

# Combination of mind-body physical exercise, cognitive training, and nurse-led risk factor modification for older adults with mild cognitive impairment: a randomised controlled trial (abridged secondary publication)

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## KEY MESSAGES

1. We compared the effects of health advice alone, nurse-led risk factor modification (RFM) alone, and a combination of cognitive training, mind-body physical exercise, and nurse-led RFM on preventing cognitive decline in older adults with mild cognitive impairment (MCI).
2. Although Alzheimer's Disease Assessment Scale–Cognitive Subscale scores significantly improved from baseline across all three groups, the combination and nurse-led RFM groups did not demonstrate additional benefits relative to the health advice group.
3. Future research should focus on identifying the characteristics of older adults with MCI who derive the most benefit from interventions, and on more accurately describing the natural history of MCI.

4. Future studies can also explore optimal intervention dosage, including the intensity, duration, and formats of physical exercise and cognitive training.
5. Early identification of MCI and improved strategies for participant retention, with more intensive follow-up, may be needed.

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## Introduction

Dementia and cognitive impairments are major public health challenges. According to the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), in older adults at risk of dementia, interventions combining exercise, cognitive training, dietary changes, and vascular risk monitoring can significantly enhance cognitive function, compared with regular health advice.<sup>1</sup> Nurse-led care can achieve health outcomes comparable to those of doctor-led care. However, there is a lack of randomised controlled trials evaluating the effectiveness of nurse-led risk factor modification (RFM) or its combination with physical exercise and cognitive training on cognitive function in older adults.<sup>2</sup> This study aimed to compare the effects of health advice alone, nurse-led RFM alone, and a combination of cognitive training, mind-body physical exercise, and nurse-led RFM on preventing cognitive decline in older adults with mild cognitive impairment (MCI).

## Methods

Older adults aged 60 to 80 years with MCI (based on a

score of 19 to 25, adjusted for education, on the Hong Kong version of the Montreal Cognitive Assessment<sup>3</sup> [HK-MoCA]) and without any life-threatening diseases were recruited from various primary care and community settings. Individuals with a diagnosis of dementia, participation in a concurrent lifestyle modification programme, a history of bipolar disorder or psychosis, or communication difficulties were excluded. Psychotropic medications were required to remain stable for at least 3 months prior to the baseline assessment and throughout the study. Participants were randomly assigned to receive health advice alone, nurse-led RFM alone, or a combination of cognitive training, mind-body physical exercise, and nurse-led RFM for 15 months.

Health advice was delivered through pamphlets emphasising healthy diets and promoting physical, cognitive, and social activities aimed at managing risk factors, preventing cognitive decline, and reducing disability.

Nurse-led RFM was based on the FINGER trial protocol.<sup>1</sup> A nurse with >20 years of experience offered personalised lifestyle modifications on a quarterly basis. A physician also reviewed blood test results, physical examination findings, and cardiovascular

and metabolic health. Key risk factors considered included poor control of blood pressure, glucose, and lipid levels, as well as body mass index  $>25 \text{ kg/m}^2$ , smoking, physical inactivity, and unhealthy diet. Dietary goals included increasing fruit and vegetable intake, choosing low-fat meat products, limiting sucrose to 50 g/day, and consuming two or more servings of fish weekly. Motivational interviewing techniques were used to promote behavioural change. Cardiovascular risk was assessed using the QRISK3 score, with the goal of maintaining 10-year cardiovascular risk  $<10\%$ .

The combination of mind-body physical exercise, cognitive training, and nurse-led RFM included practising the 24-form simplified Tai Chi for 30 minutes three times per week, led by a trained Tai Chi master or physical therapist. Participants were encouraged to continue practising using audio or video recordings afterwards. Additionally, three 1-hour group cognitive sessions per week were provided, involving leisure activities that required substantial cognitive engagement.

Assessments were conducted at baseline and at 6, 12, and 15 months. At baseline, participants met with primary care clinicians for a health examination and medical history review. The nurse provided both verbal and written guidance on physical and cognitive activities, as well as dietary recommendations to enhance vascular health and mitigate risks. Outcome measures included the Chinese version of the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog), the Clinical Dementia Rating Scale–Sum of Boxes, the Disability Assessment for Dementia, the European Quality of Life Questionnaire, five-level version and its visual analogue scale, the Geriatric Depression Scale, the Geriatric Anxiety Scale, a dietary adherence score derived from a shortened Food Frequency Questionnaire, the Physical Activity Scale for the Elderly, the Alcohol Use Disorders Identification Test–Concise, and health service utilisation.

A linear mixed model was used to assess changes and between-group differences in outcomes across the three groups over time. Outcome scores were the dependent variables, whereas the intervention group, time, and their interaction served as predictors. The intention-to-treat principle was followed.

## Results

In total, 129 male and 327 female participants (mean age, 70.1 years) were equally randomised into one of the three groups. The groups were comparable at baseline (Table 1). Attendance rates for the nurse-led RFM sessions were 88.8% in the combination group and 92.5% in the RFM group. Within the combination group, 55.1% of participants attended the exercise sessions, whereas 54.6% attended the

cognitive sessions.

ADAS-Cog scores significantly improved across all three groups at 6, 12, and 15 months ( $P<0.05$ ). Estimated between-group treatment effects revealed no significant differences in ADAS-Cog scores or any secondary outcomes among groups at any follow-up time (Table 2).

Compared with those who completed all assessments, participants who missed any follow-up assessment had worse baseline ADAS-Cog scores ( $11.9\pm 4.9$  vs  $10.4\pm 4.1$ ,  $P=0.006$ ) and HK-MoCA scores ( $22.2\pm 2.1$  vs  $22.7\pm 1.9$ ,  $P=0.048$ ).

## Discussion

Significant ADAS-Cog improvements were observed across all three groups at each follow-up. Even the minimal health advice intervention led to cognitive improvements in many participants with MCI. These improvements may be attributable to the natural course of MCI, regression to the mean, and practice effects. Epidemiological study results suggest that approximately 45% of patients remain stable, whereas up to 44% revert to normal cognition within 1 year.<sup>4,5</sup> Regression to the mean, in which extreme cognitive scores tend to normalise over time, suggests that the ADAS-Cog improvements could reflect natural fluctuations rather than genuine cognitive enhancement. Additionally, practice effects may have contributed to improvements observed in the health advice group; participants might also have benefited from unrecorded interventions, given that they were already active older adults within community and primary care settings.

The RFM group showed a non-significant trend towards better ADAS-Cog outcomes, compared with the health advice group. According to a scoping review, none of four nurse-led interventions targeting cognitive outcomes in dementia or MCI demonstrated significant positive effects. Most studies excluded patients with MCI or those at an early stage of dementia. Participants at lower risk may be less likely to benefit from interventions, suggesting that not all individuals with MCI require immediate intervention. Therefore, future research should prioritise early identification of high-risk MCI patients and more intensive follow-ups in this population.

There were no additional benefits in cognitive function or any secondary outcomes in the combination group, compared with the RFM and health advice groups. The attendance rates for physical exercise and cognitive training sessions exceeded 50% and were comparable to the 60% for physical activity and 47.2% for cognitive training noted in the FINGER study.<sup>1</sup> Future research should focus on identifying the optimal frequency and intensity of interventions that are both acceptable and effective for individuals with MCI.

TABLE I. Characteristics of participants at baseline.

Characteristic	Total (n=456)*	Combination (n=152)*	Risk factor modification (n=152)*	Health advice (n=152)*	P value
Age, y	70.1±4.9	70.9±4.8	69.8±5.0	69.6±4.8	0.061
Male	129 (28.3)	49 (32.2)	39 (25.7)	41 (27.0)	0.403
Married	285 (62.5)	95 (62.5)	92 (60.5)	98 (64.5)	0.777
Education >6 y	243 (53.3)	80 (52.6)	79 (52.0)	84 (55.3)	0.831
No. of people living together	1.6±1.4	1.5±1.2	1.8±1.5	1.5±1.2	0.084
Living alone	92 (20.2)	30 (19.7)	36 (23.7)	26 (17.1)	0.355
No. of children					0.914
0	37 (8.1)	11 (7.2)	13 (8.6)	13 (8.6)	
1	84 (18.4)	25 (16.4)	30 (19.7)	29 (19.1)	
≥2	335 (73.5)	116 (76.3)	109 (71.7)	110 (72.4)	
Employed	32 (7.0)	9 (5.9)	11 (7.2)	12 (7.9)	0.790
Family monthly income ≥HK\$4000	237 (52.0)	78 (51.3)	89 (58.6)	70 (46.1)	0.078
Recipient of Comprehensive Social Security Assistance	20 (4.4)	10 (6.6)	2 (1.3)	8 (5.3)	0.066
Medical comorbidities					0.338
0-1	106 (23.2)	31 (20.4)	39 (25.7)	36 (23.7)	
2-3	157 (34.4)	62 (40.8)	45 (29.6)	50 (32.9)	
≥4	193 (42.3)	59 (38.8)	68 (44.7)	66 (43.4)	
Ever smoker	69 (15.1)	23 (15.1)	24 (15.8)	22 (14.5)	0.950
Hong Kong version of Montreal Cognitive Assessment	22.6±2.0	22.6±1.9	22.8±1.9	22.4±2.1	0.276
Alzheimer's Disease Assessment Scale-Cognitive Subscale	10.7±4.3	10.2±3.9	10.9±4.7	11.0±4.3	0.241
Clinical Dementia Rating Scale-Sum of Boxes	1.6±0.9	1.5±0.8	1.6±1.0	1.6±0.8	0.698
Disability Assessment for Dementia	98.0±3.4	98.1±3.1	97.9±3.6	98.1±3.4	0.795
European Quality of Life Questionnaire (five-level version)	0.86±0.15	0.86±0.14	0.86±0.15	0.87±0.14	0.790
European Quality of Life Questionnaire (visual analogue scale)	69.5±14.1	70.5±13.4	69.3±14.6	68.8±14.3	0.558
Geriatric Depression Scale	4.2±3.5	3.8±3.2	4.3±3.7	4.5±3.6	0.231
Geriatric Anxiety Scale	4.6±5.6	4.2±5.4	4.5±5.4	5.1±5.9	0.369
Physical Activity Scale for the Elderly	91.1±40.6	92.2±40.9	91.6±36.8	89.6±44.0	0.844
Dietary adherence score	7.0±1.3	7.1±1.3	6.9±1.3	7.0±1.4	0.407
Alcohol Use Disorders Identification Test-Concise	0.8±1.5	0.8±1.4	0.8±1.6	0.8±1.4	0.926
No. of health service utilisations	6.3±6.4	6.4±6.9	6.3±6.4	6.3±5.9	0.975

\* Data are presented as mean±standard deviation or No. (%) of participants.

This study had several limitations. First, no assessment was conducted at 3 months after the initial 3-month intervention; the cognitive training and exercise programmes lasted only 3 months. Due to resource constraints, only a 6-month follow-up was performed. Second, a substantial proportion of participants improved with the minimal health advice intervention alone, making it difficult to detect

between-group differences. The broad MCI criteria (an HK-MoCA score of 19 to 25) may have included participants with milder cognitive impairment who improved naturally without intervention. Third, the compliance rates for exercise and cognitive training were only 50%; these likely were affected by the COVID-19 pandemic, which may have influenced outcomes in the intervention group.

TABLE 2. Estimated treatment effects between groups at 6-, 12-, and 15-month follow-ups.

Outcome	Treatment effect (95% confidence interval)		
	Combination vs health advice	Risk factor modification vs health advice	Combination vs risk factor modification
<b>Alzheimer's Disease Assessment Scale–Cognitive Subscale</b>			
6 months	-0.2 (-1.3 to 0.8)	-0.8 (-1.9 to 0.2)	0.6 (-0.4 to 1.6)
12 months	0.1 (-1.1 to 1.4)	-0.9 (-2.2 to 0.3)	1.1 (-0.2 to 2.3)
15 months	0.3 (-1.0 to 1.7)	-0.6 (-1.9 to 0.8)	0.9 (-0.4 to 2.2)
<b>Clinical Dementia Rating Scale–Sum of Boxes</b>			
6 months	-0.1 (-0.3 to 0.1)	-0.1 (-0.3 to 0.1)	0.0 (-0.2 to 0.2)
12 months	0.0 (-0.2 to 0.2)	0.1 (-0.2 to 0.3)	-0.1 (-0.3 to 0.2)
15 months	-0.1 (-0.3 to 0.1)	-0.1 (-0.4 to 0.1)	0.0 (-0.2 to 0.3)
<b>Disability Assessment for Dementia</b>			
6 months	0.6 (-0.2 to 1.4)	0.8 (-0.1 to 1.6)	-0.1 (-1.0 to 0.7)
12 months	0.3 (-0.6 to 1.2)	0.2 (-0.8 to 1.1)	0.1 (-0.8 to 1.0)
15 months	0.1 (-0.8 to 1.1)	0.2 (-0.7 to 1.2)	-0.1 (-1.0 to 0.8)
<b>European Quality of Life Questionnaire (five-level version)</b>			
6 months	0.03 (-0.01 to 0.06)	0.03 (-0.01 to 0.06)	0.00 (-0.03 to 0.04)
12 months	0.01 (-0.03 to 0.05)	0.01 (-0.03 to 0.05)	0.00 (-0.04 to 0.04)
15 months	0.04 (-0.01 to 0.09)	0.02 (-0.03 to 0.07)	0.02 (-0.02 to 0.07)
<b>European Quality of Life Questionnaire (visual analogue scale)</b>			
6 months	-0.2 (-3.3 to 2.9)	0.9 (-2.3 to 4.2)	-1.1 (-4.2 to 2.0)
12 months	0.6 (-3.3 to 4.5)	-0.2 (-4.2 to 3.8)	0.8 (-3.0 to 4.7)
15 months	-0.3 (-4.6 to 3.9)	-0.3 (-4.7 to 4.0)	0.0 (-4.2 to 4.2)
<b>Geriatric Depression Scale</b>			
6 months	0.1 (-0.6 to 0.8)	-0.2 (-1.0 to 0.5)	0.3 (-0.4 to 1.1)
12 months	-0.1 (-1.0 to 0.8)	-0.3 (-1.2 to 0.6)	0.2 (-0.7 to 1.1)
15 months	0.6 (-0.4 to 1.6)	-0.4 (-1.4 to 0.6)	1.0 (0.0 to 1.9)
<b>Geriatric Anxiety Scale</b>			
6 months	0.5 (-0.7 to 1.7)	0.0 (-1.1 to 1.2)	0.5 (-0.7 to 1.6)
12 months	0.6 (-0.9 to 2.1)	0.6 (-0.8 to 2.1)	0.0 (-1.5 to 1.4)
15 months	1.3 (-0.4 to 2.9)	-0.3 (-1.9 to 1.3)	1.5 (0.0 to 3.1)
<b>Physical Activity Scale for the Elderly</b>			
6 months	-3.5 (-12.9 to 5.9)	-3.1 (-12.3 to 6.1)	-0.1 (-9.5 to 9.2)
12 months	1.3 (-10.5 to 13.0)	-5.1 (-16.5 to 6.2)	6.7 (-4.6 to 18.0)
15 months	-1.0 (-13.8 to 11.8)	-9.1 (-21.4 to 3.3)	8.2 (-3.8 to 20.1)
<b>Dietary adherence score</b>			
6 months	0.3 (-0.1 to 0.6)	0.3 (0.0 to 0.7)	-0.1 (-0.4 to 0.3)
12 months	0.3 (-0.1 to 0.7)	0.3 (-0.1 to 0.7)	0.0 (-0.4 to 0.4)
15 months	0.3 (-0.1 to 0.7)	0.2 (-0.2 to 0.6)	0.1 (-0.3 to 0.5)
<b>Alcohol Use Disorders Identification Test–Concise</b>			
6 months	0.0 (-0.3 to 0.2)	0.1 (-0.2 to 0.3)	-0.1 (-0.4 to 0.1)
12 months	0.1 (-0.2 to 0.4)	0.0 (-0.4 to 0.3)	0.1 (-0.2 to 0.5)
15 months	0.1 (-0.2 to 0.5)	0.0 (-0.4 to 0.3)	0.1 (-0.2 to 0.5)
<b>No. of health service utilisations</b>			
6 months	-0.4 (-2.1 to 1.2)	0.4 (-1.4 to 2.2)	-0.9 (-2.8 to 1.1)
12 months	-0.3 (-2.3 to 1.7)	1.4 (-0.7 to 3.6)	-1.8 (-4.1 to 0.6)
15 months	0.3 (-1.8 to 2.4)	0.2 (-2.2 to 2.5)	0.2 (-2.3 to 2.6)

## Conclusion

A combination of cognitive training, mind-body physical exercise, and nurse-led RFM did not provide additional benefits over health advice alone regarding cognitive function improvement among older adults with MCI. Future research should focus on identifying specific characteristics of older adults with MCI who are most likely to benefit from interventions and on more accurately describing the natural history of MCI. Additionally, it is essential to explore optimal dosages, including the intensity, duration, and formats of physical exercise and cognitive training, to improve cognitive function and ensure high compliance. Early identification of MCI and better retention strategies with more intensive follow-up may be needed.

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## Disclosure

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1. Xu Z, Zhang D, Yip BH, et al. Combined mind-body physical exercise, cognitive training, and nurse-led risk factor modification to enhance cognition among older adults with mild cognitive impairment

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