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The optimal exercise intensity to improve sperm quality and quantity: A protocol for systematic review and network meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

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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 12 February 2025 and was last updated on 12 February 2025.

INTRODUCTION

Review question / Objective Review question: What is the most effective intensity of exercise training for improving sperm quality and quantity?
Objective: This study aims to systematically evaluate the impact of exercise interventions of varying intensities on sperm quality and quantity through a network meta-analysis of rodent animal studies, providing robust scientific evidence for the development of personalized exercise intervention strategies to improve male fertility in clinical practice.

Rationale It was reported that infertility affects about 17.5% of couples worldwide, of which about 50% is caused by male factors. A recent meta-analysis showed that the global male sperm concentration has declined by 62% in 50 years and the rate of decline is accelerating. Therefore, effective interventions to improve male reproductive function are urgently needed. Exercise training is widely recommended to improve the body's antioxidant capacity and as a healthy lifestyle. Indeed, whether exercise training have a positive effect on improving male reproductive function seems to be influenced by factors such as the exercise intensity. Treadmill training, one type of the exercise training, has been widely used in animal models to evaluate its effects on sperm quality and quantity. However, there are no studies that have systematically analyzed the effects of different intensities of treadmill training on sperm quality and quantity.

Condition being studied Male reproductive dysfunction.

METHODS

Search strategy PubMed, Embase, Web of Science Core Collection, The Cochrane Library, CINAHL, China National Knowledge Infrastructure

(CNKI), Wanfang Data, and SinoMed were systematically searched to identify relevant publications from databases' inception to June 4, 2024. The MeSH/Emtree terms and entry terms targeting exercise, training, physical activity, sperm quality and quantity, and rats/mice were employed to develop a comprehensive set of search strategies. There were no language restrictions. Additionally, China Dissertations Database (CDDB), Chinese Doctoral Dissertations/Master's Theses Full-text Database (CDFD-CMFD) were searched for grey literature. The reference list of all the included studies was manually reviewed to capture any relevant publications that the database searches might have missed.

Participant or population Mammalian male animals, such as mice and rats.

Intervention Studies that employed treadmill training with a clear description of the exercise intensity, while no restrictions on the frequency, time of per session, and duration of treadmill training.

Comparator Studies that used sedentary control or any other intensity of treadmill training different from the intervention groups.

Study designs to be included Randomized controlled studies.

Eligibility criteria Studies met the following criteria were included: (1) Animals: rodent models, such as mice and rats; (2) Intervention: treadmill training with a clear description of the exercise intensity, while no restrictions on the frequency, time of per session, and duration of treadmill training. (3) Control: sedentary control or any other type of treadmill training different from the intervention groups. (4) Outcomes: the primary outcome was sperm concentration and the secondary outcomes were sperm count, sperm motility, sperm viability, sperm abnormality rate, and sperm normal rate. Studies reporting any of these measures were eligible. (5) Study design: randomized controlled trials (RCTs).

The exclusion criteria for this systematic review and meta-analysis were as follows: (1) Studies conducting multiple interventions involving treadmill training where the isolated effect of treadmill training on the sperm quality and quantity could not be determined. (2) Studies with insufficient data that could not be synthesized. (3) Conference abstracts. (4) Studies without full-text available. (5) Studies with duplicate data.

Information sources A total of eight databases, including PubMed, Embase, Web of Science Core Collection, The Cochrane Library, CINAHL, China National Knowledge Infrastructure (CNKI), Wanfang Data, and SinoMed, were systematically searched to identify research focused on the relationship between exercise training and sperm quality and quantity from databases' inception to June 4, 2024. Additionally, China Dissertations Database (CDDB), Chinese Doctoral Dissertations/Master's Theses Full-text Database (CDFD-CMFD) were searched for grey literature. The reference list of all the included studies and relevant reviews was manually reviewed to capture any relevant publications that the database searches might have missed.

Main outcome(s) The main outcome was sperm concentration (million/ml). Mean and standard deviation (SD) or standard error (SE) for outcomes were extracted.

Additional outcome(s) The secondary outcomes were sperm count (million), sperm motility (%), sperm viability (%), sperm abnormality rate (%), and sperm normal rate (%). Mean and standard deviation (SD) or standard error (SE) for outcomes were extracted.

Data management Two reviewers performed data extraction independently, coving the following information: (1) Basic information of included studies: publication year and first author. (2) Characteristics of the animal models: lineage, age, weight, health conditions (such as diabetic, fatty acid liver), and sample size. (3) Details about the intervention: type, intensity, frequency, time of per session, and duration. The frequency of treadmill training was recorded as the total number of weekly training sessions, including the number of exercises performed multiple times daily. If the training intensity and time per session were increased gradually over several weeks, the average of the total intensity and duration was taken. (4) Details about the control. (5) Outcomes: mean and standard deviation (SD) or standard error (SE) for outcomes were extracted. The WebPlotDigitizer 4.7 were used to extracted data via figures when the primary data were not reported. If there were any disagreement, two reviewers discussed or consulted with the third reviewer to resolve the issue.

Quality assessment / Risk of bias analysis Two independent reviewers assessed the risk of bias of animal studies using the SYstematic Review Centre for Laboratory animal Experimentation (SYRCLE) risk of bias tool. The SYRCLE's tool,

developed in line with the Cochrane Collaboration's Risk of Bias (RoB) Tool, provides a standardized framework tailored to the unique aspects of animal research. It comprises 10 key items that evaluate six specific domains of bias: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. The evaluation results of the 10 items are represented as "Yes", "No", and "Uncertain", where "Yes" indicates a low risk of bias, "No" indicates a high risk of bias, and "Uncertain" signifies an uncertain risk of bias.

Strategy of data synthesis Pairwise meta-analysis
The conventional pairwise meta-analysis was performed through Review Manager Version 5.4. Giving that all the outcomes included in the meta-analysis are continuous variables, mean difference (MD) with 95% confidence interval (CI) were selected to express the pooled effect size. Regarding the methods for data synthesis, the random-effects model were employed because of the heterogeneity of animal models and the details of the treadmill training between included studies. Statistical heterogeneity between eligible studies were evaluated by Cochran's Q test and I2 test.
Network meta-analysis
The random effects network meta-analysis were conducted using STATA 15.0. First, we plotted network maps to visually represent the relationships among different treadmill trainings being compared. Second, we employed the design-by-treatment interaction model and a loop-specific approach to assess global and local inconsistency, respectively. The consistency model were applied for the network meta-analysis in the absence of no significant inconsistency. Third, we selected MD with 95% CI to express the pooled effect size. Fourth, we estimated the rank probabilities of different types of treadmill training for each outcome using the surface under the cumulative ranking curve (SUCRA). SUCRA value ranges from 0% to 100%, with higher values indicating a greater likelihood of being the most effective intervention. Fifth, comparison-adjusted funnel plots were employed to evaluate potential publication bias.

Subgroup analysis Subgroup analysis were performed to investigate differences in the primary outcome, sperm concentration, between healthy and unhealthy animals.

Sensitivity analysis None planned.

Language restriction None.

Country(ies) involved China.

Keywords exercise; male infertility; sperm quality; sperm quantity; systematic review; network meta-analysis.

Contributions of each author
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