## **RESEARCH ARTICLE**



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# Effects of comprehensive intervention on life quality among the elderly with Alzheimer Disease and their caregivers based on mixed models

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# Abstract

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**Aims:** We conducted a multi-sectoral comprehensive intervention for elderly Alzheimer Disease patients and their caregivers to improve their quality of life. **Design:** Randomized controlled trial.

**Methods:** From June to June in 2019, 150 Alzheimer Disease patients were randomly selected from a nursing home in Zhejiang province of China, they were randomly divided into the intervention group and the control group. And they were given comprehensive and routine interventions respectively for six months. We used mixed models in our analyses to see how outcomes changed over time and how they were affected by the intervention, which could also solve the problems of missing values and data correlation.

**Results:** After six months, compared with the control group, the communication ability, housework handling ability, self-care ability and life quality of the patients in the intervention group were improved, and the quality of life and caring ability of their caregivers were also significantly improved.

**Conclusion:** The multi-sectoral collaborative care model proposed in this study integrated resources from several departments, effectively improved the quality of life of patients and their caregivers, and provided a way of care services for patients with Alzheimer Disease.

**Impact:** Multi-sectoral comprehensive intervention would improve the life quality of elderly patients with Alzheimer Disease and their caregivers.

#### KEYWORDS

Alzheimer Disease, caregivers, elderly, mixed models, nursing intervention

Yang li, Xuan Cheng contributed equally to this work

Trial Registration: China Clinical Trial Registration Center (CciCTR), Registration number: ChiCTR1900023777 (June 11, 2019).

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# INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disease accompanied by cognitive and physical decline, which is mainly characterized by memory impairment and daily living ability decline, which is the most common type of dementia (Association, 2015). The prevalence among the elderly is higher which poses a great threat to the health of the elderly, and it has become a serious public health problem worldwide. According to the world health organization, there are 46.8 million AD patients and the number will be 131.5 million by 2050 in the world (Association, 2015). In the present study, we conducted a multi-sectoral comprehensive intervention for elderly AD patients and their caregivers to improve their quality of life.

# 2 | BACKGROUND

China is facing a huge challenge of population ageing. By the end of 2014, there were about 137 million people aged 65 and above, the number of AD elderly people has ranked the first in the world, and the number of patients is still increasing year by year (Chan KY et al., 2013). With the progression of AD, the cognitive function of patients continues to decline, leading to the loss of self-care ability. Patients with AD need special care, which would have a significant impact on life quality. Some of the patients show obvious mental behaviour abnormalities, such as anxiety, delusion, irritability, aggression, which also increases the mental and economic burden of the family.

AD is not curable, but intervention in early-stage is more effective (Pedro Carmona et al.,2016). It starts insidiously and aggravates memory disorder slowly, and is often ignored and considered as a normal ageing phenomenon. Patients often delay early diagnosis and treatment. A number of studies have shown that early intervention for AD patients could control the cognitive function impairment better, reduce the functional and behavioural disorders, and prolong the time of patients' self-care (Association, 2015).

The severity of AD clinical symptoms is closely related to its nursing effect. In China, nursing care intervention of AD patients is still in its infancy, we mainly pay attention to the clinical care for symptoms, and the rehabilitation is not enough, the life quality of patients with AD has also not been given enough attention (Barton et al., 2016). AD patients' caregivers usually lack nursing and rehabilitation knowledge of AD, most of them also lack social support. Nursing work serious affects their life quality.

In the present study, we conducted a multi-sectoral comprehensive intervention (MSI) for elderly AD patients and their caregivers to improve their life quality. The theories supporting the development of the intervention were that MSI members had rich experience in geriatric disease diagnosis and treatment and they cooperated with the staff of the nursing homes. They not only had a clear work purpose but also helped each other to coordinate and utilized the resources of all parties to the greatest extent, so as to optimize the cooperation. The care model could provide guidance and development of care technology for AD patients in nursing homes, and also could maximize the quality of care for AD patients. At the same time, online real-time communication among MSI members could timely understand the demand characteristics and dynamic changes of AD patients and their caregivers, provide professional opinions, further improve the service level and service consistency

We used several scales to evaluate the effect of intervention and compared it with the conventional care model, the scales we used included mini-mental state examination (MMSE), activities of daily living questionnaire (ADLQ), quality of life Alzheimer's disease (QOL-AD), neuropsychiatric inventory (NPI), Zarit Caregiver Burden Interview (Zarit).

of the care team, which could improve the quality of care.

Repeated measurements from patients were likely to be more similar to each other, so we chose mixed models to solve the problem of data correlation. Meanwhile, using mixed models, reasonably valid estimates of treatment effects could often be obtained even when the missing values were not completely random and additional methods for handling missing data, such as multiple imputations, were generally not required (Detry and Ma, 2016).

#### 3 | METHODS

#### 3.1 | Aims

The aim of the study was to conduct a multi-sectoral comprehensive intervention for elderly Alzheimer Disease patients and their caregivers to improve their quality of life.

## 3.2 | Design

This study was a randomized controlled trial, and the random effect optimization model was used to calculate the sample size, and relevant parameters were set (primary outcome was QOL-AD score, test level was 0.05, power was 98%). The sample size was calculated to be about 58 cases, and the final sample size was 75 cases in the intervention group and the control group respectively, which was taking into account the situation of dropouts. On the basis of the previous project, and considering the convenience of the intervention project implementation, 150 AD patients were randomly selected from a nursing home in Zhejiang province from June 12 to June 28 in 2019, and they were randomly divided into the intervention group and the control group with 75 cases each.

The random sampling of the patients was performed by a blinded research leader. After baseline assessments, patients were divided into two groups by the same blinded research leader. The research leader generated the random allocation sequence and assigned participants to interventions, physicians and nurses enrolled participants. Random allocation sequence was generated by random numbers tables, all patients were randomly selected by the researchers and assigned to each group using random number tables.

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# 3.3 | Participants

#### 3.3.1 | Inclusion criteria

Subjects aged 65 years or more, who were diagnosed as AD by NIA-AA criteria, lived in the selected nursing homes and agreed with participating in the project. We got informed consent from the participants and their family or legal guardians.

#### 3.3.2 | Exclusion criteria

Subjects with consciousness disorders, serious suicidal tendency, deaf, unable to communicate, serious disability that unable to participate in activities. Criteria for suspension: patients or their families are unwilling to continue to participate in the study, patients with severe physical diseases after enrolment, and other reasons for violation of this study, such as leaving nursing homes.

## 3.3.3 | Termination criteria

Patients with sudden cerebrovascular or cardiovascular events or other severe unexpected responses not related to the intervention.

#### 3.4 | Intervention protocol

The intervention was carried out for six months (from July 2019-December 2019). The control group was given routine intervention treatment in accordance with medical advice, which mainly including of drug intervention and health education, and their caregivers were given basic health consultation services. The intervention group was given multi-sectoral cooperative care model intervention in addition to routine intervention, and their caregivers were given systematic training besides health consultation services. A multi-sectoral cooperative medical team was set up to conduct a comprehensive intervention on the intervention group, including neurologists, nurses, patients' caregivers, family members, rehabilitation therapists and social workers. According to the individual characteristics of the participants, the nursing goals and plans were formulated and implemented. The principle of care was to help patients maintain and improve their functions through daily living ability training, cognitive training, rehabilitation exercise and other activities. Meanwhile, special training was given to caregivers including the nursing knowledge for AD patients and ways to relieve the psychological pressure.

Multi-sectoral cooperative comprehensive intervention was mainly divided into five parts: (a) Self-care training: In order to slow down the functional degradation of patients, maintain and enhance the existing life skills of patients, provide certain sensory stimulation, activities including dressing up, folding clothes, making delicious food were conducted, which were led by caregivers through daily life. (b) Exercise rehabilitation: The main purpose was to enhance the physical activity of patients. The activities mainly included simple stretching exercises, walking. Patients in wheelchairs could do hand exercises. Activities were conducted by physical therapists twice a week. (c) Cognitive memory: In order to maintain patients' memory, exercise concentration and maintain the cognition of surrounding things, activities including text matching and other games were conducted by rehabilitation therapists two to four times a week. (d) Social interest: To exercise patients' hand-brain coordination ability, provide sensory stimulation and social opportunities, and maintain the familiarity with the outside world, the activities including writing calligraphy, finger painting, reading newspapers and so on were conducted by nursing staffs four to five times a week. (e) Nursing training: For the patients' caregivers, rehabilitation therapists and nurses gave them systematic training about self-health knowledge and problem behaviour processing skills, combined with the mental behaviour problems treatment, in order to reduce the pressure of caregivers and improve their nursing ability.

#### 3.5 | Data collection

#### 3.5.1 | Randomization and blinding

After collecting the baseline data, all patients were divided into either an intervention group or the control group by coded randomizations by an independent person. SAS package 9.4 was used to produce computerized random number. An independent, blinded statistician who was not involved in the research process prepared and managed the random number table. In the treatment process, subjects were divided into two groups. Intervention group and the control group did not know which group they were in. None of the MSI numbers participated in data analysis.

#### 3.5.2 | Measured variables

The study was conducted in nursing homes. The demographic information was obtained from subjects and caregivers at the beginning, including age, areas of residence, education, occupation, family income, and health behaviours such as smoking, alcohol and illness history. Physical examinations performed by trained nurses including height and weight.

Tests and scales including MMSE, CDR, ADLQ, QOL-AD were carried out to evaluate the intervention effects well and comprehensively. MMSE was an accurate and rapid reflection of the mental state and the degree of cognitive impairment of the subjects. We could understand the intervention effect better by the MMSE scores which were compared between the two groups. The ADLQ scale mainly measured the dependence of AD patients on daily living activities. The QOL-AD scale was filled by patients and caregivers respectively, and the higher the score, the higher the quality of life. CDR collected the information obtained by doctors through talking with patients and their families,

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which was refined to complete the assessment of the cognitive impairment degree of patients. The Zarit caregiving burden scale, caregiving ability scale and functional social support scale mainly evaluated the caregiver's care burden, care ability and functional social support ability respectively. The total score of Zarit scale was 88 points, and the higher the score, the heavier the burden of caring. All of the tests were administered and scored by specifically trained psychiatrists. Follow-up evaluation was conducted in the 6th month. All of the information were collected by trained nurses.

MMSE scale was simple and easy to use, which including of time orientation, location orientation, immediate memory, attention and computation, delayed memory, language, visual space. MMSE scored below 20 among the illiterate (among participants with primary school education level (1–6 years) or below 27 among participants with middle school or higher education level (>7 years) were considered as positive results (Chan et al., 2013). ADLQ mainly measured the degree of dependence on daily life activities of AD patients, which was divided into six parts, including self-care, housework, leisure activities and so on. The higher the scores, the higher the degree of dependence on daily life activities. QOL-AD scale was filled out by patients and caregivers, respectively, and 13 aspects including physical health status, memory, overall feeling of oneself and life status of patients and caregivers were assessed. Higher scores indicated higher life quality.

#### 3.6 | Ethical considerations

The protocol of this study was approved by the Medical Ethics Committee of Zhejiang Hospital. The study was also conducted in accordance with the Helsinki Declaration (World Medical Association, 1964). Consolidated Standards of Reporting Trials (CONSORT) recommendations (Moher et al., 2012; Pandis et al. 2017) were followed when preparing the research protocol. Written informed consent was obtained from patients and their families and they were informed about the potential benefits, risks, alternatives and responsibilities during the study by the main researchers. If older people with AD unable to give valid consent, written informed consent was obtained from participants' legal representatives prior to the inclusion. The trial and experimental protocols were approved by the institutional review board of Zhejiang hospital and registered (ChiCTR1900023777, date of registration: June 11, 2019). All methods were performed in accordance with the relevant guidelines and regulations. The conduct of the study was monitored by an independent data and safety monitoring committee. We confirmed that all ongoing and related trials for this intervention are registered.

## 3.7 | Data analysis

Epidata 3.0 was used for data entry and validation and SAS 9.4 for data management and analysis. Sociodemographic characteristics

of participants were summarized using frequencies (percentages) or means and standard deviations, and they were compared by the Student's *t*-test and  $\chi^2$  test, respectively. Significance level was set at *p* <.05 for all hypothesis tests.

We used mixed models in our analyses to see how outcomes changed over time and how they were affected by the intervention. The model included fixed effects for the intervention group, time of measurement, and the model was adjusted by some baseline characteristics such as age, gender, educational level, and so on. An interaction term between intervention group/control group and time was also included to determine if the two interventions led to different recovery trajectories over time. In addition, the model included a random effect for the baseline value, addressing the variability in the starting point for each patient.

#### 3.8 | Validity and reliability

MMSE, CDR scale has been widely used in many countries and region, and its reliability, validity and sensitivity had been highly affirmed. ADLQ scale has been verified by Johnson et al. (Johnson et al., 2004), which has high reliability and validity with the Cronbach's  $\alpha$  coefficient of 0.96, and it is 0.73 in this study. Zhang Huimin et al. translated QOL-AD scale into Chinese version with Cronbach's  $\alpha$  coefficient of 0.835, and it was 0.814 and 0.717 in this study for patients and caregivers respectively (Liu FL, 2012).

## 4 | RESULTS

# 4.1 | Sociodemographic characteristics of participants

From June 12–June 28 2019, 150 subjects were recruited, with 75 cases in intervention group and the control group, respectively. After six months of intervention (July 2019–December 2019), 10 cases were excluded from intervention group: one was severe physical illness, four were leaving nursing homes, and five refused. 14 cases were excluded from control group, two were severe physical illness, four were leaving nursing homes, eight refused. A total of 126 subjects were included in the final analysis, 65 in intervention group and 61 in control group (response rate was 84.0%) (Figure 1). There were no heterogeneities between the excluded patients and the included patients.

Table 1 presents baseline demographic and clinical characteristics. A total of 126 patients with AD completed the study, 65 in the intervention group and 61 in the control group. The average age of the subjects was 85.36 years, and there were more female compared with male (96 & 30, p < .0001). There were 31.71% Illiterates, 68.85% blue-collar workers, 71.31% living alone, and there were only 15.08% having drug use for AD. Many of the included participants had cardio-cerebral vascular disease, 65.32% had hypertension, 21.77% had diabetes, 20.97% had a stroke, and 38.71% had



**FIGURE 1** Flowchart of enrollment of participants in the study

coronary heart disease. The average BMI was 20.97. The two groups did not differ significantly in age (p = .65), gender (p = .14), educational level (p = .49), profession before retired (p = .74), state of marriage (p = .08) and other characteristics (Table 1).

# 4.2 | Primary outcomes for the intervention and control groups at baseline, third month, and sixth month

The control group was given conventional drug intervention and basic health education, and the intervention group was given multisectoral intensive intervention in addition to conventional intervention. The assessment was conducted at baseline and the 6th month. Table 2 showed that the effects of interventions in the two groups both had some degrees of improvement. In the intervention group, except for the scores of the judgement and the ability to solve the problem, the scores all improved. And in the control group, in addition to the orientation force and self-care ability, the scores improved (all, p < .005). In the ADL scale, except for shopping ability, the intervention group showed improvement in self-care ability, housework and leisure ability, and communication ability (all, p < .005), while the control group showed improvement in self-care ability, housework and leisure ability (p < .005). For the NPI scale, the control group showed improvement in patients and their caregivers, but no effect was found in the intervention group. In the MMSE scale evaluation, orientation, memory, attention and calculation ability

of the intervention group and the control group were all decreased (all, p < .005), while the communication ability of the intervention group was improved (p < .05). Both the QOL and Zarit scales for patient caregivers showed significant improvement in the intervention group and the control group (Table 2).

# 4.3 | Comparison of primary outcomes between intervention and control groups

After six months' interventions, the intervention group was given multi-sectoral collaborative intervention on the basis of routine intervention to improve the quality of life of patients and their caregivers. The results showed that, compared with the control group, the patients' communication ability, family affairs processing ability, self-care ability, and housework and leisure activities were significantly improved by the intensive intervention (Table 3). Meanwhile, compared with the control group, the quality of life, caring ability and functional social support of the caregivers in the intervention group were also improved. The burden on caregivers had decreased (Table 3).

# 5 | DISCUSSION

With the acceleration of ageing process, China has become the country with the largest number of AD patients and the fastest growth

		Nu	ursingOpen	-OpenAccess	LEY-	1417
naracteristics of ntrol groups	Characteristics	Total group (N = 126)	Control (N = 61)	Intervention (N = 65)	t/X2	р
	Age, Mean $\pm$ SD (years)	85.36 <u>+</u> 6.62	85.64 ± 6.31	85.11 ± 6.93	0.45	.65
	Gender, N(%)				2.20	.14
	Female	96 (76.19)	50 (81.97)	46 (70.77)		
	Male	30 (23.81)	11 (18.03)	19 (29.23)		
	Educational level N(%)				2.42	.49
	Illiterate (<1 year)	39 (31.71)	16 (27.12)	23 (35.94)		
	Primary (1–6 years)	38 (30.89)	22 (37.29)	16 (25.00)		
	Middle (7-12 years)	21 (17.07)	10 (16.95)	11 (17.19)		
	High (>13 years)	25 (20.33)	11 (18.64)	14 (21.88)		
	Profession				0.60	.74
	Housewife or inoccupation	8 (6.56)	4 (6.90)	4 (6.25)		
	Blue collar workers	84 (68.85)	38 (65.52)	46 (71.88)		
	White collar workers	30 (24.59)	16 (27.59)	14 (21.88)		
	State of marriage, N(%)				3.06	.08
	Married	35 (28.69)	21 (36.21)	14 (21.88)		
	living alone	87 (71.31)	37 (63.79)	50 (78.13)		
	Medical history, N(%)					
	Hypertension	81 (65.32)	36 (61.02)	45 (69.23)	0.92	.34
	Diabetes	27 (21.77)	12 (20.34)	15 (23.08)	0.14	.71
	Stroke	26 (20.97)	10 (16.95)	16 (24.62)	1.11	.29
	Coronary heart disease	48 (38.71)	22 (37.29)	26 (40.00)	0.10	.76
	Lifestyle habits, N(%)					
	Cigarette smoking	13 (10.48)	6 (10.17)	7 (10.77)	0.01	.91
	Alcohol drinking	7 (5.65)	3 (5.08)	4 (6.15)	0.07	.8
	BMI, Mean $\pm$ SD (kg/m <sup>2</sup> )	$20.97 \pm 8.58$	20.41 ± 9.94	21.49 ± 7.14	0.69	.5
	Medication use for dementia, <i>N</i> (%)	19 (15.08)	6 (9.84)	13 (20.00)	2.60	.11

# **TABLE 1**Baseline characteristics ofthe intervention and control groups

rate in the world. AD patients' memory, judgement, attention and other abilities are impaired, which affecting their ability to understand and communicate, and reducing the quality of their life. The standard treatment for improving cognition of AD participants consists of anti-AD drugs, even though this typical treatment has shown limited efficacy (Jorge Alves et al., 2013; Pepeu et al., 2010), therefore, nonpharmacological interventions have been considered as a complementary option of intervention (Olazara et al., 2004). Several studies had shown that the intervention of AD patients might be helpful. Clare's team showed that cognitive rehabilitation could produce significant improvements in ratings of goal performance and satisfaction (Clare L et al., 2010), and Lowenstein's team showed improvements in patients' task performance after cognitive training (Loewenstein DA et al., 2004). Maria Dolores Onieva-Zafra, 2018. confirmed the valuable effect of music therapy and reminiscence therapy together with reality orientation techniques on depression in patients with mild Alzheimer disease (Maria Dolores et al., 2018).

Effective nursing interventions can delay the progress of AD patients, reduce medical and care costs, and improve the quality of life of patients (Bernard et al., 2016). Caring for people with AD is a long-term process and includes many challenges for caregivers. Caregivers face a variety of demands over time while caring for people with AD (Jones et al., 2017; Largent, 2019; Anne et al., 2016), and they often have feelings of anxiety, disappointment, depression, depression, apathy, and often have low life quality. But there were few studies about it. In this study, we focussed on the intervention ways not only for the patients with AD, but also for their caregivers. And we used mixed-effect model to analyse the intervention effect. The advantage of the linear mixed-effect model is the ability to use all available longitudinal data, including the data from dropouts (Hallikainen et al., 2018). The mixed-effect model can also solve the problem of correlation at different time points. After six months' short-term intervention, patients in the intervention group and the control group showed improved self-care ability, leisure activity ability, and the quality of life of patients in both groups was improved to some degrees. Compared with the control group, the communication ability, housework handling ability, self-care ability and life quality of the patients in the intervention group were improved. The quality

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TABLE 2         Primary outcomes for the intervention and	d control groups at baseline, th	nird month and sixth n	nonth		
		Score, mean (SD)			
Group	Outcomes	Baseline	6th Month	F	<i>p</i> value
Intervention	MMSE (patients)	$12.68 \pm 6.53$	$12.63 \pm 5.56$	0.01	.99
	Orientation	$4.52 \pm 2.78$	$4.98 \pm 2.62$	4.8	.2
	Memory	$1.58\pm1.13$	$1.83 \pm 1.11$	2.85	.06
	Attention and numeracy	$1.09 \pm 1.41$	$1.18 \pm 1.38$	1.3	.28
	Recollections	$0.95 \pm 1.12$	$0.82 \pm 1.07$	2.21	.11
	Communication	$4.52 \pm 2.06$	$5.82 \pm 2.18$	4.23	.017
	CDR (patients)	$1.72 \pm 0.88$	$1.85 \pm 0.89$	7.43	.0009
	Memory	$1.65\pm0.96$	$1.67 \pm 0.93$	8.64	с.
	Orientation	$1.58\pm0.94$	$1.65\pm0.88$	9.23	2
	Judging and solving problems	$1.60 \pm 0.98$	$1.75 \pm 0.88$	1.84	.16
	Social affairs	$1.82 \pm 1.00$	$1.87 \pm 0.93$	3.73	.027
	Family affairs	$1.88 \pm 1.03$	$2.32 \pm 0.83$	6.11	.003
	Self-care ability	$1.45 \pm 0.86$	$1.68\pm0.92$	8.27	.0004
	ADL (patients)	$53.14 \pm 9.16$	$56.63 \pm 10.79$	7.75	.0003
	Self-care ability	$9.23 \pm 4.60$	$11.97 \pm 4.72$	5.56	.004
	Housework and Leisure activities	$14.62 \pm 3.48$	$16.08 \pm 2.39$	14.76	<.0001
	Shopping and consumption	$17.49 \pm 1.99$	$17.23\pm2.04$	1.57	.21
	Communication	$8.57 \pm 2.96$	$11.29 \pm 2.74$	8.17	.0005
	NPI				
	Severity of symptom (patients)	$3.38 \pm 3.92$	$3.68\pm4.24$	0.21	.81
	Degree of distress (caregivers)	$1.72 \pm 2.87$	$1.02 \pm 1.74$	1.7	.19
	QOL-AD (patients)	$26.48 \pm 10.51$	$29.73 \pm 9.14$	2.16	12
	QOL-AD (caregivers)	$1.72\pm2.87$	$1.85 \pm 1.74$	8.02	.003
	Zarit (caregivers)	$28.10 \pm 15.05$	$17.51 \pm 10.92$	11.47	<.0001
	Evaluation of care ability (caregivers)	$57.13 \pm 17.82$	$61.40 \pm 16.44$	1.41	.25
	Evaluation of functional social support (caregivers)	$57.94 \pm 15.76$	$55.31 \pm 19.28$	2.08	.13

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		Score, mean (SD)			
Group	Outcomes	Baseline	6th Month	F	<i>p</i> value
Control	MMSE (patients)	$15.44 \pm 7.82$	$12.18 \pm 7.68$	26.28	<.0001
	Orientation	$5.28 \pm 3.44$	$4.02 \pm 3.51$	15.18	<.0001
	Memory	$1.77 \pm 1.07$	$1.49 \pm 1.16$	2.7	.07
	Attention and numeracy	$1.39\pm1.58$	$1.05 \pm 1.38$	2.38	.098
	Recollections	$1.23 \pm 1.19$	$0.62 \pm 0.99$	8.14	.0005
	Communication	$5.77 \pm 2.36$	$5.00 \pm 2.39$	9.01	.0003
	CDR (patients)	$1.41 \pm 0.92$	$1.71 \pm 0.96$	14.63	<.0001
	Memory	$1.39\pm0.85$	$1.68\pm0.89$	9.37	.0002
	Orientation	$1.29 \pm 1.02$	$1.47 \pm 1.10$	10.03	Ŀ
	Judging and solving problems	$1.35 \pm 0.99$	$1.65 \pm 0.95$	7.95	.0006
	Social affairs	$1.50 \pm 1.04$	$1.74 \pm 1.04$	4.78	.0104
	Family affairs	$1.51 \pm 1.02$	$1.77 \pm 1.07$	5.44	.0057
	Self-care ability	$1.07 \pm 1.13$	$1.26 \pm 1.05$	1.92	.152
	ADL (patients)	$37.23 \pm 21.34$	$39.56 \pm 19.69$	5.18	.001
	Self-care ability	$6.07 \pm 6.29$	7.77 ± 6.85	15.68	<.0001
	Housework and Leisure activities	$11.86 \pm 5.89$	$12.62 \pm 5.02$	8.67	.0003
	Shopping and consumption	$12.85 \pm 6.58$	$12.03 \pm 5.21$	0.49	.36
	Communication	$6.43 \pm 4.51$	$7.13 \pm 4.94$	23.93	.08
	IdN				
	Severity of symptom (patients)	$1.78 \pm 2.76$	$4.22 \pm 5.15$	9.11	.0003
	Degree of distress (caregivers)	$1.23 \pm 2.30$	$3.34 \pm 4.48$	7.47	.001
	QOL-AD (patients)	$29.88 \pm 7.22$	$24.80 \pm 8.48$	11.4	<.0001
	QOL-AD (caregivers)	$1.23 \pm 2.30$	$2.34 \pm 4.48$	4.25	.02
	Zarit (caregivers)	$29.50 \pm 16.57$	$32.69 \pm 15.55$	0.2	.82
	Evaluation of care ability (caregivers)	$52.83 \pm 14.79$	$39.00 \pm 17.41$	8.95	.0004
	Evaluation of functional social support (caregivers)	$54.40 \pm 17.09$	$54.73 \pm 21.28$	0.25	.78

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# TABLE 3 Comparison of primary outcomes between intervention and control groups

		Score, mean (SD)		Mean		
Outcomes	Group	Baseline	6th Month	difference	F	p value
MMSE (patients)	Intervention	$12.68 \pm 6.53$	$12.63 \pm 5.56$	-0.05	0.45	.5
	Control	$15.44 \pm 7.82$	$12.18\pm7.68$	-3.26		
Orientation	Intervention	$4.52 \pm 2.78$	$4.98 \pm 2.62$	0.46	1.62	.11
	Control	$5.28 \pm 3.44$	$4.02\pm3.51$	-1.26		
Memory	Intervention	$1.58 \pm 1.13$	$1.83 \pm 1.11$	0.25	0.44	.51
	Control	$1.77 \pm 1.07$	$1.49 \pm 1.16$	-0.28		
Attention and numeracy	Intervention	$1.09 \pm 1.41$	$1.18 \pm 1.38$	0.09	2.4	.09
	Control	$1.39 \pm 1.58$	$1.05 \pm 1.38$	-0.34		
Recollections	Intervention	0.95 ± 1.12	$0.82 \pm 1.07$	-0.13	0.001	.99
	Control	$1.23 \pm 1.19$	0.62 ± 0.99	-0.61		
Communication	Intervention	$4.52 \pm 2.06$	$5.82 \pm 2.18$	1.30	2.29	.03
	Control	5.77 ± 2.36	5.00 ± 2.39	-0.77		
CDR (patients)	Intervention	$1.72\pm0.88$	$1.85 \pm 0.89$	0.13	1.62	.21
	Control	$1.41\pm0.92$	$1.71\pm0.96$	0.30		
Memory	Intervention	$1.65 \pm 0.96$	$1.67 \pm 0.93$	0.02	1.15	.29
	Control	$1.39\pm0.85$	$1.68 \pm 0.89$	0.29		
Orientation	Intervention	$1.58\pm0.94$	$1.65 \pm 0.88$	0.07	0.88	.35
	Control	$1.29 \pm 1.02$	$1.47 \pm 1.10$	0.18		
Judging and solving	Intervention	$1.60\pm0.98$	1.75 ± 0.88	0.15	0.53	.47
problems	Control	$1.35 \pm 0.99$	1.65 ± 0.95	0.30		
Social affairs	Intervention	$1.82 \pm 1.00$	$1.87\pm0.93$	0.05	1.91	.17
	Control	$1.50 \pm 1.04$	$1.74 \pm 1.04$	0.24		
Family affairs	Intervention	$1.88 \pm 1.03$	$2.32\pm0.83$	0.44	5.16	.03
	Control	$1.51 \pm 1.02$	1.77 ± 1.07	0.26		
Self-care ability	Intervention	$1.45\pm0.86$	$1.68 \pm 0.92$	0.23	10.14	.0019
	Control	$1.07 \pm 1.13$	$1.26 \pm 1.05$	0.19		
ADL(patients)	Intervention	53.14 ± 9.16	56.63 ± 10.79	3.49	3.13	0.04
	Control	$37.23 \pm 21.34$	39.56 ± 19.69	2.33		
Self-care ability	Intervention	9.23 ± 4.60	11.97 ± 4.72	2.74	7.76	.023
	Control	$6.07\pm6.29$	7.77 ± 6.85	1.70		
Housework and Leisure	Intervention	$14.62\pm3.48$	$16.08 \pm 2.39$	1.46	3.49	.004
activities	Control	11.86 ± 5.89	$12.62 \pm 5.02$	0.76		
Shopping and	Intervention	17.49 ± 1.99	17.23 ± 2.04	-0.26	2.87	.1
consumption	Control	$12.85 \pm 6.58$	$12.03 \pm 5.21$	-0.82		
Communication	Intervention	8.57 ± 2.96	11.29 ± 2.74	2.72	4.33	.04
	Control	$6.43 \pm 4.51$	7.13 ± 4.94	0.70		
NPI						
Severity of symptom	Intervention	$3.38 \pm 3.92$	$3.68 \pm 4.24$	0.30	0.02	.89
(patients)	Control	$1.78 \pm 2.76$	$4.22\pm5.15$	2.44		
Degree of distress	Intervention	$1.72\pm2.87$	$1.85 \pm 1.74$	0.13	1.36	.2
(caregivers)	Control	$1.23 \pm 2.30$	$2.34 \pm 4.48$	1.11		
QOL-AD (patients)	Intervention	$26.48 \pm 10.51$	29.73 ± 9.14	3.25	1.17	.28
	Control	29.88 ± 7.22	$24.80 \pm 8.48$	-5.08		

#### TABLE 3 (Continued)

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		Score, mean (SD)		Mean		
Outcomes	Group	Baseline	6th Month	difference	F	p value
QOL-AD (caregivers)	Intervention	$25.63 \pm 10.60$	31.95 ± 7.55	6.32	8.08	.005
	Control	27.29 ± 7.56	24.58 ± 7.57	-2.71		
Zarit (caregivers)	Intervention	$28.10 \pm 15.05$	17.51 ± 10.92	-10.59	13.75	.0004
	Control	29.50 ± 16.57	32.69 ± 15.55	3.19		
Care ability (caregivers)	Intervention	57.13 ± 17.82	$61.40 \pm 16.44$	4.27	31.84	<.0001
	Control	52.83 ± 14.79	39.00 ± 17.41	-13.83		
Functional social support (caregivers)	Intervention	57.94 ± 15.76	55.31 ± 19.28	-2.63	0.001	.99
	Control	54.40 ± 17.09	$54.73 \pm 21.28$	0.33		

of life and caring ability of the caregivers in the intervention group were significantly enhanced, and the care burden reduced. However, there was no significant improvement in patients' directivity, memory and computing ability through intervention, which was similar to the results of Anne's team (Anne M. K et al., 2016).

The life ability of AD patients was significantly correlated with the life quality of patients and was affected by many factors. Cognitive status, age, other diseases and nutritional status might all affect the life ability of patients (Floriane et al., 2013). In this study, patients were provided with rehabilitation and nursing intervention through multi-sectoral cooperation mode, which could maximize the promotion and retention of their daily living activities, reduce their dependence on daily living activities, slow down the occurrence of disability, and improve the self-care ability and life quality of AD patients.

Previous cross-sectional studies showed that irritability and agitation were the primary contributors to overall AD caregivers' burden (Alzheimer's Association, 2015). Timely intervention for patient caregivers could relieve their tension and anxiety (Wood and Jeffrey, 1999). The ability of caregivers also directly affected the life quality of patients. This study found that after 36 hr of systematic training, caregivers' ability of care was improved, especially their ability identifying and dealing with behavioural and mental problems of AD was significantly improved. Meanwhile, the stress management and adjustment ability of caregivers were also enhanced, and the psychological and emotional support degree was increased. And the quality and satisfaction of patients' care were improved.

# 6 | LIMITATIONS

There were several limitations. Firstly, the sample size was relatively small and the intervention time was short. The selected subjects were mostly old patients with severe AD. Secondly, we didn't collect the baseline information of caregivers. Thirdly, there was potential contamination of the control group and intervention group given by they were living in the same nursing home. Therefore, a larger scale, longer period of study, including more information and carried out in multicenter are needed in the further.

# 7 | CONCLUSIONS

As the ageing process accelerates, the number of AD patients is increasing. The health status of AD patients and their caregivers affects each other, improving the quality of their life is an urgent problem to be solved in the ageing society. Practitioners should ascertain the patient's and caregiver's well-being in collaboration with the patients and the caregivers. The multi-sectoral collaborative care model proposed in this study integrated resources from several departments effectively improved the quality of life of patients and their caregivers, and provided a way of nursing care services for patients with AD and their caregivers.

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#### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

#### AUTHOR CONTRIBUTIONS

Substantial contributions to conception and design were JIN Xiaoqing, YAN Jing. Acquisition of data, or analysis and interpretation of data was ZHENG Pinpin, XUAN Cheng. Drafting the article or revising it critically for important intellectual content was YANG Li. All authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE [https://www. icmje.org/recommendations/]): substantial contributions to conception and design, acquisition of data or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content.

#### DATA AVAILABILITY STATEMENT

The data used to support the findings of this study are available from the corresponding author upon request.

#### REFERENCES

Alves, J., Magalhães, R., Thomas, R. E., Gonçalves, O. F., Petrosyan, A., & Sampaio, A. (2013). Is there evidence for cognitive intervention in alzheimer disease? A systematic review of efficacy, feasibility, and cost-effectiveness. *Alzheimer Disease and Associated Disorders*, 27(3), 195–203. https://doi.org/10.1097/WAD.0b013e31827bda55

- Koivisto, A. M., Hallikainen, I., Välimäki, T., Hongisto, K., Hiltunen, A., Karppi, P., Sivenius, J., Soininen, H., & Martikainen, J. (2016). Early psychosocial intervention does not delay institutionalization in persons with mild alzheimer disease and has impact on neither disease progression nor caregivers' well-being: ALSOVA 3-year follow-up. International Journal of Geriatric Psychiatry, 31, 273–283.
- Association, A. (2015). Alzheimer's disease facts and figures in 2015. Alzheimer's Dement, 11(3), 332–384.
- Bernard, B. L., Bernard, B. L., Bracey, L. E., Lane, K. A., Ferguson, D. Y., LaMantia, M. A., LaMantia, M. A., Sujuan Gao, S., Miller, D. K., & Callahan, C. M. (2016). Correlation between caregiver reports of physical function and performance-based measures in a cohort of older adults with alzheimer disease. *Alzheimer Disease and Associated Disorders*, 30, 169–174. https://doi.org/10.1097/WAD.000000000 000101
- Carmona, P., Molina, M., & Toledano, A. (2016). Blood-based biomarkers of alzheimer's disease: Diagnostic algorithms and new technologies. *Current Alzheimer Research*, 13, 450-464. https://doi. org/10.2174/1567205013666151116130301
- Chan, K. Y., Wang, W., Wu, J. J., Liu, L., Theodoratou, E., Car, J., Middleton, L., Russ, T. C., Deary, I. J., Campbell, H., Wang, W., & Rudan, I. (2013). Epidemiology of alzheimer's disease and other forms of dementia in China, 1990–2010: A systematic review and analysis. *The Lancet*, 381, 2016–2023. https://doi.org/10.1016/S0140-6736(13)60221-4
- Clare, L., Linden, D. E., & Woods, R. T. (2010). Goal-oriented cognitive rehabilitation for people with early-stage Alzheimer disease: a singleblind randomized controlled trial of clinical efficacy. *The American journal of geriatric psychiatry: Official journal of the American association for geriatric psychiatry*, 18,928–939.
- Detry, M. A., & Ma, Y. (2016). Analyzing repeated measurements using mixed models. Journal of the American Medical Association, 315(4), 407–408. https://doi.org/10.1001/jama.2015.19394
- Floriane, D-C, Rouch, I., Martin-Gaujard, G., Relland, S., & Krolak-Salmon, P. (2013). Effect of a nonpharmacological intervention on behavior disturbances in Alzheimer disease and associated disorders. *Geriatr Psychol Neuropsychiatr Vieil*, 11(3), 323–330. https://doi. org/10.1684/pnv.2013.0421
- Hallikainen, I., Koivisto, A. M., & Välimäki, T. (2018). The influence of the individual neuropsychiatric symptoms of people with alzheimer disease on family caregiver distress-A longitudinal ALSOVA study. *International Journal of Geriatric Psychiatry*, 22(2), 1–6. https://doi. org/10.1002/gps.4911
- Johnson, N., Barion, A., Rademaker, A., Rehkemper, G., & Weintraub, S. (2004). The activities of daily living questionnaire: A validation study in patients with dementia. *Alzheimer Disease & Associated Disorders*, 18(4), 223–230.
- Jones, R. W., Lebrec, J., Kahle-Wrobleski, K., Dell'Agnello, G., Bruno, G., Vellas, B., Argimon, J. M., Dodel, R., Haro, J. M., Wimo, A., & Reed, C. (2017). Disease progression in mild dementia due to alzheimer disease in an 18-month observational study (GERAS): The impact on

costs and caregiver outcomes. *Dementia and geriatric cognitive disorders extra*, 7, 87–100. https://doi.org/10.1159/000461577

- Largent, Emily A. (2019). Preclinical alzheimer disease and the dawn of the pre-caregiver. JAMA Neurology, 11, 1–2.
- Liu, F. L., Wang, S. H., Feng, X. M. et al (2012). The present situation and countermeasures of quality of life in patients with mild cognitive impairment (MCI). *Chinese Journal of Modern Nursing*, 18(6), 742–744.
- Loewenstein, D. A., Acevedo, A., Czaja, S. J., & Duara, R. (2004). Cognitive rehabilitation of mildly impaired Alzheimer disease patients on cholinesterase inhibitors. *The American Journal of Geriatric Psychiatry*, 12, 395–402. https://doi.org/10.1097/00019442-200407000-00007
- Onieva-Zafra, M. D., Hernández-Garcia, L., Gonzalez-del-Valle, M. T., Parra-Fernández, M. L., & Fernandez-Martinez, E. (2018). Music Intervention with reminiscence therapy and reality orientation for elderly people with alzheimer disease living in a nursing home. *Holistic Nursing Practice*, 32(1), 43–50. https://doi.org/10.1097/HNP.00000 0000000247
- Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gøtzsche, P. C., Devereaux, P. J., Elbourne, D., Egger, M., & Altman, D. G. (2012). CONSORT. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *International Journal of Surgery*, 10, 28–55. https://doi.org/10.1016/j. ijsu.2011.10.001
- Olazarán, J., Muñiz, R., Reisberg, B., Peña-Casanova, J., del Ser, T., Cruz-Jentoft, A. J., Serrano, P., Navarro, E., García de la Rocha, M. L., Frank, A., Galiano, M., Fernández-Bullido, Y., Serra, J. A., González-Salvador, M. T., & Sevilla, C. (2004). Benefits of cognitive motor intervention in MCI and mild to moderate Alzheimer Disease. *Neurology*, *63*, 2348–2353. https://doi.org/10.1212/01.WNL.0000147478.03911.28
- Pandis, N., Chung, B., Scherer, R. W., Elbourne, D., & Altman, D. G. (2017) CONSORT. 2010 Statement: Extension checklist for reporting within person randomised trials. *BMJ: British Medical Journal/British Medical Association*, 357, j2835.
- Pepeu, G., & Giovannini, M. G. (2010). Cholinesterase inhibitors and memory. Chemico-Biological Interactions, 187, 403–408. https://doi. org/10.1016/j.cbi.2009.11.018
- World Medical Association (1964). Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964.
- Wood, S., & Jeffrey, L. (1999). Cummings. Measuring outcomes in alzheimer's disease research-assessment of the effectiveness of interventions. Disease Management and Health Outcomes, 5, 1–12.

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