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Effects of a multicomponent intervention to slow mild cognitive impairment progression: A randomized controlled trial

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ABSTRACT

Background: Mild cognitive impairment affects 36% of people aged ≥65 years in China, around 50% of whom will develop dementia within 3 years. Early intervention can slow disease progression and delay the onset of dementia; however, whether a multicomponent intervention can decelerate the progression of mild cognitive impairment remains unknown.
Objective: To evaluate the effects of a multicomponent intervention to slow mild cognitive impairment progression in Chinese patients.
Design: Randomized controlled trial.
Setting(s) and participants: This study was conducted in two large regional communities in Guangzhou, China. Patients aged ≥ 65 years diagnosed with mild cognitive impairment were included.
Methods: A total of 112 eligible participants were assigned to receive either a 6-month multicomponent intervention or usual care from September 2019 until January 2021. Data were collected at the beginning of the study and at 1, 3, and 6 months thereafter. The primary outcomes were cognitive function, comprehensive physical capacity, depression, and quality of life. Analysis followed the intention-to-treat principle. A generalized estimating equation was used to determine intervention effects.
Results: At baseline, clinical characteristics did not differ significantly between groups. Significant interaction effects between time and group were detected ($p < 0.001$), indicating that the scores of five outcomes (cognitive function, short physical performance battery, timed up and go test, quality of life, and depression) of intervention and control groups changed differently over time. Participants in the intervention group were found to have a significantly greater improvement in cognitive function, physical function, quality of life, and fewer depression symptoms compared with the control group at baseline and follow-up periods.
Conclusions: This study demonstrates the beneficial effects of a multicomponent intervention on cognitive function, physical function, depression symptoms, and quality of life in people with mild cognitive impairment in the East Asia region. The effectiveness and feasibility of this intervention program suggest that its application should be promoted in community settings to delay the progression of disease in people with mild cognitive impairment.
Registration number: *ChiCTR1900026042*
Tweetable abstract: The multicomponent intervention improves cognitive/physical function, depression, and quality of life, slowing cognitive impairment progression.

What is already known

- Nearly 10 million people in China are currently living with dementia, representing the largest national population with this condition worldwide.
- Approximately 36% of people aged ≥ 65 years are living with mild cognitive impairment, and the incidence of dementia

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among these patients is 15% after 1 year, 40% after 2 years, and 53% after 3 years.
- Early and effective intervention in people with mild cognitive impairment can slow the progression of disease and delay dementia onset.

What this paper adds

- The multicomponent intervention is helpful in improving the cognitive function of patients with mild cognitive impairment.
- The multicomponent intervention can enhance the physical function of patients with mild cognitive impairment
- The multicomponent intervention is helpful in improving the mental state and quality of life of older adults with mild cognitive impairment.

1. Background

Dementia is a leading cause of disability and dependence in people older than 65 years worldwide and the fourth-largest killer after heart disease, cancer, and stroke (Prince et al., 2015). At present, the number of patients with dementia in China is approximately 10 million, ranking highest worldwide. The World Alzheimer Report indicated that the prevalence of dementia in China (6.19%) is higher than the prevalence in sub-Saharan Africa (5.47%) and central Europe (5.18%) and lower than that reported in Latin America (8.41%) and Southeast Asia (7.64%) in patients aged 60 years and older (Jia et al., 2020). By 2040, the number of patients with dementia in China will be the equivalent of the sum of those in all developed countries, and by 2050, the number of dementia patients in China is predicted to reach 30 million (Li, 2015). The Chinese Dementia Commission reported that the average treatment cost for a patient with dementia in China is approximately US$173,000, and the direct economic burden of dementia in China is expected to be about US$11.5 billion per year by 2050, far more than 1% of Chinese gross domestic product (Li, 2015).

The progressive development of dementia and the accompanying pathological changes are impossible to reverse and there is no specific treatment. Therefore, early intervention that aims to slow down or prevent the onset of dementia is particularly important. Mild cognitive impairment is a high-risk state for dementia that represents an early stage of the condition and has attracted the attention of scholars in China and elsewhere. Mild cognitive impairment is a transition stage between normal aging and dementia, and the risk of developing dementia is 10 times higher in people with mild cognitive impairment than in older people of the same age without mild cognitive impairment (Huh et al., 2011). The prevalence of mild cognitive impairment among individuals more than 65 years old is up to 36% in China, and mild cognitive impairment develops into dementia at a rate of 15% after 1 year, 40% after 2 years, and 53% after 3 years (Liu, 2014). Nevertheless, mild cognitive impairment is a clinically heterogeneous unstable state. Patients with mild cognitive impairment may progress to dementia, maintain mild cognitive impairment, or revert to normal cognitive function (Roberts et al., 2014; Vermunt et al., 2019). The different prognoses in mild cognitive impairment provide a good opportunity to delay or prevent progression to dementia. This study was focused on early intervention to delay or prevent mild cognitive impairment progression and reduce the incidence of dementia, thus reducing the economic and care burden on families and society.

Previous studies on dementia prevention have commonly used cognitive or physical training as a single intervention method, which did not result in optimal effects (Hong et al., 2017; Jeong et al., 2016; Song et al., 2018). Experts from the Cambridge Institute of Public Health and the U.K. Cognitive Functioning and Aging Research Prevention Working Group noted that intervention for dementia prevention should be multicomponent, multifactorial, multilevel, and individualized, and only comprehensive intervention addressing multiple risk factors can achieve optimal effects (Olanrewaju et al., 2015; Rodriguez et al., 2020). Previous studies have found that combined or comprehensive intervention could slow the functional decline of patients with mild cognitive impairment (Bae et al., 2019; Xu et al., 2020; Park et al., 2019b; Park et al., 2019a). For example, Bae et al. (2019) found that a 24-week multicomponent intervention combining physical, cognitive, and social activities was effective in improving cognitive function and maintaining physical activity in older adults with mild cognitive impairment.

A study conducted in France revealed that simultaneous aerobic and cognitive training are beneficial for executive functions and functional abilities in older adults with mild cognitive impairment (Combourieu et al., 2018). A systematic review reported the positive effects of the multicomponent interventions to improve cognitive-motor abilities in older adults at risk of developing dementia (Yang et al., 2020). However, a study that used nurse-led integrated management of vascular risk factors for the prevention and treatment of dementia in healthy middle-aged populations found no significant differences in the incidence of dementia between the intervention and control groups (Moll et al., 2016). Another randomized controlled trial, applying a combined intervention among young and middle-aged adults at high-risk of dementia, confirmed that the combined intervention maintained or improved the cognitive function of the subjects (Kivipelto et al., 2013; Ngandu et al., 2015). Rigorous intervention studies involving multicomponent interventions are still needed to determine their effects on slowing down the progression of mild cognitive impairment.

Based on the assessment of risk and protective factors for dementia, the aim of this study was to further evaluate the effects of a multicomponent intervention program on cognitive function, comprehensive physical ability, depression, and quality of life in community-dwelling patients with mild cognitive impairment. Intervention was delivered in community health care centers. Detailed information on the intervention has been published (Lyu et al., 2020).

2. Methods

2.1. Study design and settings

A randomized controlled design was applied in this study (Registration number: ChiCTR1900026042). This study was conducted in two large regional communities in Guangzhou, China. A flowchart showing the research design is presented in Fig. 1. All screened patients with mild cognitive impairment were randomly assigned to one of the two groups: the intervention group that received a 6-month multicomponent intervention and a control group that received usual care. The two groups were then followed prospectively at 1, 3, and 6 months after intervention to assess the effectiveness of the intervention compared with usual care.

2.2. Participants

Patients who attended the community health care centers for physical examination from September 2019 to May 2020 were invited to participate in the study if they met the following inclusion criteria: 1) had been diagnosed with mild cognitive impairment according to the criteria for mild cognitive impairment (Petersen et al., 1997); 2) if on medication (cholinesterase inhibitor or memantine) had been taking it for at least 1 month prior to

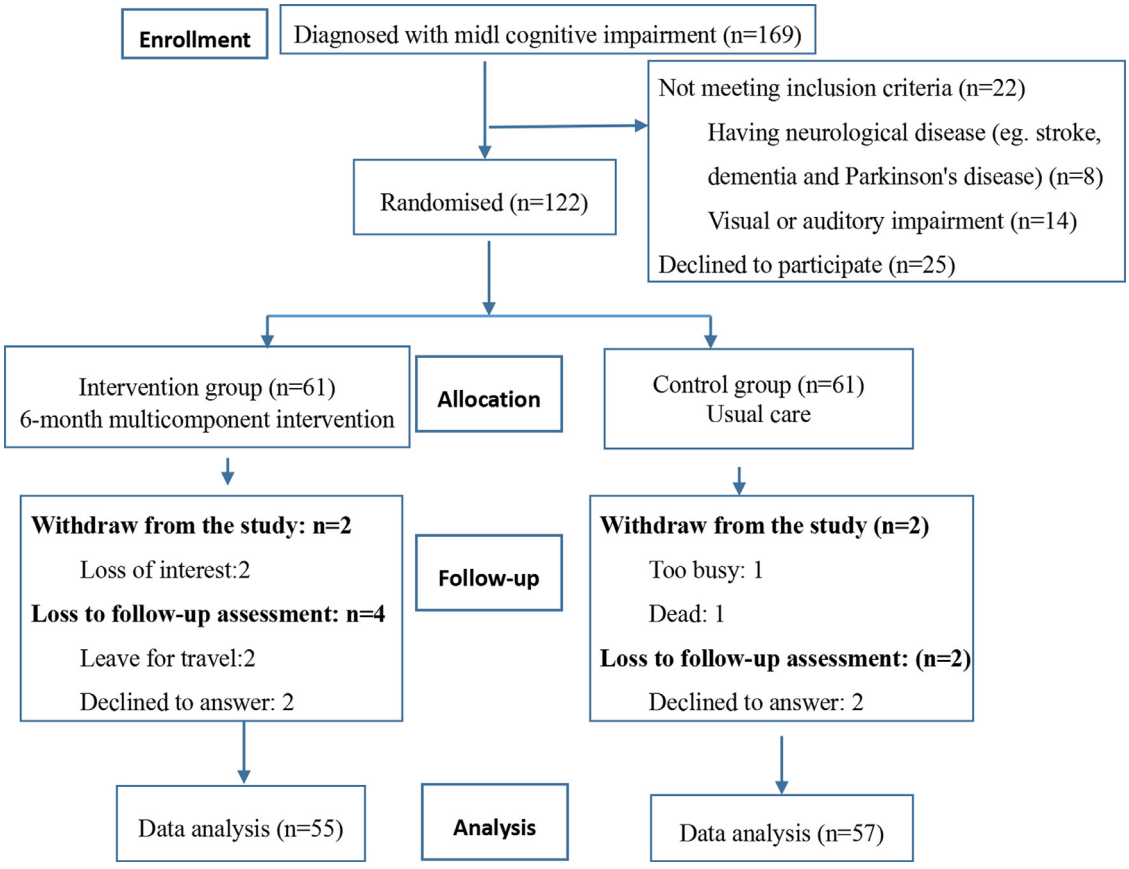

Fig. 1. The Consolidated Standards of Reporting Trials Diagram.

baseline measurement; 3) there must be a caregiver willing to accompany the patient during the intervention (spouse, child, care assistant); 4) able to complete the provided exercise program, according to assessment using the Physical Activity Readiness Questionnaire (Adams, 1999) (if all answers to the questionnaire were no, that indicated that patients could safely complete the intervention independently or with the help of the caregiver for a period of 6 months); and 5) Berg Balance Scale (Lima et al., 2018) score > 40, no risk of falling. The exclusion criteria were as follows: 1) suffering from other serious neurological or mental disorders (e.g., delirium) or brain injury; 2) having a history of severe head trauma; 3) having severe visual or hearing impairment (deaf or hard of hearing; visually impaired; both sight and hearing loss); 4) suffering from severe physical disease or other conditions preventing completion of the intervention. After recruitment, subjects were randomized into the intervention and control groups.

2.3. Sample size estimation

Sample size calculation for the tests of two means (intervention and control groups) in a repeated measures design was performed (Brown and Prescott., 2006; Liu and Wu, 2005). We used PASS 12 to calculate the sample size. PASS is a powerful sample-size program and supports repeated-measures design (Hintze, 2013).

The main outcome indicator of this study was cognitive function, which was measured by the Montreal Cognitive Assessment test. We referred to another study conducted by Xu in 2020 for the sample size calculation (Xu et al., 2020). Xu and associates applied a multidimensional intervention based on the concept of the International Classification of Functioning, Disability and Health and aimed to explore its short-term effect on the improvement of cognitive function in individuals with mild cognitive impairment (Xu et al., 2020). The a and $ß$ values were the probability of class I and II errors; $a = 0.05$ and $ß = 0.1$. The number of time points (repeated measurements) at which each subject is 3. The difference between the means of the intervention and control groups under the alternative hypothesis was 3.46. The standard deviation was 1.61, the same for both groups. Calculation using these parameters generated a required sample size for each group of 29 subjects. The dropout rate in previous studies was at least 25% (Song and Yu, 2019). A high dropout rate is realistic in studies with older people because of illness, death, or cognitive deterioration (Chatfield et al., 2005). We increased the calculation by 50% for each group, resulting in a minimum sample size is 44 patients per group. In this study, we recruited 61 patients per group.

2.4. Procedure and ethical considerations

A research assistant explained the purpose of the study and the principle of confidentiality for voluntary participation in the study and personal information to subjects who met the criteria. If patients were willing to participate in the study, they were required to provide signed informed consent. A random allocation sequence was generated using SPSS according to the sequence number of participants included in the study and stored in opaque envelopes. The research assistant allocated subjects to groups by opening each envelope in turn, according to the order of entering the study. According to the distribution scheme in the envelope, the patients were divided into intervention and control groups. The control group received usual care, and the intervention group received the 6-month multicomponent intervention. Data were collected at baseline, and at 1, 3, and 6 months after the intervention.

The project received ethical approval from the Human Ethics Committee of Sun Yat-Sen University (approval number: L2018ZSLYEC-122).

2.5. Study intervention

2.5.1. The multicomponent intervention

By consulting clinical experts, we formulated a multicomponent intervention based on risk factors and protective factors that may influence the progress of mild cognitive impairment. Interventions targeted at diminishing or eliminating the risk factors and enhancing protective factors can slow down the progression of disease. Lyu and Yang systematically searched PUBMED up to January 1, 2020 to identify systematic reviews and meta-analyses of observational studies examining associations of potentially modifiable factors with all types of dementia within the most recent 5 years. Lv and Lin retrieved and abstracted the full text of potentially eligible articles. We excluded studies that investigated the association between genetic markers and risk for dementia because these factors are not modifiable. We restricted the language to English. When articles reported an overlap in the sample of participants, the article with the largest sample was included. In total, 46 articles were identified.

The literature review found that the main factors influencing progression of mild cognitive impairment to dementia were biological (age, sex), sociological (education level), genetic (family history of dementia, apolipoprotein E genes), disease (coronary heart disease, stroke, diabetes, hypertension, hypercholesterolemia, obesity), and lifestyle (insufficient physical activity, smoking, alcohol abuse, unhealthy diet) (Irwin et al., 2019; Baumgart et al., al.,2015; Zhao et al., 2018; Bellou et al., 2017). Apart from age, sex, genetic factors, and education level could not be addressed, while the remaining risk factors were considered targets for intervention. The protective factors most strongly associated with dementia risk are cognitive and physical activity. Based on the above risk and protective factors screened for those that could delay mild cognitive impairment progression, we developed a multicomponent intervention program. It included four parts: dietary guidance, physical training, cognitive training, and management and monitoring of metabolic indicators and vascular risk factors.

The intervention was delivered by 14 community healthcare workers in the two sites. Their mean age was 40.5 years (SD ± 7.2), and they had practiced as community healthcare workers for a mean of 7.5 years (SD ± 6.8). All intervention providers received 1-day training specific to the multicomponent intervention. The intervention was conducted among patients with mild cognitive impairment under supervision at the community healthcare center. Precise details of the intervention content can be found in another related publication (Lyu et al., 2020).

2.5.1.1. Dietary intervention

Patients with mild cognitive impairment and their caregivers met the community dietitians every 3–4 weeks. A total of six 10–30 min dietary face-to-face meetings were arranged. The dietitian provided information and support on lifestyle improvements, according to the specific situation of each participant, to help them build a healthy diet. After baseline measurement at the beginning of the intervention, the dietitian provided dietary guidance, based on 3-day measurements of food and nutrient intake, metabolic indicators, and vascular risk factors, provided by the participants and their caregivers, and met regularly with participants to make adjustments.

2.5.1.2. Physical Training

Physical training programs, including individualized progressive muscle strength training and aerobic exercise, were designed by rehabilitation therapists. Physical training was completed in the community fitness area in group-based (6–8 people) mode under the supervision of rehabilitation therapists and community physicians and nurses to ensure subjects' safety. Training frequency during the first month was once per week and twice per week for the remaining months. An exercise diary was completed for subjects throughout the intervention. Subjects were tested for single-repeat maximum load before muscle strength training, and exercise intensity was set between 40% and 85% of the single-repeat maximum load. Exercise intensity was adjusted according to repeated maximum load assessment of the participants. Aerobic exercise intensity was set at 50%–70% of maximum heart rate (Maximum heart rate = 220 – age). A heart rate monitor was worn on the wrist to assess energy consumption and heart rate. If the heart rate exceeded pre-set intensity parameters, sound and vibration reminders were activated.

2.5.1.3. Cognitive Training

Cognitive training was based on computer-aided cognitive training and conducted for 60–90 min per session (20-min break time at the interval) once a week at a fixed time and completed under the guidance of psychotherapists. Every patient used a personal account and password to login the training platform to complete cognitive training. Cognitive intervention mainly targeted memory but also involved attention, executive function, visual-spatial ability, language, abstraction, calculation, orientation, and other cognitive fields, with 3–7 training items in each field. Training items were selected and designed to correspond as closely as possible to activities of daily living. Each training item established strict training requirements and procedures. In the 24 types of training, there was a degree of repetition and, as training times increased, the difficulty level of each training task was gradually increased, according to the situation of the research subject.

2.5.1.4. Management and monitoring of metabolic indicators and vascular risk factors

Subjects allocated to the intervention group met with nurses four times: at the beginning of the study, then at 1 month, 3 months, and the end of the intervention (6 months). Metabolic and physiological indicators were measured, including smoking, alcohol consumption, blood pressure, body mass index, hip circumference, waist circumference, blood cholesterol, fasting blood glucose, and oral glucose tolerance test results, among other parameters. Community nurses reported the results back to the subjects, their caregivers, or family members by mail or WeChat. According to the evaluation results, subjects in the intervention group were informed orally and in writing about the importance of reducing these risk factors. Motivating subjects to change lifestyle was an important part of the intervention. When patients needed medication, they were advised to contact an appropriate physician.

2.5.2. Control intervention

The control group received usual care, which was provided to both groups by community nurses and general practitioners. It included three health education classes (45 min each) during the 6-month study period. The educational information was related to epidemiology, etiology, clinical manifestations, and prognosis of mild cognitive impairment, and it also included recommendations for appropriate participation in social activities. The classes did not contain any specific information regarding dietary guidance, physical training, cognitive exercises, and management of metabolic and vascular factors.

2.6. Measurement

2.6.1. Sociodemographic profile

Sociodemographic data were collected from the subjects and their caregivers, including age, sex, education level, marital status,

profession, family per capita monthly income, comorbidity, family history of dementia, history of medication, living conditions, and method of payment of medical expenses. This information was collected only once, at baseline, by research assistants.

2.6.2. Global cognitive function

The Montreal Cognitive Assessment test was used to quickly screen for mild cognitive impairment (Nasreddine et al., 2005; Pinto et al., 2019; Yu et al., 2012). It assesses eight aspects of cognitive function: visual-spatial executive function, naming, memory, attention, language fluency, abstract thinking, 5-min delayed memory, and orientation. It includes 15 items to generate a score of 0–30. One point was added to the test results for subjects with < 12 years of education to correct for educational bias. Higher scores indicated better cognitive function. It takes approximately 10 min to complete and had adequate internal consistency for use with patients with cognitive impairment (Huang et al., 2019).

2.6.3. Comprehensive physical function

The short physical performance battery (Treacy and Hassett, 2018) and the **timed up and go test** (Browne and Nair, 2019) are commonly used measures of physical function.

The short physical performance battery assessment comprises three sections: a series standing test, a 2.44-m walking test, and a sit-stand test (performed five times). The series standing test was administered by trained research nurses to assess patient balance while standing with feet in three positions (together side-by-side, semi-tandem, and tandem). A stopwatch was used to record the time until subjects moved or grasped the tester for support, which was recorded as the end time point. In two time trials of the 2.44-m walk test, subjects were asked to walk 2.44 m two times as fast as possible, and the shorter one was recorded or the time taken if only one time test was completed. For the sit-stand test, participants were asked to stand up and sit down five times as quickly as possible, and the time was recorded using a stopwatch.

For the timed up and go test, subjects started in a seated position. The patients stood up upon the therapist's command, walked 3 m, turned around, walked back to the chair and sat down. A timer was started when the instruction was issued and stopped when the subject was seated.

2.6.4. Depression

The 15-item Geriatric Depression Scale was developed for depression screening in older adults (Dias et al., 2017). The original scale comprised 30 items designed to assess the core symptoms of depression in old age. Each item is a single sentence, and subjects are asked to answer "yes" or "no." Ten of the 30 items are scored in reverse order (i.e., "no" indicated depression), while 20 items are scored in positive order (i.e., "yes" indicated depression). The 15-item Geriatric Depression Scale is a summary of 15 items from a previous depression scale developed by Sheikh and Yesavage in 1986 (Sheikh and Yesavage, 1986). The total score range is 0–15, with higher scores indicating greater depression and scores ≥ 8 indicating the presence of depressive symptoms. The internal consistency coefficient for this scale is 0.82 (Nyunt et al., 2009).

2.6.5. Quality of life

The quality of life of subjects was evaluated using the Quality of Life in Alzheimer's Disease scale (Park et al., 2019a). It contains 13 items. A four-grade Likert scale was adopted, with "1, 2, 3, and 4" representing "poor, average, good, and very good," respectively. The total score was the sum of the scores for all items, where higher scores indicated better quality of life. The scale has good reliability and validity Torisson et al., 2016; Picillo et al., 2019).

2.7. Data analysis

Analyses were performed using IBM SPSS (version 20.0, Chicago, IL, USA). Student's t-tests and χ^2 tests were conducted to investigate whether demographic data or outcome variables were significantly different between two groups. A generalized estimating equation was employed to analyze the effects of the multicomponent intervention on cognitive function, physical function (short physical performance battery, timed up and go test), depression, and quality of life. In situations in which more than one hypothesis is tested simultaneously, proper adjustment of statistical inference is required for multiple comparisons (Bender and Lange, 2001). We applied a Bonferroni adjustment to solve the multiple comparison problems (Chen et al., 2017) by using the significance level as α=0.05/5 = 0.01.

3. Results

3.1. Recruitment, attrition, and adherence

From September 2019 to May 2020, of 169 potential participants identified, 122 who were eligible agreed to participate into the study (Fig. 1). Participants were randomized in a 1:1 ratio to the intervention and control groups. At the end of the study, six subjects in the intervention group and four in the control group had withdrawn from the study. No significant difference was found between the patients who withdrew from the two groups. No adverse events occurred during the intervention. Analyses were limited to the 112 (91.8%) participants with complete follow-up data.

3.2. Participant characteristics

The baseline information on study subjects is presented in Table 1. The mean age of the subjects was 70.45 years, approximately 53% were female, 93% were married, and over 95% lived with a spouse or children. More than 90% ($n = 104$) of participants had health insurance. There were no significant differences in demographic data or outcome variables between the intervention and control groups at baseline.

3.3. Effects of the intervention on cognitive and physical function, depression, and quality of life

Generalized estimating equations was applied to analyze the differences between intervention and control groups. Significant interaction effects between time and group were detected ($p < 0.001$), indicating the scores of five outcomes (cognitive function, short physical performance battery, timed up and go test, quality of life, and depression) of two groups changed differently over time. Then we further applied generalized estimating equations to analyze the data of intervention and control groups, respectively. Participants in the intervention group were found to have a significantly greater improvement in cognitive function, physical function, quality of life, and fewer depression symptoms compared with the control group at baseline and follow-up periods. This indicates that the multicomponent intervention can improve patients' cognitive function, physical function, quality of life, and depressive symptoms. More details can be found in Table 2 and 3. Fig. 2 shows the changing trajectory of measurements over the three time points for the two groups.

4. Discussion

The purpose of this study was to examine the effect of a 6-month multicomponent intervention in slowing the progression of mild cognitive impairment. Our findings indicate that the 6-month

Table 1
Baseline patient demographic characteristics and outcome variables.

Variable	Total (n = 112) n (%)	Intervention (n = 55) n (%)	Control (n = 57) n (%)	t/x^2	p
Age (years, $\bar{x}$± SD)	70.19 ± 5.96	70.68 ± 5.38	70.45 ± 6.54	1.49	1.37
Sex					
Male	53 (47.32)	27 (49.09)	26 (45.61)	0.16	0.38
Female	59 (52.68)	28 (50.91)	31 (54.39)		
Education level					
Below middle school	44 (39.29)	21 (38.18)	23 (40.35)	2.07	0.56
Middle school	47 (41.96)	25 (45.46)	22 (38.60)		
Above middle school	21 (18.75)	9 (16.36)	12 (21.05)		
Marital status					
Married	104 (92.86)	50 (90.91)	54 (94.74)	4.22	0.12
Unmarried/divorced/widowed	8 (7.14)	5 (9.09)	3 (5.26)		
Residence					
Living alone	5 (4.46)	2 (3.64)	3 (5.26)	0.37	0.83
Living with spouse or children	107 (95.54)	53 (96.36)	54 (94.74)		
Source of medical funds					
Self-funded	8 (7.14)	5(9.09)	3 (5.26)	3.38	0.19
Commercial insurance	10 (8.93)	7 (12.73)	3 (5.26)		
Free state medical care	13 (11.61)	7 (12.73)	6 (10.53)		
Social medical insurance	81 (72.32)	36 (65.45)	45 (78.95)		
Family history of dementia					
Yes	30 (26.8)	14 (25.5)	16 (28.1)	2.34	0.13
No	82 (73.2)	41 (74.5)	41 (71.9)		
Outcome variables					
Cognitive function (MoCA score)	21.39 ± 1.55	21.00 ± 1.38	21.48 ± 1.42	−1.713	0.09
Physical function					
SPPB	9.79 ± 0.94	9.64 ± 0.72	9.94 ± 1.09	−1.617	0.11
TUG	9.06 ± 1.36	9.18 ± 1.63	8.94 ± 1.06	0.875	0.38
QoL (QoL-AD score)	29.40 ± 1.73	29.26 ± 1.81	29.54 ± 1.66	−0.808	0.42
Depressive symptoms (GDS score)	5.28 ± 1.48	5.44 ± 1.18	5.12 ± 1.72	1.084	0.28

SD, standard deviation; MoCA, Montreal Cognitive Assessment score; SPPB, Short Physical Performance Battery; TUG, Time Up and Go test; QoL-AD, Quality of Life-Alzheimer's disease; GDS, Geriatric Depression Scale.

Table 2
Generalized estimating equations results for the main effects and interaction effects.

Outcomes	Time effect			Group effect			Group × time effect		
	Waldx²	*df*	*P*	*Waldx²*	*df*	*P*	*Waldx²*	*df*	*P*
Cognitive function	35.728	3	< 0.01	5.255	1	0.022	303.928	3	< 0.01
SPPB	42.721	3	< 0.01	5.18	1	0.023	97.283	3	< 0.01
TUG	6.795	3	0.079	36.271	1	< 0.01	280.522	3	< 0.01
Quality of life	4.522	3	0.21	49.528	1	< 0.01	226.559	3	< 0.01
Depressive symptoms	22.683	3	< 0.01	16.456	1	< 0.01	126.102	3	< 0.01

SPPB, Short Physical Performance Battery; TUG, time up and go test.

Fig. 2. The change trajectory of measurements over the three time points for the two groups.

Table 3
Results of generalized estimating equation analysis for comparison of outcome variables between the intervention and control groups.

Outcomes	Intervention group			Control group			P_{int}
	$\bar{x}\pm SD$	β(95%CI)	p	$\bar{x}\pm SD$	β(95%CI)	p	
Cognitive function							
Baseline	21.00 ± 1.38			21.48 ± 1.42			
1st month	21.44 ± 1.50	0.44 (0.292, 0.588)	< 0.01	21.18 ± 1.37	−0.300(−0.449, −0.151)	< 0.01	< 0.01
3rd month	21.48 ± 1.54	0.48 (0.342, 0.618)	< 0.01	21.14 ± 1.26	−0.34 (−0.483, −0.197)	< 0.01	< 0.01
6th month	21.96 ± 0.64	0.96 (0.814, 1.106)	< 0.01	19.80 ± 0.86	−1.68(−1.943, 1.417)	< 0.01	< 0.01
Physical function							
SPPB							
Baseline	9.28 ± 0.72			9.94 ± 1.09			
1st month	9.52 ± 0.88	0.24 (0.052, 0.428)	0.013	10.52 ± 0.97	0.58 (0.379, 0.781)	< 0.01	< 0.01
3rd month	9.86 ± 1.08	0.58 (0.379, 0.781)	< 0.01	10.26 ± 1.01	0.32 (0.088, 0.552)	< 0.01	< 0.01
6th month	10.12 ± 0.88	0.84 (0.662, 1.018)	< 0.01	9.68 ± 1.22	−0.26(−0.525, 0.005)	0.054	< 0.01
TUG							
Baseline	9.12 ± 1.62			8.94 ± 1.06			
1st month	8.64 ± 1.61	−0.48(−0.827, −0.133)	< 0.01	9.44 ± 1.15	0.5 (0.27, 0.73)	< 0.01	< 0.01
3rd month	8.04 ± 1.65	−1.080(−1.459, −0.701)	< 0.01	10.02 ± 1.13	1.08(0.866, 1.294)	< 0.01	< 0.01
6th month	7.56 ± 1.48	−1.560(−1.949, −1.171)	< 0.01	10.88 ± 1.27	1.94 (1.678, 2.202)	< 0.01	< 0.01
Quality of life							
Baseline	29.24 ± 1.81			29.54 ± 1.66			
1st month	30.06 ± 1.82	0.82 (0.503, 1.137)	< 0.01	28.00 ± 2.08	−0.56 (−1.031, −0.089)	0.02	< 0.01
3rd month	30.88 ± 2.31	1.64 (1.261, 2.019)	< 0.01	28.98 ± 1.42	−1.54(−1.874, −1.206)	< 0.01	< 0.01
6th month	31.32 ± 2.08	2.08 (1.717,2.443)	< 0.01	27.18 ± 1.31	−2.36(−2.82, −1.9)	< 0.01	< 0.01
Depressive symptoms							
Baseline	5.44 ± 1.18			5.12 ± 1.72			
1st month	5.20 ± 1.26	−0.24 (−0.392, −0.088)	< 0.01	5.94 ± 1.63	0.88 (0.628, 1.132)	< 0.01	< 0.01
3rd month	4.52 ± 1.01	−0.92 (−1.167,−0.673)	< 0.01	6.24 ± 1.35	1.12(0.813, 1.427)	< 0.01	< 0.01
6th month	4.36 ± 1.37	−1.02(−1.265, −0.775)	< 0.01	6.20 ± 1.24	1.08 (0.739, 1.421)	< 0.01	< 0.01

$\bar{x}$, mean; SD, standard deviation; β,regression coefficient; P_{int}, P value for interaction effect test; SPPB, Short Physical Performance Battery; TUG, **time up and go test**.

multicomponent intervention can slow progression of mild cognitive impairment by improving patient cognitive and physical function, mental health, and quality of life. This may delay progression of disease among this population and decrease the economic and care burden on society and families.

Our data show that the multicomponent intervention can effectively improve cognitive and physical function in patients with mild cognitive impairment. This is supported by findings in previous studies. For example, a previous investigation found that cognitive and physical function in patients with mild cognitive impairment improved after a 24-week combined intervention (Park et al., 2019b). Another study using an intervention combining physical, cognitive, and social activities to promote community activity to improve cognitive function in older adults with mild cognitive impairment led to significant improvements in spatial working memory and maintaining physical activity in older adults with mild cognitive impairment (Bae et al., 2019). Similarly, a quasi-experimental study conducted an intervention based on the concept of the International Classification of Functioning and found significant differences between the intervention and control groups in the improvement of cognitive function after 1 week (Xu et al., 2020). However, another study applying multimodal lifestyle intervention among older adults with mild cognitive impairment did not detect significant differences between groups in cognitive function at either 12 weeks or 24 weeks follow up (Falck et al., 2020).

Physical function is helpful in reducing cognitive decline. It has been proved that physical activity can improve cognition, particularly executive functioning and memory (Nuzum et al., 2020). Although the current and previous studies have shown that comprehensive intervention can improve cognitive and physical function in people with mild cognitive impairment to some extent, the effects of physical exercise on cognitive function demands additional trials with rigorous study design.

This study also revealed that the multicomponent intervention could reduce depressive symptoms in people with mild cognitive impairment. This is in accord with another study using a multicomponent intervention, which consisted of 11 individual sessions of cognitive behavioral therapy, cognitive rehabilitation, and reminiscence therapy, that reduced depressive symptoms in people with mild cognitive impairment and dementia (Tong et al., 2021). However, in contrast to the present study, other studies using a single psychosocial intervention did not find significant changes in depressive symptoms among people with mild cognitive impairment (Clare et al., 2019; Stockwell-Smith et al., 2018). These differences can be explained by the variation in interventions employed, the outcome measurements, and/or the baseline characteristics of participants. The multicomponent intervention can improve depressive symptoms by providing peer support during group-based intervention. In general, people consider peer support as helpful, reliable, and comforting because of similar experiences, which allow patients to share their concerns and thoughts without judgment, and may be helpful in improving their depressive symptoms. Several studies using a group-based intervention model have found significant improvement of depression symptoms in people with mild cognitive impairment (Song and Yu, 2019; Tonga et al., 2021). Therefore, we suggest that group-based intervention aimed at improving depression symptoms should be further explored in future studies.

Another promising finding of the present study was that we observed significant changes in quality of life in the intervention group at the end of the intervention. This finding was consistent with findings from another study that tested a combination of cognitive and balance training, in which two groups showed significant differences in quality of life favoring the experimental group (Hagovska and Olekszyova, 2016). Similarly, another study conducted in China also found that a moderate physical exercise program for people with mild cognitive impairment led to a significantly greater improvement in quality-of-life scores compared with the control group (Song and Yu, 2019). The positive effects of the multicomponent intervention can be explained by the improvements in cognitive function, physical function, and mental state. These changes may result in positive self-perception of health,

leading to improved quality of life. Previous studies have indicated that impairment of cognitive function can impair normal daily activity, reduce social engagement, and lead to poor self-perception of health (Berg et al., 2013). Further studies are needed to confirm whether cognitive function, physical function, and/or depression mediate the effect of a multicomponent intervention on quality of life.

Based on this study, we recommend several aspects that require further research. (1) More research is needed to confirm the association among cognitive function, physical function, depression, and quality of life, and whether the multicomponent intervention can improve patient cognitive function and quality of life by enhancing psychological status and physical function. (2) Although the findings of this study showed that the change on scores of the measurements after intervention was relatively small, the change trajectory was different between groups. This indicates that the multicomponent intervention is effective in maintaining or improving the cognitive, physical, and mental status of patients with mild cognitive impairment. However, the determined intervention effect may be a result of changing the response behavior. Future studies with extended follow-up periods are needed to show/point out clinical relevance, such as whether the intervention can reduce the incidence of dementia among people with mild cognitive impairment. (3) More studies are needed to explore effective models for collaboration between hospitals and communities and provide professional support for the implementation of the multicomponent intervention in the community.

This study was conducted in two urban communities in China. Influenced by the traditional Chinese “filial piety” culture, the older people mostly live with their family members and receive more family support when they are receiving interventions. This is conducive to good adherence and expected outcomes of the intervention. Therefore, the findings of this study are more applicable for the East Asia region, where the same traditional culture is shared.

The limitations of this study are as follows: First, the duration of the multicomponent intervention was only 6 months, so it is difficult to evaluate the long-term effects of the intervention and determine whether the intervention can reduce the incidence of dementia. Second, this study was conducted in only two community health service centers in Guangzhou, which may have influenced the representativeness of the sample and could limit the generalizability of the research results to other regions. Finally, although statistical significance indicates that the multicomponent intervention is effective in slowing the progression of mild cognitive impairment, we cannot ensure whether unobserved bias (e.g., repeated measurement error, reporting bias) caused overestimation of effects.

5. Conclusions

This report presents positive findings from a study of a 6-month multicomponent intervention aimed at slowing disease progression in individuals with mild cognitive impairment in the East Asia region. The multicomponent intervention is helpful in improving cognitive and physical function, as well as mental health and quality of life.

Declaration of Competing Interest

None.

CRediT authorship contribution statement

Qiao-hong Yang: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Xia Lyu:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Qing-ran Lin:** Conceptualization, Data curation, Formal analysis, Writing – original draft. **Zi-wen Wang:** Data curation, Writing – original draft. **Li Tang:** Data curation, Writing – original draft. **Yu Zhao:** Data curation, Writing – original draft. **Qi-yuan Lyu:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing.

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References

Adams, R., 1999. Revised Physical Activity Readiness Questionnaire. Can. Fam. Physician 45, 1004–1005 992, 995.

Bae, S., Lee, S., Lee, S., Jung, S., Makino, K., Harada, K., et al., 2019. The effect of a multicomponent intervention to promote community activity on cognitive function in older adults with mild cognitive impairment: a randomized controlled trial. Complement. Ther. Med. 42, 164–169. doi:10.1016/j.ctim.2018.11.011.

Baumgart, M., Snyder, H.M., Carrillo, M.C., Fazio, S., Kim, H., Johns, H., 2015. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: a population-based perspective. Alzheimers Dement. 11 (6), 718–726. doi:10.1016/j.jalz.2015.05.016.

Berg, A.I., Wallin, A., Nordlund, A., Johansson, B., 2013. Living with stable MCI: experiences among 17 individuals evaluated at a memory clinic. Aging Ment. Health 17 (3), 293–299. doi:10.1080/13607863.2012.751582.

Bellou, V., Belbasis, L., Tzoulaki, I., Middleton, L.T., Ioannidis, J.P.A., Evangelou, E., 2017. Systematic evaluation of the associations between environmental risk factors and dementia: an umbrella review of systematic reviews and meta-analyses. Alzheimers Dement. 13 (4), 406–418. doi:10.1016/j.jalz.2016.07.152.

Bender, R., Lange, S., 2001. Adjusting for multiple testing-when and how? J. Clin. Epidemiol. 54, 343–349. doi:10.1016/s0895-4356(00)00314-0.

Browne, W., Nair, B., 2019. The timed up and go test. Med. J. Aust. 210 (1), 13–14. doi:10.5694/mja2.12045.

Brown, H., Prescott, R., 2006. Applied Mixed Models in Medicine, 2nd Ed. John Wiley & Sons Ltd, Chichester, West Sussex, England Chapter 6.

Chatfield, M.D., Brayne, C.E., Matthews, F.E., 2005. A systematic literature review of attrition between waves in longitudinal studies in the elderly shows a consistent pattern of dropout between differing studies. J. Clin. Epidemiol. 58 (1), 13–19. doi:10.1016/j.jclinepi.2004.05.006.

Chen, S.Y., Feng, Z., Yi, X., 2017. A general introduction to adjustment for multiple comparisons. J. Thorac. Dis. 9 (6), 1725–1729. doi:10.21037/jtd.2017.05.34.

Clare, L., Kudlicka, A., Oyebode, J.R., Jones, R.W., Bayer, A., Leroi, I., et al., 2019. Individual goal-oriented cognitive rehabilitation to improve everyday functioning for people with early-stage dementia: a multicentre randomised controlled trial (the GREAT trial). Int. J. Geriatr. Psychiatry 34 (5), 709–721. doi:10.1002/gps.5076.

Combourieu, D.L., Perrot, A., Belleville, S., Bloch, F., Kemoun, G., 2018. Effects of simultaneous aerobic and cognitive training on executive functions, cardiovascular fitness and functional abilities in older adults with mild cognitive impairment. Ment. Health Phys. Act. 15, 78–87. doi:10.1016/J.MHPA.2018.06.001.

Dias, F., Teixeira, A.L., Guimaraes, H.C., Barbosa, M.T., Resende, E., Beato, R.G., et al., 2017. Accuracy of the 15-item geriatric depression scale (GDS-15) in a community-dwelling oldest-old sample: the Pieta Study. Trends Psychiatry Psychother. 39 (4), 276–279. doi:10.1590/2237-6089-2017-0046.

Falck, R.S., Davis, J.C., Best, J.R., Chan, P., Li, L.C., Wyrough, A.B., et al., 2020. Effect of a multimodal lifestyle intervention on sleep and cognitive function in older adults with probable mild cognitive impairment and poor sleep: a randomized clinical trial. J. Alzheimers Dis. 76 (1), 179–193. doi:10.3233/JAD-200383.

Hagovska, M., Olekszyova, Z., 2016. Impact of the combination of cognitive and balance training on gait, fear and risk of falling and quality of life in seniors with mild cognitive impairment. Geriatr. Gerontol. Int. 16 (9), 1043–1050. doi:10.1111/ggi.12593.

Hintze J. PASS 12. Kaysville, Utah: NCSS, LLC; 2013. Available at: www.ncss.com

Hong, J., Kim, J., Kim, S.W., Kong, H.J., 2017. Effects of home-based tele-exercise on sarcopenia among community-dwelling elderly adults: body composition and functional fitness. Exp. Gerontol. 87 (Pt A), 33–39. doi:10.1016/j.exger.2016.11.002.

Huang, Y.Y., Qian, S.X., Guan, Q.B., Chen, K.L., Zhao, Q.H., Lu, J.H., et al., 2019. Comparative study of two Chinese versions of montreal cognitive assessment for screening of mild cognitive impairment. Appl. Neuropsychol. Adult. 1–6. doi:10.1080/23279095.2019.1602530.

Huh, Y., Yang, E.J., Lee, S.A., Lim, J.Y., Kim, K.W., Paik, N.J., 2011. Association between executive function and physical performance in older Korean adults: findings from the Korean Longitudinal Study on Health and Aging (KLoSHA). Arch. Gerontol. Geriatr. 52 (3), e156–e161. doi:10.1016/j.archger.2010.10.018.

Irwin, M.R., Vitiello, M.V., 2019. Implications of sleep disturbance and inflammation for Alzheimer's disease dementia. Lancet Neurol. 18 (3), 296–306. doi:10.1016/S1474-4422(18)30450-2.

Jeong, J.H., Na, H.R., Choi, S.H., Kim, J., Na, D.L., Seo, S.W., et al., 2016. Group- and home-based cognitive intervention for patients with mild cognitive impairment: a randomized controlled trial. Psychother. Psychosom. 85 (4), 198–207. doi:10.1159/000442261.

Jia, L.F., Quan, M.N., Fu, Y., Zhao, T., Li, Y., Wei, C.B., Tang, Y., et al., 2020. Dementia in China: epidemiology, clinical management, and research advances. Lancet Neurol. 19 (1), 81–92. doi:10.1016/S1474-4422(19)30290-X.

Kivipelto, M., Solomon, A., Ahtiluoto, S., Ngandu, T., Lehtisalo, J., Antikainen, R., et al., 2013. The finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER): study design and progress. Alzheimer's Dementia 9 (6), 657–665. doi:10.1016/j.jalz.2012.09.012.

Li, A., 2015. Dementia in China (2010–2050) Estimate using the 2010 Census. Soochow University, Soochow, China.

Lima, C.A., Ricci, N.A., Nogueira, E.C., Perracini, M.R., 2018. The Berg Balance Scale as a clinical screening tool to predict fall risk in older adults: a systematic review. Physiotherapy 104 (4), 383–394. doi:10.1016/j.physio.2018.02.002.

Liu, M., 2014. The Effects of Multi-Component Exercise Training on Physical Function and Cognitive Functions of the Elderly With Mild Cognitive Impairment in the Community. Zhongnan University, Changsha, China.

Liu, H., Wu, T., 2005. Sample size calculation and power analysis of time-averaged difference. J. Modern Appl. Statis. Methods 4 (2), 434–445. doi:10.22237/jmasm/1130803680.

Lyu, Q., Cheung, D., Lai, H., Wang, X., Qiu, J., Huang, Y., et al., 2020. A multicomponent integrative intervention to slow down the progression of mild cognitive impairment: a protocol for a randomized controlled trial. Res. Nurs. Health 43 (4), 307–316. doi:10.1002/nur.22050.

Moll, V.C.E., Richard, E., Eurelings, L.S., van Dalen, J.W., Ligthart, S.A., van Bussel, E.F., et al., 2016. Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial. Lancet 388 (10046), 797–805. doi:10.1016/S0140-6736(16)30950-3.

Nasreddine, Z.S., Phillips, N.A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., et al., 2005. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. J. Am. Geriatr. Soc. 53 (4), 695–699. doi:10.1111/j.1532-5415.2005.53221.x.

Ngandu, T., Lehtisalo, J., Solomon, A., Levalahti, E., Ahtiluoto, S., Antikainen, R., et al., 2015. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. Lancet 385 (9984), 2255–2263. doi:10.1016/S0140-6736(15)60461-5.

Nuzum, H., Stickel, A., Corona, M., Zeller, M., Melrose, R.J., Wilkins, S.S., 2020. Potential Benefits of Physical Activity in MCI and Dementia. Behav. Neurol. 2020, 7807856. doi:10.1155/2020/7807856.

Nyunt, M.S., Fones, C., Niti, M., Ng, T.P., 2009. Criterion-based validity and reliability of the geriatric depression screening scale (GDS-15) in a large validation sample of community-living Asian older adults. Aging Ment. Health 13 (3), 376–382. doi:10.1080/13607860902861027.

Olanrewaju, O., Clare, L., Barnes, L., Brayne, C., 2015. A multimodal approach to dementia prevention: a report from the Cambridge institute of public health. Alzheimers Dement 1 (3), 151–156. doi:10.1016/j.trci.2015.08.003.

Park, E.Y., Park, S.M., Kim, J.H., 2019a. Psychometric properties of the geriatric quality of life-dementia in older adults with dementia or mild cognitive impairment living in nursing homes. BMC Geriatr. 19 (1), 281. doi:10.1186/s12877-019-1307-8.

Park, H., Park, J.H., Na, H.R., Hiroyuki, S., Kim, G.M., Jung, M.K., et al., 2019b. Combined intervention of physical activity, aerobic exercise, and cognitive exercise intervention to prevent cognitive decline for patients with mild cognitive impairment: a randomized controlled clinical study. J. Clin. Med. 8 (7). doi:10.3390/jcm8070940.

Petersen, R.C., Smith, G.E., Waring, S.C., Ivnik, R.J., Kokmen, E., Tangelos, E.G., 1997. Aging, memory, and mild cognitive impairment. Int. Psychogeriatr. 9 (Suppl 1), 65–69. doi:10.1017/s1041610297004717.

Picillo, M., Cuoco, S., Amboni, M., Bonifacio, F.P., Bruno, A., Bruschi, F., et al., 2019. Validation of the Italian version of carers' quality-of-life questionnaire for parkinsonism (PQoL Carer) in progressive supranuclear palsy. Neurol. Sci. 40 (10), 2163–2169.

Pinto, T., Machado, L., Costa, M., Santos, M., Bulgacov, T.M., Rolim, A., et al., 2019. Accuracy and psychometric properties of the Brazilian version of the montreal cognitive assessment as a brief screening tool for mild cognitive impairment and Alzheimer's disease in the initial stages in the elderly. Dement. Geriatr. Cogn. Disord. 47 (4–6), 366–374. doi:10.1159/000501308.

Prince, M.J., Wu, F., Guo, Y., Gutierrez, R.L., O'Donnell, M., Sullivan, R., et al., 2015. The burden of disease in older people and implications for health policy and practice. Lancet 385 (9967), 549–562. doi:10.1016/S0140-6736(14)61347-7.

Roberts, R.O., Knopman, D.S., Mielke, M.M., Cha, R.H., Pankratz, V.S., Christianson, T.J., et al., 2014. Higher risk of progression to dementia in mild cognitive impairment cases who revert to normal. Neurology 82 (4), 317–325. doi:10.1212/WNL.0000000000000055.

Rodriguez, T.F., Jackson, J., Ware, C., Churchyard, R., Hanseeuw, B., 2020. Interdisciplinary and transdisciplinary perspectives: on the road to a holistic approach to dementia prevention and care. J. Alzheimers Dis. Rep. 4 (1), 39–48. doi:10.3233/ADR-180070.

Sheikh, J.I., Yesavage, J.A., 1986. Geriatric depression scale (GDS): recent evidence and development of a shorter version. Clin. Gerontol. 5 (1–2), 165–173. doi:10.1300/J018v05n01_09.

Song, D., Yu, D., Li, P., Lei, Y., 2018. The effectiveness of physical exercise on cognitive and psychological outcomes in individuals with mild cognitive impairment: a systematic review and meta-analysis. Int. J. Nurs. Stud. 79, 155–164. doi:10.1016/j.ijnurstu.2018.01.002.

Song, D., Yu, D., 2019. Effects of a moderate-intensity aerobic exercise programme on the cognitive function and quality of life of community-dwelling elderly people with mild cognitive impairment: a randomised controlled trial. Int. J. Nurs. Stud. 93, 97–105. doi:10.1016/j.ijnurstu.2019.02.019.

Stockwell-Smith, G., Moyle, W., Kellett, U., 2018. The impact of early psychosocial intervention on self-efficacy of care recipient/carer dyads living with early-stage dementia-A mixed-methods study. J. Adv. Nurs. 13. doi:10.1111/jan.13710.

Tonga, J.B., Saltyte, B.J., Arnevik, E.A., Werheid, K., Korsnes, M.S., Ulstein, I.D., 2021. Managing depressive symptoms in people with mild cognitive impairment and mild dementia with a multicomponent psychotherapy intervention: a randomized controlled trial. Int. Psychogeriatr. 1–15. doi:10.1017/S1041610220000216.

Torisson, G., Stavenow, L., Minthon, L., Londos, E., 2016. Reliability, validity and clinical correlates of the Quality of Life in Alzheimer's disease (QoL-AD) scale in medical inpatients. Health Qual. Life Outcomes 14, 90. doi:10.1186/s12955-016-0493-8.

Treacy, D., Hassett, L., 2018. The short physical performance battery. J. Physiother. 64 (1), 61. doi:10.1016/j.jphys.2017.04.002.

Vermunt, L., van Paasen, A., Teunissen, C.E., Scheltens, P., Visser, P.J., Tijms, B.M., 2019. Alzheimer disease biomarkers may aid in the prognosis of MCI cases initially reverted to normal. Neurology 92 (23), e2699–e2705. doi:10.1212/WNL.0000000000007609.

Xu, S., Meng, G., Chen, P., Fang, M., Jin, A., 2020. Multidimensional intervention in individuals with mild cognitive impairment: a pilot nonrandomized study. Ann. Palliat. Med. doi:10.21037/apm-20-346.

Yang, C., Moore, A., Mpofu, E., Dorstyn, D., Li, Q., Yin, C., 2020. Effectiveness of combined cognitive and physical interventions to enhance functioning in older adults with mild cognitive impairment: a systematic review of randomized controlled trials. Gerontologist 60 (8), 633–642. doi:10.1093/geront/gnz149.

Yu, J., Li, J., Huang, X., 2012. The Beijing version of the Montreal Cognitive Assessment as a brief screening tool for mild cognitive impairment: a community-based study. BMC Psychiatry 12, 156. doi:10.1186/1471-244X-12-156.

Zhao, C., Noble, J.M., Marder, K., Hartman, J.S., Gu, Y., Scarmeas, N., 2018. Dietary Patterns, Physical Activity, Sleep, and Risk for Dementia and Cognitive Decline. Curr Nutr Rep 7 (4), 335–345. doi:10.1007/s13668-018-0247-9.