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Comparative Effectiveness of Cognitive–Physical Combined Interventions in Older Adults with Mild Cognitive Impairment: A Systematic Review and Network Meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data extraction.

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 29 August 2026 and was last updated on 29 August 2026.

INTRODUCTION

Review question / Objective To investigate the comparative efficacy of different modes of combined cognitive-physical training for older adults with mild cognitive impairment (MCI) by employing both traditional pairwise and network meta-analyses. Specifically, this review aims to address the following research questions:
1.What is the comparative efficacy of combined cognitive-physical training versus single-modality interventions (exercise or cognitive training alone) and control conditions on cognitive, psychological, and functional outcomes in older adults with mild cognitive impairment?
2.What are the factors related to the intervention effects?
3.Which specific components constitute the optimal intervention strategy?
PICOS Framework:
Participants: Older adults aged 60 and older who have been clinically diagnosed with MCI.
Interventions:Three types of combined interventions: Virtual Reality-based Cognitive-Physical Training (VRCP) is characterized by virtual environments and real-time multidimensional interaction, integrating virtual.

Condition being studied Mild cognitive impairment (MCI) represents a critical transitional stage between normal age-related cognitive decline and overt dementia, which is commonly identified in clinical practice using standardized screening tools, typically indicated by a Mini-Mental State Examination (MMSE) score ranging from 24 to 27 or a Montreal Cognitive Assessment (MoCA) score of less than 26.

METHODS

Search strategy PubMed
#1 "Cognitive Dysfunction"[Mesh] OR "mild cognitive impairment"[Title/Abstract] OR "MCI"[Title/Abstract] OR "cognitive impairment*"[Title/Abstract] OR "cognitive disorder*"[Title/Abstract] OR "cognitive decline"[Title/Abstract] OR "cognitive dysfunction"[Title/Abstract]

#2 "Exercise Therapy"[Mesh] OR "Exercise"[Mesh] OR "Resistance Training"[Mesh] OR "Muscle Stretching Exercises"[Mesh]
#3 "exercis*"[Title/Abstract] OR "physical activit*"[Title/Abstract] OR "physical exercise*"[Title/Abstract] OR "exercise training"[Title/Abstract] OR "exercise therap*"[Title/Abstract] OR "exercise intervention*"[Title/Abstract] OR "motor training"[Title/Abstract] OR "motor exercis*"[Title/Abstract] OR "motor stimulation"[Title/Abstract] OR "aerobic exercise*"[Title/Abstract] OR "resistance training"[Title/Abstract] OR "resistance exercis*"[Title/Abstract] OR "strength training"[Title/Abstract] OR "strength exercis*"[Title/Abstract] OR "endurance training"[Title/Abstract] OR "balance training"[Title/Abstract] OR "muscle.

Participant or population Older adults aged 60 and older who have been clinically diagnosed with MCI.

Intervention Three types of combined interventions: Virtual Reality-based Cognitive-Physical Training (VRCP) is characterized by virtual environments and real-time multidimensional interaction, integrating virtual environments or active video gaming (e.g., VR games and cybercycling) with physical tasks such as boxing and resistance training. Conventional Cognitive-Physical Training (CCPT) relies on traditional clinical tools and non-virtual computerized programs, pairing standard cognitive software (e.g., CogniPlus) or mental tasks (e.g., word pairing, numerical calculations) with conventional physical activities like aerobic gymnastics and pedaling. Traditional Chinese Mind-Body based Cognitive-Physical Training (TCCP) integrates high-level cognitive demands, such as precise breath coordination, complex sequence memorization, and mental simulations (e.g., simulating the tension of archery), into traditional Eastern physical practices.

Comparator Exercise alone; cognitive intervention alone; active control (any placebo intervention used to neutralize the effects of nontherapeutic components of the tested intervention, such as health education); passive control (usual care, no treatment).

Study designs to be included Only randomized controlled trials (RCTs) were included.

Eligibility criteria Articles meeting any of the following criteria were excluded: (1) Studies published in languages other than English or Chinese. (2) Studies involving additional interventions with potential cognitive therapeutic effects (e.g., cognitive-behavioral therapy or reminiscence therapy). (3) Conference abstracts, reviews, study protocols, and letters to the editor. (4) Studies with incomplete data that precluded comprehensive analysis or outcome assessment.

Information sources Four English databases (Cochrane Library, PubMed, Web of Science, EMBASE) and three Chinese databases (CNKI, Wan Fang Database, Chinese Biomedical Literature Database) were searched from inception to 2nd April 2025. The searching was limited to articles published in English and Chinese.

Main outcome(s) Main outcomes:
Global cognition, executive function, memory function, activities of daily living (ADL) and depressive symptoms.
Measures of effect:
The intervention effect size was measured by the standardized mean difference (SMD) and 95% confidence interval.

Additional outcome(s) Additional outcomes:
Balance, gait performance.
Measures of effect:
The intervention effect size was measured by the standardized mean difference (SMD) and 95% confidence interval.

Quality assessment / Risk of bias analysis The Cochrane risk of bias tool was used for quality appraisal.

Strategy of data synthesis Pairwise meta-analysis was conducted using RevMan 5.4 software, and data pooling was performed when at least three studies reported on the same outcome. Mean change scores from baseline and their standard deviations (SDs) were extracted directly or calculated from the published data. Standardized mean differences (SMDs) and 95% confidence intervals (CIs) were utilized as the summary statistics of effect size.Heterogeneity was assessed utilizing the Q test and I 2 index, with a random-effects model applied when significant heterogeneity was detected ($p<0.1$ or $I^2 \geq 50\%$); otherwise, a fixed-effects model was adopted. Subsequently, subgroup and sensitivity analyses were performed to explore potential sources of heterogeneity, identify factors influencing intervention effects, and verify the stability of the findings.
Using Stata 18.0 software, network meta-analysis was conducted based on a frequentist framework to assess the comparative effects of different

combination components. A random-effects model was used t.

Subgroup analysis To further explore potential sources of heterogeneity, subgroup analyses were stratified by the type of intervention, training duration, and types of control.

Sensitivity analysis To verify the robustness of the pooled results, sensitivity analyses will be conducted for outcomes that demonstrate substantial heterogeneity. We will employ a 'leave-one-out' approach to systematically identify potential outliers. By sequentially excluding these outlier studies and recalculating the summary estimates, we aim to determine whether the overall conclusions are disproportionately driven by any single trial.

Country(ies) involved China.

Keywords Combined interventions; Exercise; Cognitive intervention; Mild cognitive impairment; Network meta-analysis.

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