang, M; Liang, ZG.

Corresponding author:
Biao Li

libiao@hfnu.edu.cn

Author Affiliation:
School of Physical Science, Hefei Normal University.

ADMINISTRATIVE INFORMATION

Support - KYSR2025032.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202580014

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 4 August 2025 and was last updated on 4 August 2025.

INTRODUCTION

Review question / Objective The objective of this systematic review and meta-analysis is to address the following question: In populations with or without insulin resistance (including humans or animal models), does exercise intervention (compared to non-exercise) regulate the expression of insulin signaling pathway-related proteins (with a focus on key effectors such as p-AKT) in controlled studies. Specifically, we aim to systematically evaluate the association between exercise intervention and changes in the expression of insulin signaling pathway-related proteins to clarify the regulatory role of exercise in the insulin signaling pathway.
Population (P): Populations with or without insulin resistance, including human subjects or animal models relevant to insulin signaling pathway research.
Intervention (I): Exercise intervention, including but not limited to aerobic exercise, resistance exercise, or combined exercise, with specified type, intensity, frequency, and duration.
Comparator (C): Non-exercise intervention.
Outcomes (O): Changes in the expression level of insulin signaling pathway-related proteins, including key molecules such as p-AKT, IR , IRS-1 , and PI3K .
Study design (S): Controlled studies, including randomized controlled trials and non-randomized controlled trials.

Rationale Exercise is widely recognized as a cost-effective non-pharmacological intervention for improving metabolic health, but its specific regulatory effects on insulin signaling pathway-related proteins remain inconsistent across existing studies. Variations in exercise protocols (e.g., type, intensity, duration), study populations (e.g., healthy individuals vs. those with insulin resistance), and methodological approaches have led to conflicting findings, making it difficult to draw definitive conclusions about the role of exercise in modulating this pathway .Given the controversies and gaps in current knowledge, this systematic review and meta-analysis aims to integrate relevant controlled studies to quantify the effect of exercise

intervention on the expression of insulin signaling pathway-related proteins. By providing a comprehensive evaluation, this study will contribute to a more robust understanding of exercise's regulatory role in the insulin signaling pathway and support evidence-based recommendations for metabolic health management.

Condition being studied The insulin signaling pathway is a key regulatory network in glucose metabolism and insulin sensitivity. This pathway relies on the coordinated activity of multiple proteins, including insulin receptor (IR), insulin receptor substrate 1 (IRS-1), phosphatidylinositol 3-kinase (PI3K), and phosphorylated AKT (p-AKT), whose expression and function directly influence insulin-mediated glucose uptake and metabolic regulation. Dysregulation of these proteins is closely associated with insulin resistance, a pathological state characterized by impaired cellular response to insulin, which serves as a core driver of metabolic diseases such as type 2 diabetes mellitus.
Exercise as a modulator of the insulin signaling pathway has gained increasing attention. However, existing studies on the effect of exercise on the expression of insulin signaling pathway-related proteins have reported inconsistent results, with variations in findings attributed to differences in study design, exercise protocols, and population characteristics.

METHODS

Search strategy Four databases will be used to perform the search: PubMed, Embase, Cochrane Library, and Web of Science. Medical subject heading (MeSH) keywords and free words will be used to search each database for the concepts: "exercise intervention" and "insulin signaling pathway".

Participant or population Insulin resistance patients, insulin resistance animal models, and their respective controls without insulin resistance.

Intervention The intervention of interest is exercise intervention, including aerobic exercise, anaerobic exercise, or resistance exercise, with clear descriptions of exercise type, intensity, frequency, duration, and implementation mode to explore its regulatory effect on the expression of insulin signaling pathway-related proteins.

Comparator Non-exercise intervention and non-exercise control groups in human and animal models.

Study designs to be included Controlled studies, including randomized controlled trials (RCTs) and non-randomized controlled trials, that investigate the effect of exercise intervention on the expression of insulin signaling pathway-related proteins in human or animal models.

Eligibility criteria Eligible studies must meet the following criteria: (1) study population includes humans or animal models with or without insulin resistance; (2) study designs are controlled studies, including randomized controlled trials and non-randomized controlled trials; (3) intervention is exercise intervention (including aerobic exercise, anaerobic exercise, or resistance exercise) with clear description of exercise type, intensity, frequency, and duration; (4) comparator is non-exercise intervention or non-exercise control groups; (5) study reports at least one of the following outcomes: changes in the expression level of insulin signaling pathway-related proteins (e.g., IR, IRS-1, PI3K, p-AKT).

Information sources PubMed, Embase, Cochrane Library, and Web of Science.

Main outcome(s) The primary outcome is the association between exercise intervention and changes in the expression level of insulin signaling pathway-related proteins, including key molecules such as insulin receptor (IR), insulin receptor substrate 1 (IRS-1), phosphatidylinositol 3-kinase (PI3K), and phosphorylated AKT (p-AKT). Specifically, outcomes will include quantitative data on the expression levels of these proteins in response to exercise intervention, measured through laboratory assays (e.g., Western blot, immunohistochemistry) in human or animal models.

Data management Records will be kept in endnote and extracted data will be kept in excel.

Quality assessment / Risk of bias analysis Two reviewers will independently assess the quality of included studies using the Newcastle-Ottawa Scale (NOS) for case-control studies, where one star is awarded for each item in the Selection and Exposure categories, two stars for Comparability, and a maximum score of nine indicates the highest quality; disagreements will be resolved by consultation with a third reviewer.

Strategy of data synthesis Narrative synthesis and quantitative synthesis (meta-analysis) using Review Manager, version 5.3.

Subgroup analysis Subgroup analyses will be performed based on exercise type (aerobic, anaerobic, resistance) and population type (humans, animal models) to explore potential variations in outcomes.

Sensitivity analysis Sensitivity analysis will be performed if relevant.

Country(ies) involved China.

Keywords insulin resistance; exercise intervention; insulin signaling pathway; systematic review; meta-analysis.

Contributions of each author

Author 1 - Biao Li - Conceptualization, validation, investigation, writing—original draft preparation.
Email: libiao@hfnu.edu.cn
Author 2 - Siyuan Hu - Methodology, writing—review and editing.
Email: husiyuan@hnucm.edu.cn
Author 3 - Meng Zhang - Conceptualization, methodology, formal analysis, resources, data curation, visualization.
Email: zhangmeng@hfnu.edu.cn
Author 4 - Zhange Liang - Supervision, project administration, writing—review and editing.
Email: zhangel@hfnu.edu.cn