Clinical Practice Guideline for Non-pharmacological Interventions in Older Adults with Cognitive Decline: Physical Activity Postprint

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Abstract

Cognitive decline refers to functional impairment in one or more cognitive domains, primarily affecting the elderly population. Based on the degree of cognitive function impairment, it mainly includes subjective cognitive decline (SCD), mild cognitive impairment (MCI), and dementia. Populations with SCD and MCI have a higher risk of progression to dementia, severely impacting patients' quality of life and creating a substantial burden for families and society. Numerous studies have demonstrated that physical activity is one of the effective non-pharmacological interventions for cognitive decline. However, there is currently no unified standard for physical activity intervention protocols for cognitive decline, and no relevant physical activity guidelines that consider the values and preferences of Chinese elderly with cognitive decline, which hinders the dissemination and application of evidence to some extent. This guideline aims to develop the "Clinical Practice Guideline for Non-pharmacological Interventions in Elderly with Cognitive Decline: Physical Activity" suitable for China' s national conditions, based on existing evidence and considering the values and preferences of Chinese elderly with cognitive decline, following the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Ultimately, eight recommendations for physical activity in elderly with cognitive decline were formulated, with the goal of reducing the incidence of cognitive decline and preventing or delaying the progression from cognitive decline to dementia.

Full Text

Introduction

Cognitive decline refers to impaired function in one or more cognitive domains, primarily affecting elderly populations. Based on the degree of cognitive impairment, it mainly includes subjective cognitive decline (SCD), mild cognitive impairment (MCI), and dementia. SCD describes a state where patients subjectively perceive a decline in cognitive performance compared to previous levels, yet objective neurological assessment reveals no pathological changes. MCI involves mild memory impairment that does not compromise daily living abilities but fails to meet diagnostic criteria for dementia, representing a pre-dementia condition. Both SCD and MCI carry a high risk of progression to dementia.

In the "Chinese Alzheimer' s Disease Biomarker and Lifestyle Study" cohort, the conversion rates for SCD and dementia were X% and X% respectively over X years among X participants. An Italian prospective study reported that approximately X% of MCI patients progress to dementia. Systematic reviews indicate that about X% of MCI cases develop dementia, underscoring the critical importance of early intervention. As a pre-dementia state with reversible potential, MCI provides an optimal "window of opportunity" for dementia prevention. Early intervention in SCD and MCI populations offers new strategies to prevent or delay disease progression.

Non-pharmacological interventions (NPIs) represent effective approaches for cognitive decline and dementia, primarily encompassing exercise intervention, cognitive intervention, dietary intervention, and traditional Chinese medicine intervention. Physical activity, defined as any bodily movement produced by skeletal muscles that requires energy expenditure—including both daily activities and structured exercise—constitutes a key component of NPIs.

The mechanisms through which physical activity improves cognitive function operate at multiple levels. At the molecular level, physical activity promotes the generation of brain-derived neurotrophic factor (BDNF) in blood, facilitating neuronal growth. Concurrent increases in vascular endothelial growth factor (VEGF) and insulin-like growth factor (IGF-1) may enhance cognition by improving vascular survival, growth, and neurovascular generation. At the brain structural level, physical activity increases brain volume in white and gray matter regions and hippocampal volume, enhances cerebral blood flow, and improves brain perfusion. At the hormonal level, physical activity modulates the hypothalamic-pituitary-adrenal (HPA) axis, such as by reducing cortisol secretion to delay cognitive decline. Additionally, physical activity can improve cognitive function by enhancing mood and self-perception.

As physical activity is commonly adopted among cognitive decline populations, relevant guidelines are needed for scientific direction. In YEAR, the American Academy of Neurology (AAN) first updated its MCI population guidelines, establishing recommendations for physical activity. However, specific guidelines

tailored to Chinese cognitive decline populations remain necessary.

Methods

Expert Consultation

A panel of X experts from medicine, neurology, exercise rehabilitation, cognitive rehabilitation, general practice, nursing, and related fields conducted two rounds of consultation. The expert group followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group methodology to evaluate clinical questions and outcome indicators, supplementing potentially omitted important questions while ranking the importance of clinical questions and outcomes. In importance scoring, X points indicated importance, X points indicated criticality for decision-making, and X points indicated unimportance. Experts also discussed the accuracy of clinical question and outcome indicator formulations, ultimately establishing the guideline' s clinical questions and corresponding outcome indicators (see Table X).

Literature Search and Evidence Integration

Literature Search Strategy Based on prioritized clinical questions, the secretariat developed search strategies and retrieved clinical practice guidelines, best practices, expert consensus, systematic reviews, and randomized controlled trials (RCTs), with particular emphasis on systematic reviews and meta-analyses. Other literature categories served as supplementary references.

Inclusion criteria were: (1) Non-pharmacological physical activity interventions; (2) Study subjects: elderly with SCD and MCI; (3) Control groups with different measures including blank control and health education; (4) Outcome indicators including cognitive function and subdomains, physical function, and psychological indicators. The search deadline was X (see search strategy in Table X).

Literature Inclusion and Exclusion Criteria For guidelines: Inclusion: (1) Latest version by search date; (2) Clear recommendations; (3) Contains physical activity recommendations for elderly with cognitive decline. Exclusion: (1) Non-Chinese/English guidelines; (2) Direct translations of foreign guidelines or duplicate publications; (3) Normative documents or consensus opinions.

For systematic reviews: Inclusion: (1) Systematic review or meta-analysis; (2) Content matches search strategy. Exclusion: (1) Unable to obtain full text after contacting authors X times; (2) Non-Chinese/English literature.

Literature Screening and Quality Assessment X secretariat members independently screened literature by title, abstract, and full text according to inclusion and exclusion criteria. Disagreements were resolved through discussion among X people or by a third member.

Quality assessment was conducted independently by X secretariat members. Guidelines were evaluated using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument, while systematic reviews were assessed using the Risk of Bias in Systematic Reviews (ROBIS) tool. Disagreements were resolved through discussion or third-party consultation.

Evidence Integration X secretariat members used standardized extraction forms to retrieve and integrate information from included evidence, including: literature type, author, year, sample size, study subjects, interventions, control groups, intervention effects, and outcome indicators.

When integrating evidence from different sources, consistent recommendations or conclusions across literature were addressed by adopting higher-quality, more recent evidence. Complementary recommendations on the same topic were merged according to logical relationships. Inconsistencies were resolved by tracing evidence sources and identifying reasons for different recommendations, prioritizing higher-quality, more recent literature. Multi-strategy recommendations were split into separate components. Disagreements were resolved through discussion or by a third member.

Evidence Quality Grading and Recommendation Formulation The guideline secretariat extracted and verified evidence addressing clinical questions. The GRADE evidence quality evaluation and grading system was applied, considering X downgrade factors (risk of bias, inconsistency, imprecision, publication bias, indirectness) and X upgrade factors (large effect size, confounding factor bias, dose-response relationship). Evidence quality was classified as high, moderate, low, or very low.

For important areas lacking ideal evidence in existing literature, consensus was developed based on indirect evidence or expert clinical experience as Good Practice Statements (GPS). The secretariat sent preliminary recommendations and evidence summary tables to the consensus expert group. Experts used the GRADE system to vote on recommendation direction and strength, with primary determinants being benefit-harm trade-offs, supplemented by evidence quality and patient/family values and preferences (obtained through interviews with target populations).

Five recommendation strengths were established: strong for, weak for, unclear, weak against, and strong against. For a recommendation to be classified as strong for or strong against, at least X% of participants had to agree; recommendations for or against an intervention required X% agreement. Standards not meeting these thresholds yielded no recommendation (Table X). Final consensus was achieved through voting and an external review meeting.

The secretariat discussed, revised, and refined expert opinions, extracting X recommendations regarding physical activity type, frequency, time, intensity, and exercise management for Chinese elderly with cognitive decline (SCD/MCI).

Recommendations

Theme 1: General Principles of Physical Activity

General Recommendation: All elderly with cognitive decline (SCD/MCI) should engage in physical activity, reducing bed rest and sedentary time. Physical activity includes both daily activities and structured exercise (see Table X for X recommendations).

Theme 2: Aerobic Exercise

Recommendation: Elderly with cognitive decline should perform aerobic exercise as the primary exercise modality.

Frequency: At least X times per week.

Intensity: Moderate [Rating of Perceived Exertion (RPE) X] to vigorous intensity.

Time: Weekly cumulative moderate-intensity activity of X minutes or vigorous-intensity activity of X minutes, or equivalent combinations.

Type: Walking, jogging, table tennis, cycling, swimming, or other continuous rhythmic endurance exercises involving large muscle groups.

Evidence Summary: A systematic review (n=X) investigating physical activity effects on MCI elderly found that physical activity intervention improved overall cognitive function [standardized mean difference (SMD) = X, 95% CI (X, X)], delayed memory [SMD = X, CI (X, X)], and executive function [SMD = X, CI (X, X)]. Subgroup analysis revealed that moderate-intensity and other exercise types such as mind-body exercise were effective.

Theme 3: Resistance Exercise

Recommendation: Elderly with cognitive decline should engage in resistance exercise, initially using equipment or body weight. Professional or trained caregiver supervision is recommended.

Frequency: At least X times per week.

Intensity: Moderate (RPE X) to vigorous (RPE X). Progress gradually from low intensity by increasing resistance, repetitions, or frequency to avoid injury.

Type: Stair climbing, resistance bands, dumbbells, sandbags, or other resistance exercises involving large muscle groups.

Evidence Summary: A systematic review (n=X) demonstrated that resistance exercise significantly improved overall cognitive function [SMD = X, CI (X, X)] and executive function [SMD = X, CI (X, X)]. Subgroup analysis found that resistance exercise at X times per week for X weeks significantly improved MCI elderly' s body mass index [SMD = X, CI (X, X)].

Theme 4: Comprehensive Physical Activity

Recommendation: Elderly with cognitive decline should perform comprehensive physical activity. Mind-body exercise as a multimodal comprehensive activity can improve balance, stability, and coordination.

Time: At least X minutes per session, with intervention duration lasting at least X months.

Frequency: X times or more per week.

Type: Tai Chi, Baduanjin, and similar mind-body exercises.

Evidence Summary: A systematic review (n=X) including X studies found that mind-body exercise significantly improved overall cognitive function scores in cognitive decline elderly [weighted mean difference (WMD) = X, CI (X, X)] and language function [SMD = X, CI (X, X)]. Memory function also improved after mind-body exercise intervention [SMD = X, CI (X, X)]. Tai Chi intervention for X months, X times per week, X minutes per session, improved overall cognitive function [SMD = X, CI (X, X)], memory function [SMD = X, CI (X, X)], and visuospatial ability [SMD = X, CI (X, X)]. Baduanjin intervention for X months, X times per day, also significantly improved overall cognitive function scores [WMD = X, CI (X, X)].

Theme 5: Exercise Management

Pre-Exercise Consultation: Consult professional healthcare providers to develop personalized exercise prescriptions based on comprehensive assessment of physical fitness, disease status, exercise environment, and available resources.

Exercise Process: Warm-up exercise (X minutes), formal exercise, and stretching (flexibility exercise) should constitute key exercise components, with caregiver supervision when necessary. Equipment-based exercise requires prior training and supervision. Stretching: upper and lower limb muscle stretching, X seconds per muscle group, X repetitions, total X minutes, with intensity producing a stretching sensation without pain.

Post-Exercise: Gradually reduce intensity with appropriate stretching to allow heart rate to decline slowly. Post-exercise stretching can alleviate muscle soreness.

Exercise Safety: Reduce exercise-related injuries through proper warm-up, gradual intensity progression, and appropriate volume. Exercise within tolerance limits, preventing cardiovascular events and falls. If discomfort occurs during exercise, stop slowly and rest.

Recommendation Rationale: Most reported exercise-related adverse events result from inappropriate exercise, making scientific exercise management essential. Cognitive decline elderly populations typically exhibit poor mobility, high fall risk, poor balance, and neuropsychiatric symptoms, requiring additional

considerations during physical activity. Pre-exercise warm-up and post-exercise stretching (flexibility exercise) are suitable for functionally impaired individuals such as 高龄的认知衰退老年人, effectively increasing joint range of motion, flexibility, and balance while maximizing intervention effects and reducing injury risk.

Analysis revealed that after several months, both overall cognitive function and activities of daily living showed improvement. However, adverse events such as fractures, bone and joint pain, and falls may occur during exercise. For elderly individuals with comorbid chronic conditions, exercise prescriptions should adhere to the most conservative values recommended by healthcare professionals to ensure total exercise volume does not exceed cardiopulmonary tolerance, thereby ensuring safety. Even those with severe cognitive impairment can engage in physical activity, though they may require personalized assistance and continuous monitoring during training.

Formal exercise encompasses aerobic exercise, resistance training, and comprehensive physical activities. Healthcare professionals should flexibly adjust single-type or combined exercise interventions based on individual patient characteristics. Age-appropriate safety measures are recommended, including installing handrails on exercise equipment, wearing suitable clothing and footwear, and providing caregiver supervision when necessary. International physical activity guidelines consistently emphasize the importance of scientific exercise management for ensuring both efficacy and safety. Therefore, this guideline recommends that elderly individuals with cognitive decline undergo professional consultation, exercise capacity assessment, and risk evaluation before initiating physical activity, with development of individualized exercise prescriptions to maximize benefits.

Research demonstrates that professional medical guidance, group-based programs, gamification, and multimodal interventions effectively improve cognitive function in older adults. Healthcare providers should develop tailored physical activity interventions based on individual patient needs.

This guideline was developed using the updated international methodology for evidence-based clinical guideline creation. First, clinical questions and outcome indicators were identified through a Delphi process. Second, systematic literature searches, screening, and appraisal were conducted, incorporating patient values and preferences to weigh benefits and harms. Important clinical questions received graded recommendations, with consensus on recommendations and strength achieved through expert consultation and external review. Finally, the Chinese Clinical Practice Guideline for Non-pharmacological Interventions in Elderly Populations with Cognitive Decline was formulated.

Analysis and Findings (continued)

Physical Activity

The guidelines can provide decision-making support for Chinese hospital and community staff regarding physical activity interventions for elderly individuals with cognitive decline. However, several limitations exist in the guideline development process: this study only included literature published in Chinese and English, which may have omitted relevant research in other languages.

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Note: Figure translations are in progress. See original paper for figures.