

Effects of a Structured Cognitive-Based Intervention in Older Adults With Mild Cognitive Impairment: A Randomized Clinical Trial

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Abstract

Background

Evidence remains limited on whether structured cognitive training provides additional benefit when added to multimodal non-pharmacological programs for older adults with mild cognitive impairment (MCI).

Methods

In this randomized controlled trial, 631 older adults were screened for eligibility, 161 met the study criteria, and 146 were enrolled and randomized 1:1 to the intervention or active control group (73 per group) using computer-generated block randomization with block sizes of 4 and 6. Both groups received cognitive-health education, home-based cognitive activities, and standardized physical exercise. The intervention group additionally received 12 weeks of supervised structured multidomain cognitive training with individualized starting levels and progressive adjustment of task difficulty. The primary outcome was change in Montreal Cognitive Assessment (MoCA) total score from baseline to 3 and 12 months, analyzed using intention-to-treat linear mixed-effects models.

Results

The intervention group showed greater improvement in MoCA total score than the control group at 3 months ($\beta = 0.525$; 95%CI, 0.227 to 0.822; $p = 0.001$) and 12 months ($\beta = 1.627$; 95%CI, 1.325 to 1.929; $p < 0.001$). Per-protocol findings were consistent. No consistent between-group differences were observed for depressive symptoms, instrumental functioning, or physical performance. Exploratory analyses suggested greater improvement in attention at both follow-ups and in language and abstraction at 12 months.

Conclusion

Adding structured multidomain cognitive training to a shared multimodal program resulted in greater improvement in global cognition at both follow-ups. Further pragmatic evaluation of this noncomputerized approach in routine and resource-constrained settings is warranted.

Trial registration:

The trial was registered at ClinicalTrials.gov (registration number: NCT06453746; June 12, 2024), available at <https://clinicaltrials.gov/study/NCT06453746>.

Background

Cognitive decline during the mild cognitive impairment (MCI) stage is clinically important because it often represents an early trajectory toward loss of functional independence and dementia.(1) Longitudinal studies have reported conversion rates from MCI or amnesic MCI to Alzheimer's dementia ranging from approximately 10% to 33% within 1 year in clinic-based populations, with higher cumulative rates over longer follow-up periods.(2) In

addition to dementia risk, MCI is associated with increased functional vulnerability, caregiver burden, psychological distress, and reduced independence.(3, 4) Importantly, MCI may represent a potentially modifiable stage before more advanced neurodegenerative impairment becomes established.(5)

Previous studies and meta-analyses suggest that cognitive training, multidomain interventions, and cognitive rehabilitation may support cognitive performance and delay functional decline in selected populations.(6, 7) However, many studies provide limited detail regarding how cognitive activities are organized, adapted, progressed, and integrated over time within a coherent therapeutic framework.(8) Consequently, it remains unclear whether observed benefits arise primarily from the activities themselves or from the structured manner in which they are implemented over time. In addition, many previous studies have used passive or methodologically heterogeneous control conditions, limiting the ability to distinguish intervention-specific cognitive effects from nonspecific influences related to physical activity or general cognitive engagement.(9, 10)

These issues may be particularly relevant in low- and middle-income settings (LMICs), where scalable and clinically accessible interventions are needed. Although technology-assisted cognitive interventions have shown promising findings,(11) implementation may remain limited by infrastructure requirements, cost, digital literacy variability, and restricted accessibility across healthcare settings, particularly among older adults with lower familiarity or engagement with technology-based interventions.(12)

Against this background, the present study examined whether a structured multidomain cognitive-based program integrated within a multimodal non-pharmacological framework could improve cognitive outcomes over time in older adults with MCI.

Methods

Study design and participants

This randomized parallel-group clinical trial was conducted between June 2024 and June 2026 at a secondary-level public hospital in Viet Nam to evaluate the effects of a structured cognitive training program in older adults with MCI. The study followed the Consolidated Standards of Reporting Trials (CONSORT) statement (*Supplementary Appendix 1*).(13)

Eligible participants were aged ≥ 60 years, met Petersen's criteria(1) and the International Working Group criteria(5) for MCI, were able to read or write Vietnamese and attend scheduled hospital visits, and had supervision available for daily activities when necessary. Individuals with clinically stable chronic conditions, including hypertension and type 2 diabetes mellitus, were eligible provided that no acute exacerbation or medication changes had occurred within the previous 3 months to minimize acute illness-related effects on cognitive assessment and ensure safety during physical performance testing.

Exclusion criteria included severe visual or hearing impairment interfering with cognitive assessment; acute or uncontrolled medical conditions affecting cognition or contraindicating physical performance testing; participation in another cognitive intervention within the previous 3 months; use of medications with clinically significant cognitive effects (sedatives, anticholinergics, or antipsychotics); psychiatric disorders affecting cognition; regular alcohol consumption ≥ 60 g/day (approximately ≥ 5 standard drinks; 1.5 L of 5% beer or 180 mL of 40% spirits); or a GDS-15 score ≥ 5 .

Criteria for MCI Classification

The framework used to identify MCI in this study has been described previously in detail.(14) Because classification was based on screening instruments rather than comprehensive neuropsychological and diagnostic evaluations, participants were considered to have screen-detected MCI rather than clinically confirmed MCI. In this study, “MCI” refers to screen-detected MCI identified using the following screening criteria(1, 5): (i) subjective cognitive complaints, (ii) Mini-Mental State Examination (MMSE) scores of 24–29, (iii) relatively preserved instrumental functioning on the Lawton IADL scale (score ≥ 5),(15) and (iv) absence of a prior clinical diagnosis of dementia. The Vietnamese MMSE was used solely for initial screening and eligibility classification. The version administered was obtained from the Vietnamese Ministry of Health technical guideline for rehabilitation, which provides the corresponding Vietnamese-language administration and scoring format.(16) Changes in cognition over time were evaluated using the Montreal Cognitive Assessment (MoCA), as described below.

Sample size Calculation

Sample size estimation used a conservative two-group mean comparison approach for a parallel-group design with equal allocation because reliable estimates of within-subject correlation for repeated-measures calculations were unavailable in comparable populations.(17) Given that mixed-effects models generally improve statistical efficiency by incorporating within-subject correlations, this approach was considered conservative for trial planning.(18)

Assuming a two-sided α of 0.05 ($Z_{(1-\frac{\alpha}{2})}=1.96$), 80% power ($Z_{(1-\beta)} = 0.84$), a standard deviation of 1.0, and a minimum clinically relevant between-group difference of 0.5 points,(19) the minimum required sample size was 63 participants per group. We recruited 73 participants in each group to account for potential attrition during the follow-up.

Randomization and blinding process

A total of 146 participants were randomized in a 1:1 ratio to the intervention or control group using a computer-generated block randomization sequence with block sizes of 4 and 6. The sequence was generated by an independent research assistant (TNNL) who was not involved in participant recruitment, outcome assessment, or intervention delivery. Allocation concealment was maintained using sequentially numbered, opaque, sealed envelopes, and group assignment was performed only after baseline assessment and eligibility confirmation.

Because of the behavioral nature of the intervention, participants and researchers delivering the intervention could not be blinded to group allocation. Outcome assessments were conducted by staff who were not involved in the informed-consent process or intervention delivery. However, participants were aware of the activities they received, and the informed-consent materials described the group-specific study procedures. Therefore, inadvertent disclosure of group allocation could not be excluded, and complete assessor masking was not considered assured.

Intervention

Intervention

Figure 1 Study intervention framework and timeline (Figure created by the authors).

Intervention Procedures

Participants in both groups received the same multimodal background program, consisting of cognitive health education, guided home-based cognitive activities, and a standardized physical exercise program (*Fig. 1*).

The physical exercise program included moderate-intensity aerobic training with standardized warm-up, aerobic exercise, and cool-down components under the supervision of trained research personnel (*Supplementary Appendix 2*). Exercise frequency and overall activity were aligned with World Health Organization physical activity recommendations for older adults,(20) with intensity and pacing gradually adjusted according to individual tolerance.

Participants in both groups also completed standardized home-based cognitive activities four times per week (*Supplementary Appendix 3*). Each session included brief relaxation exercises and simple cognitive tasks involving memory, arithmetic, word generation, and puzzles.

Control Group

Participants allocated to the control group (CG) received the multimodal background program described above and therefore served as an active control. At week 20, CG participants attended a time-matched 90-minute hospital-based booster session consisting of general health education and relaxation activities without structured multidomain cognitive training.

Intervention Group

In addition to the multimodal background program, participants in the intervention group (IG) received supervised structured multidomain cognitive training over 12 weeks. The training used individualized starting levels and progressive adjustment of task difficulty based on participant performance. The cognitive training component was developed with reference to the updated Medical Research Council framework for developing and evaluating complex interventions.(21) The adaptation algorithm incorporated predefined tailoring variables, decision points, intervention options, and decision rules consistent with adaptive-intervention design principles.(22) Each supervised session comprised five components (*Supplementary Appendix 4*):

1. attentional preparation, using guided breathing and relaxation techniques to facilitate attentional readiness and reduce distraction;
2. prospective-memory and episodic-recall activities, comprising sticky-note strategy training, intervention-specific structured home-task assignments, and recall of prior-session activities. These activities were intended to support remembering to carry out previously formed intentions at an appropriate future time, whereas episodic-recall activities focused on retrieving previously completed activities and experiences;
3. progressively complex multidomain cognitive exercises, engaging attention, working memory, executive function, language, abstraction, and visuospatial processing through structured cognitive and problem-solving tasks;

4. ADL/IADL-oriented functional-cognition activities, emphasizing the sequencing, planning, and organization of cognitively demanding everyday tasks to support functional relevance; and
5. structured relaxation, intended to reduce cognitive fatigue and support attentional recovery after cognitively demanding activities.

IG participants underwent individualized entry-level assignment and subsequent adaptation of task difficulty. Before the first supervised cognitive-training session, participants were assigned to one of four hierarchical starting levels (Levels A, B, C, D) according to baseline global cognitive and working-memory performance, operationalized using the MoCA total score and digit-span performance, as detailed in *Supplementary Appendix 5*. This entry-level assignment was intended to provide an appropriate initial degree of cognitive challenge while reducing the likelihood of either excessive task difficulty or insufficient cognitive engagement.

To ensure intervention fidelity, all supervised sessions were delivered using standardized session checklists aligned with the predefined five-component structure and hierarchical progression framework. The checklists documented delivery of the required intervention components, assigned difficulty level, and progression decisions. Details are provided in *Supplementary Appendix 5*.

At week 20, IG participants attended a 90-minute hospital-based booster session to reinforce the multidomain cognitive strategies practiced during the 12-week cognitive training program.

Outcome measures

The primary outcome was longitudinal change in cognitive performance assessed using the MoCA. Secondary outcomes included depressive symptoms assessed with the GDS-15, physical performance assessed using selected Senior Fitness Test (SFT) components (Chair Stand, Arm Curl, Two-Minute Step, and Timed Up and Go tests), and functional ability assessed with the Lawton IADL scale. Assessments were conducted at baseline (T0), immediately post-intervention at 3 months (T1), and 12 months from baseline (T2).

Montreal Cognitive Assessment

The MoCA was used as the primary cognitive outcome because of its sensitivity for detecting subtle cognitive deficits in older adults with MCI and its suitability for tracking cognitive changes over time.(23, 24)

The authorized Vietnamese version (*Version 7.1; MoCA Test Inc., Québec, Canada*) was administered. The MoCA is a 30-point multidomain cognitive assessment in which higher scores indicate better cognitive performance. For domain-specific analyses, items were categorized into visuospatial and executive function using Trail Making B, cube copying, and clock drawing (5 points); naming using a three-item animal naming task (3 points); attention using digit span, vigilance, and serial subtraction tasks (6 points); language using sentence repetition and verbal fluency tasks (3 points); abstraction using a verbal abstraction task (2 points); delayed recall/short-term memory using a five-word recall task (5 points); and orientation using six time-and-place orientation items (6 points).(25, 26)

Previous psychometric studies have demonstrated acceptable structural validity and composite reliability across clinical populations, with reported composite reliability coefficients ranging from 0.74 to 0.95.(27)

15-item Geriatric Depression Scale

Depressive symptoms were assessed using the Vietnamese version of the GDS-15, a 15-item dichotomous (yes/no) instrument evaluating emotional and behavioral experiences during the previous week, with higher scores indicating greater depressive symptom burden. Previous studies have demonstrated good screening performance and strong agreement with the original 30-item version in older adults ($r = 0.966$).⁽²⁸⁾

Lawton Instrumental Activities of Daily Living Scale

Functional independence was assessed using the Lawton IADL scale, which evaluates instrumental activities required for independent community living, including telephone use, shopping, food preparation, housekeeping, laundry, transportation, medication management, and financial management. Scores range from 0 to 8, with higher scores indicating greater independence. The Vietnamese version used in national health surveys under Ministry of Health guidance was applied.⁽²⁹⁾

Senior Fitness Test

Physical performance was assessed using selected components of the SFT, a standardized functional fitness battery for older adults with high reliability (intraclass correlation coefficients 0.80–0.98) and good validity compared with established physical fitness measures.⁽³⁰⁾

- - The Chair Stand test assessed lower-limb strength and endurance by recording the number of sit-to-stand repetitions completed within 30 seconds.
- - The Arm Curl test evaluated upper-limb strength and endurance using the maximum number of elbow flexion repetitions completed within 30 seconds with a standardized hand weight.
- - Aerobic endurance was assessed using the Two-Minute Step test, in which participants marched in place for two minutes while raising the knees to a predetermined height; rest periods and light balance support were permitted if necessary.
- - Agility and dynamic balance were evaluated using the Timed Up and Go test, in which participants stood from a chair, walked around a marker positioned 2.44 m away, and returned to the seated position as quickly and safely as possible without running; two trials were performed, and the shortest completion time was analyzed.

Pilot study

Before the main trial, a pilot study was conducted in a comparable outpatient population of older adults with MCI to evaluate the feasibility of the study procedures and internal consistency of the study instruments.⁽³¹⁾ The pilot demonstrated high feasibility, with an enrollment rate of 89.4% and completion rate of 98%. Acceptable internal consistency was observed for the MoCA (Cronbach's $\alpha = 0.68$), GDS-15 ($\alpha = 0.71$), and Lawton IADL ($\alpha = 0.73$).

Ethics

The study was approved by the Biomedical Research Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (reference number: 625/HĐĐĐ-ĐHYD, dated 05 May 2024) and by the Ethics Committee of Nhan Dan Gia Dinh Hospital (reference number: 65/NDGD-HĐĐĐ, dated 17 May 2024). The study adhered to the ethical principles outlined in the revised 1987 Declaration of Helsinki, and written informed consent was provided by all participants. The trial was registered at ClinicalTrials.gov (registration number: NCT06453746; June 12, 2024).

Statistical methods

The primary analysis followed the intention-to-treat principle and included all randomized participants in their originally assigned groups. Changes in the MoCA total score were analyzed using linear mixed-effects models with fixed effects for randomized group, assessment time, and the group-by-time interaction, with a participant-specific random intercept. Secondary outcomes were analyzed using the same mixed-effects framework to account for within-participant correlations and maintain consistency of treatment-effect estimation across outcomes.(32)

No adjustment for multiple comparisons was applied to secondary and exploratory outcomes. Missing follow-up data were handled using maximum likelihood estimation within the mixed-effects models.

A per-protocol analysis was conducted as a supportive analysis to evaluate the consistency of the primary findings among participants with sufficient adherence and no protocol deviations. Adherence was assessed separately for each intervention component. Attendance at hospital-based physical-exercise, cognitive-health-education, supervised cognitive-rehabilitation, and week-20 booster sessions was ascertained from date-stamped encounter records in the hospital's electronic registration and medical record system. Completion of home-based cognitive activities was recorded in participant diaries and reviewed during follow-up contacts, with caregiver confirmation when available.

Adequate adherence to the intervention components provided to both groups was defined as attendance at $\geq 75\%$ of the hospital-based physical-exercise and cognitive health education sessions, and completion of $\geq 75\%$ of the home-based cognitive activities. These thresholds were predefined as pragmatic indicators of sufficient exposure while allowing for occasional missed sessions in an older population with screen-detected MCI.(33, 34)

Because supervised cognitive rehabilitation was provided only to the intervention group, IG participants were required to attend $\geq 85\%$ of the supervised cognitive-rehabilitation sessions. This criterion was informed by previous cognitive-training literature suggesting more consistent effects when adherence exceeded 80–85%.(35, 36) Both IG and CG participants were required to attend the time-matched week-20 booster session.

Results

Participant characteristics

A total of 631 older adults were screened for eligibility, of whom 161 met the study criteria and 146 were randomized (73 per group; Fig. 2). At the end of the intervention period, 71 participants in the intervention group and 69 in the control group met the predefined adherence criteria for inclusion in the per-protocol population. Attrition across the intervention and follow-up periods was relatively balanced between groups and was primarily attributable to relocation, loss of contact, personal scheduling constraints, or reduced interest in continued participation, without an apparent pattern suggestive of intervention-related cognitive intolerance or differential dropout. At 12 months, 67 participants in each group completed the outcome assessments. All 146 randomized participants were included in the intention-to-treat analysis.

Of the 146 randomized participants, 140 completed the 3-month assessment and 134 completed the 12-month assessment. The mean age of the 146 randomized participants at baseline was 69.30 years (SD, 4.08). Among

participants assessed at each time point, the groups remained descriptively similar in age, gender, and educational attainment. Observed mean MoCA scores increased in both groups at 3 months, with a larger between-group separation at 12 months, whereas no consistent pattern was evident across the other observed outcomes (Table 1).

Table 1
Participant characteristics by assessment time.

T0			T1			T2		
Intervention (n = 73)	Control (n = 73)	p	Intervention (n = 72)	Control (n = 68)	p	Intervention (n = 67)	Control (n = 67)	p
Age (Mean±SD)								
69.33 ± 4.16	69.27 ± 4.03	0.936	69.39 ± 4.15	69.37 ± 4.08	0.976	69.40 ± 4.13	69.25 ± 4.09	0.834
Gender (%)		0.403*			0.704*			0.598*
Female								
39 (53.4)	44 (60.3)		39 (54.2)	39 (57.4)		38 (56.7)	41 (61.2)	
Male								
34 (46.6)	29 (39.7)		33 (45.8)	29 (42.6)		29 (43.3)	26 (38.8)	
Education (%)		0.295*			0.438*			0.195*
Less than senior high school								
22 (30.1)	28 (38.4)		21 (29.2)	24 (35.3)		18 (26.9)	25 (37.3)	
Completed senior high school								
51 (69.9)	45 (61.6)		51 (70.8)	44 (64.7)		49 (73.1)	42 (62.7)	
MoCA Total Score (Mean±SD)								
22.27 ± 1.87	21.79 ± 1.72	0.110	24.40 ± 2.60	23.34 ± 1.88	0.007	24.01 ± 2.50	21.93 ± 1.68	< 0.001
GDS-15 score (Mean±SD)								
1.75 ± 1.18	1.47 ± 1.19	0.146	1.14 ± 0.81	0.87 ± 0.81	0.050	1.10 ± 1.03	0.85 ± 0.74	0.105
Lawton IADL score (Mean±SD)								
5.81 ± 1.16	5.95 ± 1.15	0.432	6.50 ± 0.96	6.79 ± 1.02	0.081	6.54 ± 0.89	6.88 ± 1.01	0.052
Senior Fitness Test								
Chair stand test (Mean±SD)								

T0			T1			T2		
Intervention (n = 73)	Control (n = 73)	<i>p</i>	Intervention (n = 72)	Control (n = 68)	<i>p</i>	Intervention (n = 67)	Control (n = 67)	<i>p</i>
13.61 ± 2.09	13.78 ± 1.91	0.620	15.00 ± 2.49	14.99 ± 2.56	0.973	13.90 ± 1.96	13.51 ± 1.75	0.230
<i>Arm curl test (Mean±SD)</i>								
15.10 ± 2.69	14.71 ± 2.51	0.375	17.24 ± 2.72	17.10 ± 2.43	0.761	16.07 ± 2.40	15.94 ± 2.61	0.757
<i>2-minute step test (Mean±SD)</i>								
81.97 ± 11.14	80.75 ± 10.98	0.506	92.56 ± 12.07	94.37 ± 10.47	0.346	83.21 ± 9.71	85.13 ± 10.01	0.261
<i>Timed Up and Go test (Mean±SD)</i>								
10.85 ± 1.44	11.13 ± 1.27	0.231	10.81 ± 1.49	11.07 ± 1.30	0.284	10.83 ± 1.47	11.16 ± 1.26	0.168
Abbreviations: GDS-15, 15-item Geriatric Depression Scale; IADL, instrumental activities of daily living; MoCA, Montreal Cognitive Assessment; IG, Intervention Group; CG, Control Group Footnotes: All <i>p</i> values were calculated using independent-samples <i>t</i> tests, except where otherwise indicated. *Pearson's χ^2 test. Follow-up <i>p</i> values represent unadjusted cross-sectional comparisons and are presented descriptively; longitudinal intervention effects were estimated using linear mixed-effects models and are reported separately.								

Primary and secondary outcomes

The intervention effect on global cognition was evident by 3 months and remained present at 12 months. Compared with the control group, the intervention group showed greater improvement in MoCA total score at both 3 months ($\beta = 0.525$; 95%CI: 0.227–0.822; $p = 0.001$) and 12 months ($\beta = 1.627$; 95%CI: 1.325–1.929; $p < 0.001$) (Table 2).

No between-group differences were observed over time for depressive symptoms or instrumental functioning. Physical-performance findings were inconsistent. Chair-stand change nominally favored the intervention group at 12 months ($\beta = 0.518$; 95%CI: 0.040–0.996; $p = 0.034$), whereas 2-minute step change favored the control group at 3 months ($\beta = -2.227$; 95%CI: -4.412 to -0.042; $p = 0.046$) and 12 months ($\beta = -2.922$; 95%CI: -5.141 to -0.702; $p = 0.010$). No between-group differences were evident for the arm-curl or Timed Up and Go tests. Because these secondary analyses were not adjusted for multiple comparisons and did not form a coherent pattern across physical outcomes, they should be interpreted as supportive rather than definitive.

Exploratory domain-level analyses showed greater between-group improvement in attention at both follow-up assessments and in language and abstraction at 12 months. No clear differences were evident across the

remaining MoCA domains. Thus, the total-score effect was not uniformly distributed across domains. These exploratory findings should be considered hypothesis-generating.

Table 2
Intervention Effects on Changes in Cognitive, Functional, and Physical Outcomes from Baseline to 3 and 12 months.

Variables	Group × time contrast	β	95%CI	<i>p</i>
Primary and secondary outcomes				
MoCA total score				
	3 months	0.525	0.227 to 0.822	0.001
	12 months	1.627	1.325 to 1.929	< 0.001
GDS-15 score				
	3 months	-0.071	-0.325 to 0.183	0.586
	12 months	-0.015	-0.273 to 0.242	0.906
Lawton IADL score				
	3 months	-0.089	-0.271 to 0.092	0.333
	12 months	-0.142	-0.327 to 0.043	0.133
Senior Fitness Test				
Chair stand test				
	3 months	0.170	-0.301 to 0.641	0.479
	12 months	0.518	0.040 to 0.996	0.034
Arm curl test				
	3 months	-0.064	-0.549 to 0.420	0.795
	12 months	-0.194	-0.687 to 0.298	0.439
2-minute step test				
	3 months	-2.227	-4.412 to - 0.042	0.046
	12 months	-2.922	-5.141 to - 0.702	0.010
Timed Up and Go test				
	3 months	-0.000	-0.064 to 0.063	0.991
	12 months	-0.005	-0.070 to 0.059	0.874
Exploratory MoCA domain outcomes				
Visuospatial and executive function				
	3 months	-0.177	-0.370 to 0.017	0.073
	12 months	0.126	-0.070 to 0.323	0.208
Naming				
	3 months	0.034	-0.105 to 0.173	0.630

Variables	Group × time contrast	β	95%CI	<i>p</i>
Attention	12 months	0.017	-0.123 to 0.158	0.809
	3 months	0.702	0.394 to 1.010	< 0.001
	12 months	0.340	0.028 to 0.653	0.033
Language	12 months	0.340	0.028 to 0.653	0.033
	3 months	-0.191	-0.429 to 0.047	0.116
	12 months	0.524	0.282 to 0.765	< 0.001
Abstraction	12 months	0.524	0.282 to 0.765	< 0.001
	3 months	0.099	-0.120 to 0.319	0.375
	12 months	0.568	0.346 to 0.791	< 0.001
Delayed recall	12 months	0.568	0.346 to 0.791	< 0.001
	3 months	0.148	-0.108 to 0.405	0.258
	12 months	0.122	-0.139 to 0.382	0.360
Orientation	12 months	0.122	-0.139 to 0.382	0.360
	3 months	-0.050	-0.292 to 0.191	0.683
	12 months	-0.041	-0.286 to 0.203	0.741
Abbreviations: β , coefficient; CI, confidence interval; GDS-15, 15-item Geriatric Depression Scale; IADL, instrumental activities of daily living; MoCA, Montreal Cognitive Assessment.				
Footnotes: Coefficients were estimated using linear mixed-effects models fitted by maximum likelihood, with the control group and baseline assessment as the reference categories. Each β represents the between-group difference in change from baseline to the specified follow-up assessment. Higher scores indicate better outcomes for the MoCA total and domain scores, Lawton IADL, Chair Stand, Arm Curl, and 2-minute Step tests; lower scores indicate better outcomes for the GDS-15 and Timed Up and Go test. Secondary-outcome and exploratory MoCA domain analyses were not adjusted for multiple comparisons and should be interpreted as supportive.				

Sensitivity analysis

A per-protocol sensitivity analysis included 140 participants who met the predefined per-protocol criteria. The findings were consistent with the primary intention-to-treat analysis. Compared with the control group, the intervention group demonstrated greater improvement in MoCA total score at both 3 months ($\beta = 0.507$; 95%CI: 0.214-0.8; $p = 0.001$) and 12 months ($\beta = 1.613$; 95%CI: 1.316–1.91; $p < 0.001$). Results for depressive symptoms, instrumental functioning, and most physical-performance findings were consistent with those of the intention-to-treat analysis. Similar patterns were observed for the chair-stand and 2-minute step tests, as well as the exploratory MoCA domains of attention, language, and abstraction.

Discussion

This RCT found that older adults with MCI who received the structured multidomain cognitive intervention showed greater cognitive improvement than those in the control group at both follow-up assessments. The larger between-group difference at 12 months suggests better maintenance of the early cognitive gain in the intervention group, whereas much of the initial improvement in the control group was not sustained. Most secondary outcomes showed no clear between-group differences, indicating that the cognitive benefit was not accompanied by broad effects on depressive symptoms, instrumental functioning, or physical performance. This interpretation is consistent with the broader multidomain-prevention literature, in which benefits are commonly characterized as improvement or maintenance of cognitive function relative to a comparison condition.(37)

The findings support the added benefit of the structured multidomain cognitive training when added to the multimodal background component. The cognitive training component combined a standardized session structure, individualized entry levels, adaptive progression, supervised delivery, reinforcement, and functionally oriented cognitive tasks. However, the trial was not designed to determine which of these features contributed most to the observed effect. Previous multidomain programs have differed substantially in content, dose, progression, and control conditions, which has limited identification of the intervention characteristics most relevant to durable cognitive benefit.(9, 38)

The present result is consistent with the SYNERGIC trial,(36) in which the addition of computerized cognitive training to aerobic–resistance exercise produced greater cognitive improvement than exercise alone in adults with MCI. The current study extends that principle to a conventional, noncomputerized approach. Its reliance on clinically accessible tasks rather than technology-intensive platforms may facilitate implementation in routine clinical and community settings, although scalability and cost-effectiveness were not directly evaluated.(39, 40)

The physical-performance findings were inconsistent. At 12 months, the chair-stand result reflected relative preservation rather than a clear gain in lower-limb strength. Performance changed little in the intervention group but declined slightly in the control group, while no between-group difference was evident at 3 months. Although the chair-stand test primarily reflects functional lower-body strength,(30) sit-to-stand performance also requires motor planning,(41) postural control,(42) and cognitive–motor integration.(43) A cognitive contribution is therefore plausible, although the present data do not establish that cognitive improvement caused the chair-stand difference.

In contrast, the negative 2-minute step coefficients indicated a smaller improvement in the intervention group than in the control group, rather than a decline from baseline, as scores increased in both groups. The test reflects exercise capacity but may also be influenced by lower-limb strength and the ability to sustain repetitive effort.(30, 44, 45) Together with the absence of between-group differences in arm-curl and TUG performance, the contrasting chair-stand and 2-minute step findings were isolated, inconsistent in direction, and based on secondary analyses without adjustment for multiple comparisons. These findings therefore provide no clear evidence of physical benefit or harm and do not explain the greater cognitive improvement in the intervention group.

Exploratory analyses suggested that the between-group differences in cognitive change were most evident in attention at both follow-up assessments and in language and abstraction at 12 months with no clear differences in the remaining cognitive domains. Although this pattern may suggest greater responsiveness of processes requiring sustained attention, cognitive control, and higher-order integration, it should not be interpreted as evidence of a specific neurocognitive mechanism. Cognitive-intervention effects in MCI can vary across domains,

and gains on global or trained cognitive measures do not necessarily generalize uniformly to other cognitive or everyday functions.(6, 7)

A strength of this trial is its use of an active control group rather than usual care or no intervention. The active control received the same background components as the intervention group, including cognitive-health education, standardized low-intensity home cognitive activities, and the same supervised and home-based physical-exercise program. The key difference between groups was the structured, supervised, and progressively adapted multidomain cognitive training provided only to the intervention group. This design reduces the likelihood that the greater between-group improvement in MoCA change from baseline was explained solely by staff contact, general cognitive stimulation, or exercise exposure.(46, 47) The consistency of the per-protocol findings with the intention-to-treat analysis provides some reassurance that the primary result was not driven solely by differential attrition or adherence.

Several limitations should be considered. First, MCI was identified using screening criteria rather than comprehensive clinical, neuropsychological, or biomarker assessment. The MoCA was used as a continuous measure of cognitive change over time rather than an eligibility criterion, supported by validation studies reporting 90–93% sensitivity and 87% specificity for detecting MCI in older adults.^(23, 48) Second, repeated administration of the same Vietnamese MoCA version (7.1) may have introduced practice effects. This version was selected because it is the validated Vietnamese MoCA version officially approved for clinical use. Practice effects are generally strongest over shorter retest intervals and may be less pronounced in people with MCI than in cognitively intact older adults.(49) Moreover, because participants were randomly assigned to study groups using block randomization, any practice effects would be expected to occur similarly in both groups and are therefore unlikely to account for the between-group differences in cognitive outcomes.(50) Finally, the structured cognitive training comprised several interacting components, including individualized starting levels, adaptive progression, supervised training, and functionally oriented tasks. The trial was not designed to isolate the contribution of individual components; therefore, the observed cognitive benefit should be attributed to the structured cognitive training as a whole rather than to any single feature.

Conclusion

Among older adults with MCI, adding a structured, progressively delivered cognitive rehabilitation program to a shared multimodal non-pharmacological platform produced greater improvement in global cognition than control at both 3 and 12 months. These findings support further pragmatic evaluation of this noncomputerized intervention in routine practice and resource-constrained settings.

Declarations

Ethics approval and consent to participate

The study was approved by the Biomedical Research Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City (reference number: 625/HĐĐĐ-ĐHYD, dated 05 May 2024) and by the Ethics Committee of Nhan Dan Gia Dinh Hospital (reference number: 65/NDGD-HĐĐĐ, dated 17 May 2024). The study adhered to the ethical principles outlined in the revised 1987 Declaration of Helsinki, and written informed consent was provided by all participants. The trial was registered at ClinicalTrials.gov (registration number: NCT06453746; June 12, 2024).

Consent for publication

Not applicable

Competing interests

The authors declare no competing interests.

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Author Contribution

KQN, KGT, and THNT contributed to the conception and design of the study, interpretation of the findings, and drafting and substantive revision of the manuscript. KQN was responsible for data collection. KQN and KGT performed the data analysis, and KGT supervised the overall process of data collection and data processing. All authors read and approved the final manuscript and agreed to be accountable for their own contributions and for the integrity of the work.

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Availability of data and materials

The datasets generated and/or analyses during the current study are available from the corresponding author on reasonable request.

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Figures

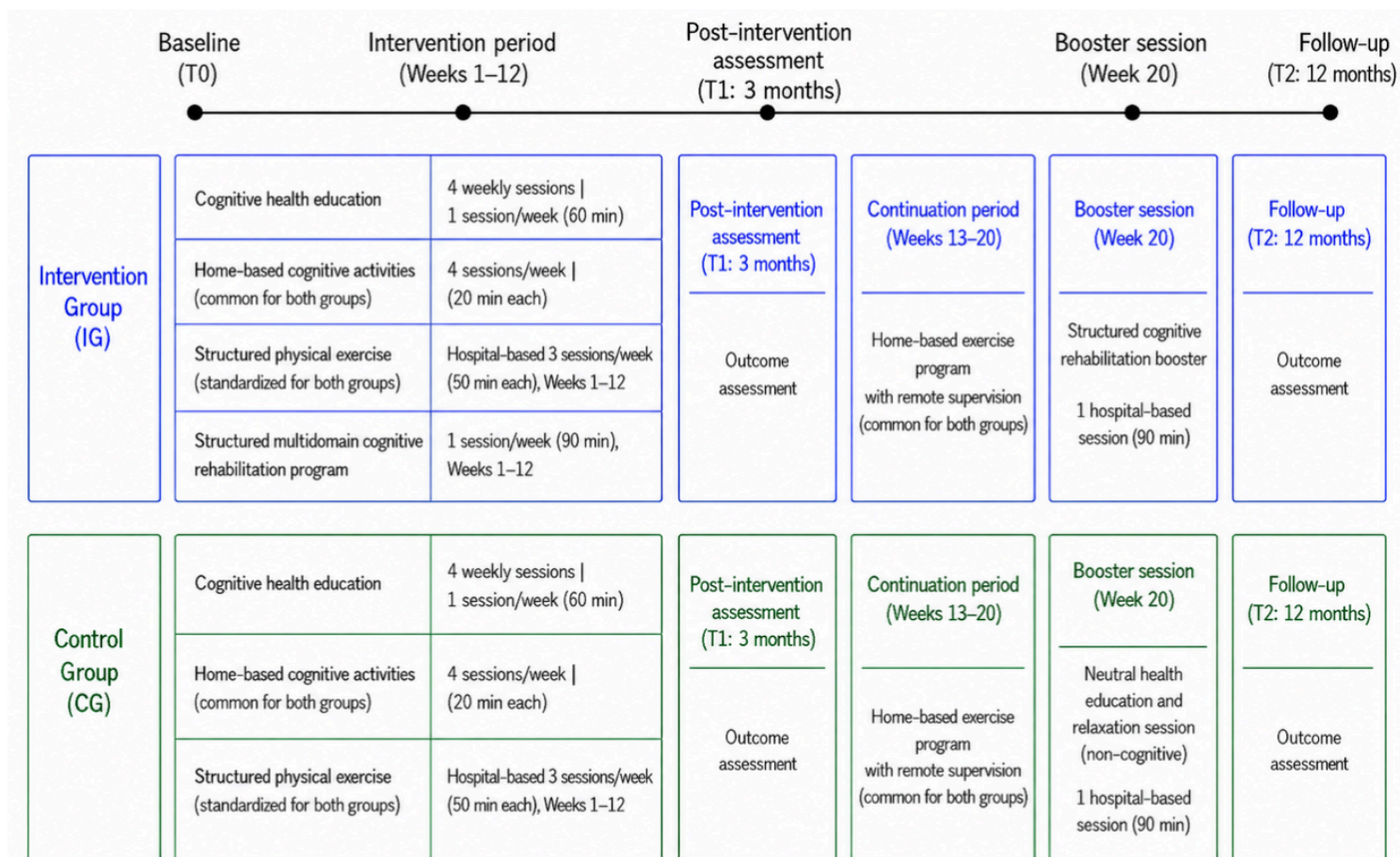


Figure 1

Study intervention framework and timeline (Figure created by the authors).

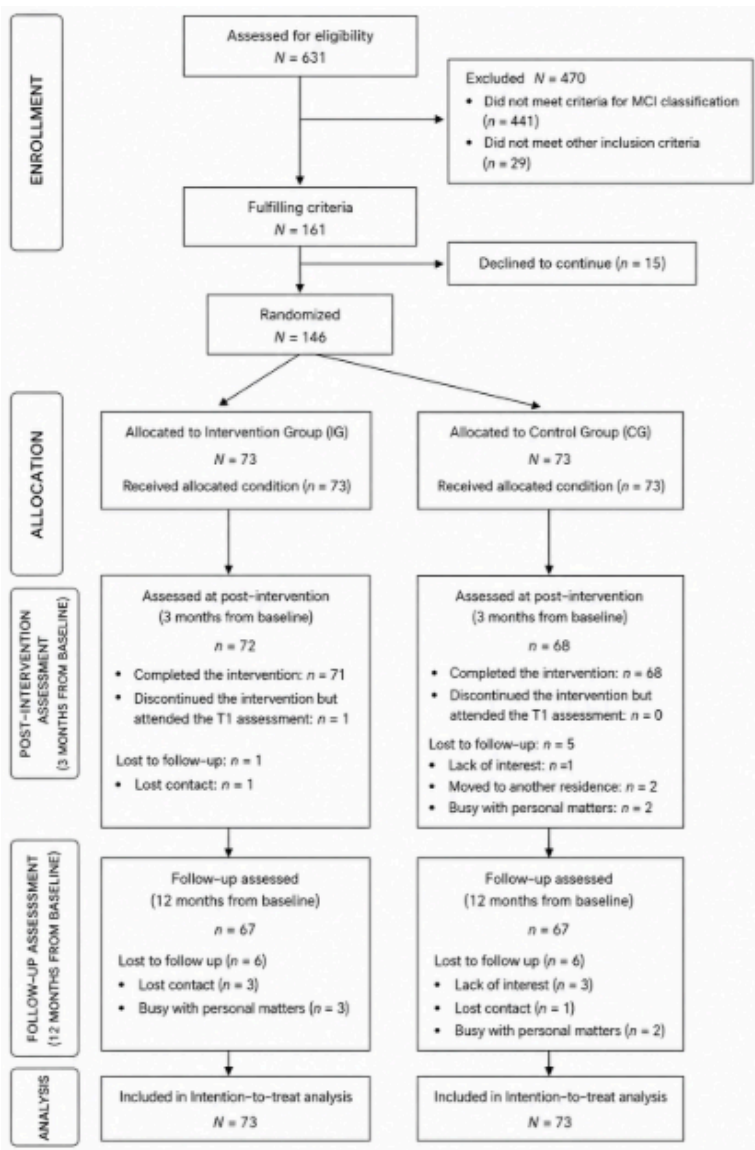


Figure 2

Flow chart of the study (Figure created by the authors).

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