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REVIEW ARTICLE

Early detection of dementia in the community under a community-based integrated care system

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Early detection of dementia is recommended in the stages from mild cognitive impairment to early dementia, excluding the asymptomatic stage. The advantages of early detection for patients and their caregivers include early receipt of pharmacological and non-pharmacological therapies, and early access to appropriate agencies and/or support networks. The disadvantages include psychological damage related to anxiety and depression, and risk of stigmatization and/or social exclusion. The possibility of false positive diagnoses is also problematic. For detection of dementia, various screening tests and questionnaires have been developed. However, none of these techniques are sensitive and specific enough to avoid false positives. Thus, these screening tools are recommended for assessment of the severity of functional decline after sufficient information has been gathered to suspect dementia. In terms of social services, early detection might delay institutionalization. However, implementation of early detection would add a heavy burden on social resources, especially human resources. For effective implementation of early diagnosis and management of dementia, measures are required to improve social and human resources, including the following: improvement of the diagnostic abilities of general practitioners, improvement of necessary care and support systems after diagnosis, and organizing volunteers to support local communities. Under a community-based integrated care system, each community will create a "tailored" system that meets the health needs, health status and values of the community. Promoting social participation and community involvement of the residents should be one of the key strategies to address the shortage of human resources. **Geriatr Gerontol Int 2014; 14 (Suppl. 2): 2–10.**

Keywords: community-based integrated care systems, early detection of dementia, social support, social resources, stigma and social exclusion.

Introduction

Early detection of dementia is encouraged for individuals with dementia and their caregivers to ensure the benefits of accessing treatment, care and support; earlier detection and intervention is one of the main policies of the Five-Year Plan for Promotion of Measures against Dementia in Japan (Orange Plan; 2013–2017). However, there are disadvantages of early detection, as well as various advantages (Table 1). The most serious issue is the shortage of social resources, particularly human resources, as a result of an enormous increase in the number of demented individuals. Early diagnosis is beneficial only when effective treatment and appropriate social services are available; for treatment and care of dementia, medication alone is not sufficient, and social services and support are crucial. The present article aims to overview the advantages and disadvantages from the perspectives of the patients, their caregivers and social services, and then to consider implementation under a community-based integrated care system.

Early detection of dementia: at which stage of dementia should treatment be started?

There is a lack of consensus regarding at which stage of dementia treatment should be started: asymptomatic stage, symptomatic prodromal stage of dementia (mild cognitive impairment [MCI]) or early-stage dementia after the onset of the disease.

Asymptomatic stage

Research study trends are moving to earlier detection of dementia, at the asymptomatic stage, aiming at the prevention of dementia. Most of these studies have focused on Alzheimer's disease (AD); clinical and epidemiological evidence generally suggests the presence of a cognitive continuum from an asymptomatic phase to onset of AD, and the pathophysiological process of AD is thought to begin many years before the diagnosis of AD dementia.[1]

Table 1 Advantages and disadvantages of early diagnosis

	Advantages	Disadvantages
Patients	Receiving pharmacological and non-pharmacological therapies	Psychological damage of anxiety and depression
	Access to appropriate agencies and support networks	Risk of withdrawal, isolation, stigma and social exclusion
	Prevention of behavioral and psychological symptoms of dementia	Risk of false positive diagnosis
Families and caregivers	Mental preparation for disease progression	Stigma and exclusion
	Access to appropriate agencies and support networks	Care burden from early stages
Social services	Net cost reduction effects including delay of institutionalized care	Shortage of social resources, including human resources

However, detection of AD in the asymptomatic stage is still in the research phase, and many challenges remain to be overcome. First of all, a firm link has not been shown between the appearance of any specific biomarker in the asymptomatic stage and the subsequent emergence of clinical symptoms of AD. As an associated issue, not all individuals who have evidence of AD pathology will necessarily progress to clinical AD dementia.[2] Regarding treatment, individuals might be left untreated with a high risk of developing AD without disease-modifying drugs. In addition, there has been little research on other causative diseases of dementia. Further research is required, because identification and classification of syndromes that will progress to subtypes of dementia are critical for the management of the diseases when modifiable therapies are available. The issue of costs cannot be ignored. In the asymptomatic stage, detection requires examination of biomarkers using costly brain-imaging techniques, such as positron emission tomography, glucose metabolism or β-amyloid accumulation.

Symptomatic prodromal stage of dementia

MCI is a prodromal stage of dementia characterized by cognitive decline greater than age-related changes, but the condition does not interfere notably with activities of daily living.[3] The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), refers to a spectrum of cognitive and functional impairments, from mild neurocognitive disorders (mild NCD) to major neurocognitive disorders (major NCD). In major NCD, deterioration of cognitive function is severe enough to interfere with independence in everyday activities, whereas capacity for independence still remains in minor NCD.[4]

With optimal intervention during the stage of MCI, development to AD could be avoided or delayed, although MCI shows a high risk of progression to

dementia, particularly of the AD type; according to one report, conversion rates to AD were 41% after 1 year, and 64% after 2 years.[5] Thus, detection at the MCI stage could be meaningful for prevention of dementia, or at least to delay the onset of dementia.

Early-stage dementia after the onset of the disease

Once dementia has developed, the best that can be done is to slow the progression of the disease. In the present article, "early" detection is considered as detection at the stage from MCI to very early-stage dementia, excluding the asymptomatic stage.

Advantages and disadvantages of early detection of dementia

Advantages and disadvantages for patients

Advantages for patients include optimizing the use of pharmacological and non-pharmacological therapies, as well as appropriate agencies and support networks provided as required after diagnosis. Early diagnosis is associated with a higher probability of prevention of behavioral and psychological symptoms of dementia (BPSD),[6] and detection of treatable causes, such as normal pressure hydrocephalus. Lifestyle-related diseases, which increase the risk of cognitive decline, might be treated from the perspective of control of the progression of dementia. Detection at the stage of MCI provides the possibility of preventing and/or slowing the development of dementia.

However, it should be noted that there is no conclusive evidence that early treatment with antidementia medication is more effective than late treatment,[7] and it is still unclear whether MCI and early-stage dementia should be medicated or not. In addition, further research is required to clarify the side-effects to the central nervous system.

The greatest disadvantages for patients are psychological damage and stigmatized labeling. A diagnosis of dementia is inevitably associated with deterioration of self-esteem and feelings of helplessness, which might be accelerated by potential loss or diminution of roles, and abrogation of control of property, money and possessions.[8,9] A diagnosis of dementia can lead to depression and anxiety, which are risk factors for developing cognitive deterioration. Regarding the influence of stress on AD pathology, the transgenic mouse model of AD showed that a synthesized adrenocortical hormone of a dexamethasone injection induced β-amyloid deposition and tau accumulation.[10] Indeed, many patients report feeling abandoned and unsupported after diagnosis.[7] A patient's mental health after diagnosis should be carefully considered, and appropriate mental support should be arranged, because an early diagnosis can accelerate the development of dementia.

Regarding stigma, it is undeniable that a diagnosis of dementia is stigmatizing, and can result in social exclusion and restriction of an individual's rights.[11–14] Withdrawal is also problematic. It is possible for individuals with MCI and very early-stage dementia to continue their social activities with the understanding of people around them. However, because of the prejudices of others, individuals with MCI or dementia tend to withdraw from social activities. In cases where the patients still work, early diagnosis might damage household income, especially with early-onset dementia. Even if the patients are capable enough to work, continuation can become difficult because of prejudices, and they might stop working.

Doctors should note that early diagnosis is not always welcomed because of the fear of negative consequences of stigmatization and isolation, despite the benefits of support and assistance. In association with stigma, risks of misdiagnosis cannot be overlooked. False positives can lead to an unjustified acquisition of a stigmatizing label and patient distress. Misdiagnosis is also associated with missing the opportunity to address treatable conditions, such as depression.

A diagnosis can change the relationships among family members, who might become overly preoccupied and burdened by the dementia. Family members might set restrictions on activities, deprive the patient's roles at home and become hypervigilant with the patient.[8]

Disclosure of a diagnosis is a controversial issue. It has been reported that one in five general practitioners (GPs) regard disclosure as more harmful than helpful.[15,16] One study reported that 51% of people with dementia reacted poorly to the diagnosis, whereas 46% reacted positively.[17] The negative impacts of disclosure identified for individuals with dementia mainly regard psychological damage as aforementioned, whereas the positive impacts include putting an end to uncertainty, confirmation of suspicions and increased understanding of problems.[8]

Advantages and disadvantages for family members and caregivers

Family members and caregivers will play vital roles in at-home care. Advantages for family members and caregivers include the provision of time to make advanced preparations. Informing the family members of the prognosis and the disease course can allow them to set up social support and make legal arrangements for the disease progression. Knowledge and anticipation of the disease can be helpful in preventing a decline of quality of life, and social support might also be helpful in alleviating distress that caregivers may experience.[18]

Regarding disadvantages, family members and caregivers will also be confronted with stigmatized labeling and exclusion. Because of prejudiced views of dementia, family members might be labeled as a "caregiver of a demented family member". If the diagnosis had a negative impact on the patient and resulted in BPSD, including depression and apathy, the psychological burden of caring might increase.

Providing adequate support to caregivers should be a part of the total care at all stages. Receiving a diagnosis of dementia can be a devastating event, and the family members of the diagnosed patient will also require careful support and assistance. In addition to mental care and support, family members and caregivers will require financial and legal advice, and other kinds of practical assistance.

Advantages and disadvantages for social services

Regarding advantages, some reports suggest cost reductions associated with early detection of dementia. An early diagnosis can result in less intensive treatment, especially that associated with BPSD, and can delay nursing home admission when patients are appropriately treated.[19,20]

A shortage of social resources, particularly human resources, is a serious concern; an increased number of patients will strain workloads across all disciplines, and many patients could be diagnosed and not receive appropriate services. Indeed, patients diagnosed in the absence of sufficient local resources report feeling abandoned and unsupported after the diagnosis.[7] To meet these demands, health practitioner education and training are an urgent issue.

Screening of cognitive decline for early detection of dementia

The first step for detection of dementia is screening for symptoms of dementia. In this section, screening measures are considered.

Screening measures

Screening is important in deciding whether or not to proceed with more specific consultation. Requirements of screening include high sensitivity and specificity, brevity, and ease of administration. As an ethical matter, psychological burden should be taken into consideration. There are two general methods to screen for dementia: patient performance-based testing and informant interviews.

Patient performance-based testing

The most widely used brief test is the Mini-Mental State Examination, which covers different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, calculations, and orientation, and a total score represents overall cognitive status.[21] As a similar test, the Montreal Cognitive Assessment was developed for evaluation of MCI,[22] and there are a number of alternatives, such as the six-item Cognitive Impairment Test the General Practitioner Assessment of Cognition and the 7-Minute Screen.[23]

These tests are not without problems. The major problem of such brief tests is variability of their sensitivity according to age and education level.[24,25] Furthermore, the ceiling effect makes these tests insensitive to the very early stages of dementia,[26] especially for highly educated individuals.[27,28] In addition, these tests falsely identify those with low education, poor cognitive functioning, aphasia or depression as demented. The fact that these tests are time-consuming is also problematic; the time to administer the Montreal Cognitive Assessment is approximately 10 min. Another serious problem is the psychological burden on patients, as cognitive tests for dementia themselves are stressful for patients.[29]

Informant interview

It should be noted that self-rating scales are not reliable for dementia detection, because subjective cognitive impairment and memory complaints are common in elderly individuals, and such complaints are correlated with depressive symptoms or personality traits, rather than cognitive decline.[30] In addition, those who are already demented tend to overestimate their function and their self-awareness of cognitive impairments diminishes as the disease progresses, especially memory.[31,32] Such deficits in self-awareness of a disease, anosognosia, is one of the typical symptoms in AD, and DSM-5 explicitly gives a warning about excessive focus on subjective symptoms because of the danger of failing to diagnose in individuals with poor insight.[4]

Regarding informant-based assessment, the Clinical Dementia Rating (CDR)[33] scale is widely used. CDR meets the requirement of accuracy, but it is not an easily administered screening tool. It is a semi-structured interview that requires trained practitioners and takes at least 30 min, which is not easily administered under time-constraint situations.

We propose a brief informant-based screening questionnaire for identifying dementia in both clinical and community-based settings: Symptoms of Early Dementia-11 Questionnaire (SED-11Q; Fig. 1).[34] This questionnaire is easily administered, and is both patient and informant friendly. Questions on early signs of dementia were selected based on clinical experiences. SED-11Q inquires about the state of ordinary daily activities often carried out by an elderly individual living independently. Quantifying difficulties in daily living can provide more sensitive information about early functional changes rather than questions on cognitive function in a single domain, as functional integrity is a key differentiating feature of dementia, and decline in multifaceted cognitive domains directly leads to functional impairments. In addition, as deficits caused by dementia are manifested in various aspects, SED-11Q includes questions on social interaction and personality. The statistically optimal cut-off value of 2/3 indicates sensitivity of 0.84 and specificity of 0.90.[34] SED-11Q is also useful to estimate deficits in self-awareness of a disease, anosognosia. Caregivers and patients are required to answer the same questions, and discrepancies between caregiver and patient assessments show the severity of anosognosia.[35]

Another brief scale including questions on cognitive abilities and daily functioning is the eight-item questionnaire, AD8.[36] AD8 consists of questions of change in memory, orientation and functional abilities by placing emphasis on intra-individual, rather than inter-individual comparisons. The statistically optimal cut-off value of 2/3 shows sensitivity of 0.74 and specificity of 0.86.

Detection of dementia should be carried out without unduly alarming the patient. Therefore, informant-based assessments are preferable. DSM-5 recommends a combination of cognitive tests and questionnaires to complement each other. However, even in combination use, it should be noted that these tests and questionnaire are not sensitive or specific enough to avoid false positives.

Methods of screening: population screening and case findings

In the community setting, two pathways for detection can be considered: community-wide population screening, and case findings at primary care and other clinics, including cases where family members notice changes in daily living and take the person suspected with dementia to a doctor.

Symptoms of Early Dementia-11 Questionnaire (SED-11Q)

Date(MM/DD/YYYY)   /   /

Patient Name :   Patient ID :

Respondent Name :   Relationship

Respondent-completed / Interview by Name:

How has the patient's daily life been for the last month?
Please answer the following questions by circling the appropriate responses
(Exclude any difficulties caused by physical issues. e.g., pain).
Please ask for any help if needed.

			N/A
He/she talks and asks about the same things repeatedly.	YES	NO	N/A Don't know
He/she has become unable to understand the context of facts.	YES	NO	N/A
He/she has become indifferent about clothing and other personal concerns.	YES	NO	N/A
He/she has begun to forget to turn off the faucet and/or close the door. and/or has become unable to clean up properly.	YES	NO	N/A
When doing two things at the same time. he/she forgets one of them.	YES	NO	N/A
He/she has become unable to take medication under proper management.	YES	NO	N/A
He/she has begun to take a longer time to do work (e.g.. household chores). which could be done quickly before.	YES	NO	N/A
He/she has become unable to make a plan.	YES	NO	N/A
He/she cannot understand complex topics.	YES	NO	N/A
He/she has become less interested and willing. and stopped hobbies. etc.	YES	NO	N/A
He/she has become more irritable and suspicious than before.	YES	NO	N/A
TOTAL SED-11Q SCORE			

He/she has delusions. e.g.. claims to have had valuables stolen.	YES	NO	N/A
He/she has illusions. e.g.. sees something that isn't there.	YES	NO	N/A

If the answer is "yes" to either of these 2 questions. then a more comprehensive medical consultation is recommended.

Figure 1 The (a) Symptoms of Early Dementia-11 Questionnaire (SED-11Q) and (b) SED-11Q for patients (SED-11Qp), cited from Maki et al.[34,35]). (a) The statistically optimal cut-off value of 2/3, which showed sensitivity of 0.84 and specificity of 0.90, can be applied in the clinical setting. In the community setting, a cut-off value of 3/4, which showed sensitivity of 0.76 and specificity of 0.96, is recommended to reduce the danger of false positives. Medical consultation is recommended whenever delusions or illusions are detected. (b) SED-11Qp asks the same questions as SED-11Q. However, the title was changed to avoid using the word "dementia". "Patient Name" and "Patient ID" have been changed to "Name" and "ID". Two additional questions on delusions and illusions were not included in SED-11Qp. The questionnaires can be completed by interview.

How do you feel?

Date(MM/DD/YYYY)   /   /

Name :   ID :

Respondent-completed / Interview by Name:

How has your daily life been for the last month?
Please answer the following questions by circling the appropriate responses
(Exclude any difficulties caused by physical issues. e.g.. pain).
Please ask for any help if needed.

			N/A Don't know
You talk and ask about the same things repeatedly.	YES	NO	N/A Don't know
You have become unable to understand the context of facts.	YES	NO	N/A
You have become indifferent about clothing and other personal concerns.	YES	NO	N/A
You have begun to forget to turn off the faucet and/or close the door. and/or have become unable to clean up properly.	YES	NO	N/A
When doing two things at the same time. you forget one of them.	YES	NO	N/A
You have become unable to take medication under proper management.	YES	NO	N/A
You have begun to take a longer time to do work (e.g.. household chores). which could be done quickly before.	YES	NO	N/A
You have become unable to make a plan.	YES	NO	N/A
You cannot understand complex topics.	YES	NO	N/A
You have become less interested and willing. and stopped hobbies. etc.	YES	NO	N/A
You have become more irritable and suspicious than before.	YES	NO	N/A
TOTAL SED-11Q SCORE			

Figure 1 *Continued*

For years, there has been a wide debate over whether or not community-wide population screening for dementia helps patients and saves healthcare costs. However, at present, there is insufficient evidence of the benefits to justify community-wide population screening from the perspective of clinical outcomes, emotional effects and cost-effectiveness.[8,37,38] The causes for concern are a lack of screening measures that are both sensitive and specific enough to detect dementia, and a shortage of local resources. As aforementioned, no tests or questionnaires are sensitive and specific enough to avoid false positives, and people would suffer from incidental findings that

were found to be false. Undergoing unnecessary procedures after screening alone could be a great mental burden, adding to anxiety and fear raised by screening results. Significant resources are required for population screening itself, and thus implementation would pose additional burdens to local communities who are already confronted with a shortage of social resources. Detection of dementia is the initial step in the medical and care process, and thus for effective implementation of population screening, medical and care follow-up systems should be required, including mental care and support.

Case findings appear to be a more appropriate method than population screening to avoid false positives.[39] In many cases, the first stage of diagnosis starts with suspicion of dementia by those who know the person well, such as family members, colleagues and neighbors.[8] GPs and primary care physicians might also be keeping watchful eyes for signs of dementia. In a survey carried out in Canada, 26% of primary care physicians claimed that they routinely checked for signs of dementia in their patients.[40] Community nurses and staff at health-care centers may notice changes in community residents, and recommend them and/or their family members to consult with doctors.[8] Screening tools could provide information to verify whether or not such suspicions should be regarded as signs of dementia, and further investigation should be required. It is recommended to use the screening tools when sufficient information has been accumulated to suspect dementia. In the case of population screening, the diagnosis process begins with screening using tests and/or questionnaires, often without any information, whereas in case findings, tests and/or questionnaires are carried out only after sufficient information is gathered to suspect dementia. In either case, ethical issues must be carefully considered, including protection of personal information, obtaining informed consent, relieving the mental burden of undergoing screening, and the problem of overcoming stigmatization and exclusion.

Issues to be addressed for effective implementation of early diagnosis

Accurate diagnosis, avoiding false positives and overdiagnosis

It is evident that effective therapy, intervention and support depend on an accurate diagnosis, and it should be noted that screening is absolutely different from diagnosis. Considering the mental burden and stigma that result from diagnosis, false positives should be carefully avoided.

One of the fundamental issues is a wide variation in GPs' abilities and confidence in diagnosing and managing dementia.[41] At present, it is a practical resolution that the responsibility of diagnosis of dementia is shared between generalists and specialists. The government launched a plan to designate Medical Centers for Dementia in 2008, and 171 hospitals had been designated up to May 2012. The functions of these centers are to establish medical–medical and medical–care cooperation in local communities. The GPs play an important gatekeeper role in referring people for diagnosis by a specialist, rather than taking on the burden of diagnosis themselves. Based on the referral, the centers diagnose patients, and once the diagnosis has been confirmed, the GPs are expected to provide both practical and emotional support for patients and their family members, and refer them for additional psychosocial support if required. If there is a need for a consultation with a specialist, the patients can revisit the center on referral by the GP. At present, the centers are overloaded because they are forced to provide daily practical and emotional support for patients as a result of the insufficient capabilities of GPs to deal with dementia. Thus, education of GPs is a pressing issue for treatment after detection of dementia. The Ministry of Health, Labor and Welfare in Japan certifies Dementia Support Doctors who lead and support the primary care doctors and other dementia care professionals, and holds the skill-up programs of dementia medicine for primary care doctors and GPs.

Human resource development under a community-based integrated care system

It is a challenge to ensure compatibility between cost-effectiveness and quality care, and quality care could be provided if there was effective cooperation and coordination between healthcare professionals and organizations.[42,43] In Japan, the long-term care insurance system aims to promote the implementation of a community-based integrated care system with the goal of deinstitutionalization and promotion of at-home care. Under the system, allocation of social resources and capital was delegated to each local government for management and implementation, and basically, services, including medical treatment, care and community life support, are provided within local communities. The policy is based on the expectation that each community will create a "tailored" system to meet the health needs, health status and values of the community.[44,45] Under the Five-Year Plan for Promotion of Measures against Dementia in Japan, the pilot project of the initial-phase intensive support teams has been launched to grope the community-based implementation methods of earlier detection and intervention; the support team consists of healthcare professionals including nurses, health nurses and occupational therapists.

Development of human resources is one of the urgent requirements. In addition to the education and training of medical and healthcare staff, community residents

are expected to act as participants, and not merely as beneficiaries of services.[46] It is vital to implement measures that involve all members of society, so that they can help and support each other towards the improvement of the living environment for the elderly. This can be achieved through cooperation and active involvement among all sectors of society, such as the national government, local governments, corporations, local communities, non-profit organizations, family members and individuals with dementia. Task shifting is one of the key concepts; that is, shifting some work carried out by healthcare professionals to volunteers in order to reduce the workload of professional workers. The policy encourages volunteers to assist in the lives of demented individuals, and good outcomes have been shown in a number of local communities. For implementation of beneficial community-based integrated care after diagnosis, promoting social participation and community involvement of the residents should be a key strategy in addressing the shortage of human resources.

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Disclosure statement

The authors declare no conflict of interest.

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ORIGINAL ARTICLE: EPIDEMIOLOGY,
CLINICAL PRACTICE AND HEALTH

Intensive rehabilitation for dementia improved cognitive function and reduced behavioral disturbance in geriatric health service facilities in Japan

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Aim: To examine the efficacy of rehabilitation for elderly individuals with dementia at intermediate facilities between hospitals and home, based on the policies for elderly individuals to promote community-based care at home and dehospitalization.

Methods: Participants were older adults with dementia newly admitted to intermediate facilities. A total of 158 in the intervention group who claimed Long-Term Care Insurance for three consecutive months, and 54 in the control group were included in the analysis. The interventions were carried out in a tailor-made manner to meet individual needs. The personal sessions were carried out three times a week for 3 months after admission by physical, occupational or speech therapists. Outcome measures were cognitive tests (Hasegawa Dementia Scale revised [HDS-R] and Mini-Mental State Examination), and observational assessments of dementia severity, activities of daily living (ADL), social activities, behavioral and psychological symptoms of dementia (BPSD) using a short version of the Dementia Disturbance Scale (DBD13), depressive mood, and vitality.

Results: Significant improvement in the intervention group was shown in cognitive function measured by HDS-R (interaction $F[1, 196] = 5.190$, $P = 0.024$), observational evaluation of dementia severity ($F[1,198] = 9.550$, $P = 0.002$) and BPSD (DBD13; $F[1,197] = 4.506$, $P = 0.035$). Vitality, social activities, depressive mood and ADL were significantly improved only in the intervention group, although interaction was not significant.

Conclusions: Significant improvement by intervention was shown in multiple domains including cognitive function and BPSD. Cognitive decline and worsening of BPSD are predictors of care burden and hospitalization, thus intensive rehabilitation for dementia was beneficial for both individuals with dementia and their caregivers. **Geriatr Gerontol Int 2014; 14: 206–211.**

Keywords: behavioral and psychological symptoms of dementia, clinical medicine, Dementia Disturbance Scale short version, dementia, geriatric medicine, rehabilitation, tailor-made.

Introduction

Promoting community-based care at home and dehospitalization is one of the main policies for elderly individuals. In order to reduce the length of hospital stay, it is recommended to establish a rehabilitation and care system for the elderly just after leaving hospital. Thus, the Japanese government established the "Geriatric Health Service Facility" in 1986 (Long-Term Care Health Facility after 2000; Roken), which is a transitional facility between hospital and home or nursing home to provide medical treatment, nursing care, and rehabilitation. Elderly individuals are admitted to Roken after their condition has become stable in hospital, and stay until they are ready to return home. After returning home, Roken offers community-based rehabilitation and various care services to support home-based care, and facilitates networks for intraregional exchanges among municipalities, local healthcare and social welfare services.

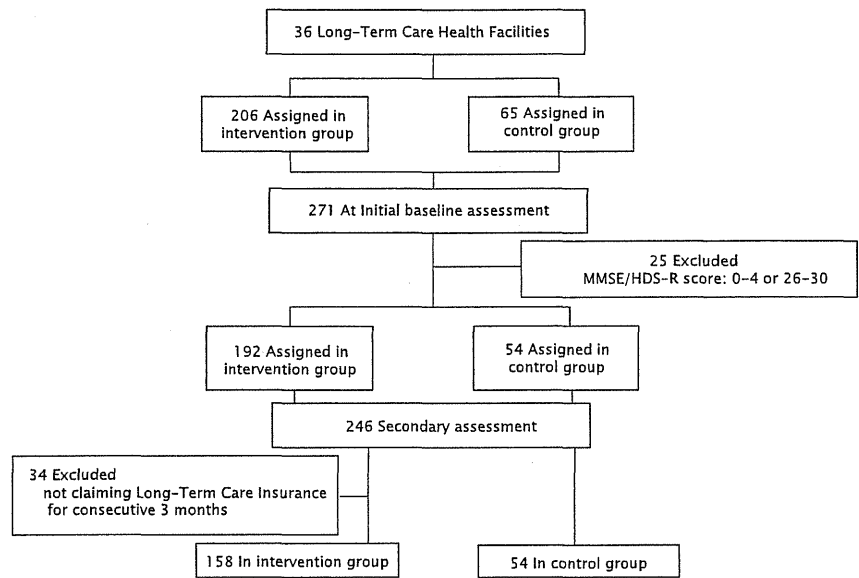Since Roken was launched, the number of inpatients with dementia has markedly increased. Hospitalization

Figure 1 Flow of participants in the intervention and control groups. HDS-R, Hasegawa Dementia Scale revised. MMSE, Mini-Mental State Examination.

itself can cause cognitive deterioration, even during a hospital stay for diseases other than dementia, and patients are often not expected to recover to their pre-hospitalization level.[1] Other predictors of hospitalization are caregivers' burden and the interrelationship with caregivers.[2] Behavioral and psychological symptoms of dementia (BPSD) are a source of distress for caregivers and a major reason for hospitalization.[3,4] Additionally, disuse syndrome is triggered by psychological factors associated with dementia, such as a depressive and apathetic mood.[5-9] Disuse syndrome can lead to deterioration of cognitive and physical function, which can result in repeated hospitalization.

To break the vicious cycle of repeated hospitalization, effective rehabilitation just after discharge from hospital is required, and Roken was singled out as the appropriate facility for the rehabilitation. Thus, in 2006, the Japanese Long-term Care Insurance system introduced intensive rehabilitation for individuals with dementia who were newly admitted to Roken, consisting of personal rehabilitation three times a week for 3 months. This rehabilitation has become widely practiced since its introduction. However, the efficacy has not been examined, although the rehabilitation is payable under long-term insurance. Thus, a model project was organized to examine the efficacy of the rehabilitation for dementia in Roken throughout Japan.

Methods

Study members

Study committee members were researchers excluding stakeholders of any Roken, and committee observers were staff of the Health and Welfare Bureau for the Elderly, Ministry of Health, Labour and Welfare. The committee designed the research, selected 36 Rokens, and interpreted the data. Data were collected by rehabilitation staff in the 36 Rokens.

Participants

The study was carried out between July 2007 and February 2008. The flow of participants is shown in Figure 1. Survey slips were sent to the facilities in July 2007. The facilities were required to send them back after the pre-intervention and post-intervention assessment, respectively. Inclusion criteria of the intervention group were: (i) newly admitted patients with dementia diagnosed by *The Diagnostic and Statistical Manual of Mental Disorders IV*; (ii) with Mini-Mental State Examination (MMSE) or Hasegawa Dementia Scale revised (HDS-R) score between 5 and 25 at pre-intervention assessment; and (iii) who claimed Long-Term Care Insurance for three consecutive months. Inclusion criteria of the control group were: (i) and (ii), and (iii) who did not receive interventions. The participants were not randomized. We received 271 responses, and among them, 212 individuals met the inclusion criteria (158 in intervention group and 54 in control group; Table 1). Informed consent was given from all participants or their responsible care giver. The research plan was approved by the Ethics Board of the Japan Association of Geriatric Health Services Facilities.

Assessment

The assessment was minimized to reduce the burden of facilities staff. As the interventions were carried out by therapists during working time, it would have been

Table 1 Demographic data

		Intervention	Control	
n		158	54	
Male/female (%)		30.2/69.8	39.6/60.4	NS
Age		84.1 ± 7.1	87.3 ± 7.1	P = 0.005[‡]
Dementia	AD	22	7	NS
	VD	52	15	NS
	DLB	3	0	NS
	FTD	2	0	NS
	Others/unknown	79	32	NS

[‡]Significant difference by two-sample *t*-test. AD, Alzheimer's disease; DLB, dementia with Lewy bodies; FTD, front-temporal dementia; M/F, male/female; NS, no significant difference by χ^2-test; VD, vascular dementia.

difficult to collect many data if the assessment were complicated. The assessment scales were chosen based on preliminary studies, which were carried out in the last 2 years.

Cognitive tests

The MMSE and HDS-R were carried out. HDS-R is similar to MMSE, but lays more weight on memory than does MMSE.

Questionnaires

For the assessment of subjective mood, the participants were required to answer the interview of a short version of the Geriatric Depression Scale (GDS;[10] scores are between 0–5, high scores indicate more depressive mood). Facility care staff assessed activities of daily living (ADL), BPSD, N-Memory Scale (NM),[11] vitality index[12] and the Social Activity Scale. ADL was assessed using the Barthel Index (scoring was changed: total assistance of 0 to independence of 3 for each item, and full score of 15).[13] In addition to ADL, the capacity for social interaction was measured using the Social Activity Scale, whose sub-items were conversation with facility staff members, conversation with other residents, organizing own belongings, participation in recreational activities, and outings (total assistance of 0 to independence of 3 for each item, and full score of 15). BPSD was evaluated using a short version of the Dementia Behavior Disturbance Scale (DBD;[13] "never" of 0 to "usually" of 3 for each item and full score of 48).[14] The NM Scale is an observational scale, which evaluates the stages of dementia in five domains: housework, social interaction and interest, communication, memory, and orientation ("impossible" of 0 to "normal" of 10 and full score of 50). The Vitality Index evaluates motivation in daily living, with sub-items of waking up, greetings, having meals, elimination, and participation in rehabilitation and/or recreation ("indifferent" of 0 to "voluntarily" of 2 and full score of 10).

Intervention

Before commencement of the study, a training workshop was held to introduce the intervention methods, whose efficacy was suggested by previous studies: such as reminiscence, reality orientation, memory rehabilitation, music therapy, physical exercise, occupational therapy, speech communication therapy and learning sessions.

The intervention was carried out in an individualized tailor-made manner.[15] First, the individual functional profiles were assessed with regard to both abilities and disabilities to evaluate how to enhance the abilities and compensate for disabilities. Second, training activities were selected; the decision was shared between therapists and participants. Each personal session was took place three times a week for 3 months after admission by physical, occupational or speech therapists. Individuals in the control group took usual group therapies including exercise, singing songs and games.

Analysis of data

The data were analyzed using the Japanese version of SPSS for Windows version 19.0 (IBM Corporation, Armonk, NY, USA). For an initial baseline comparison between the intervention and control groups, two-sample *t*-tests were carried out; there was no significant difference between the two groups for any outcome measure. Participants who underwent the initial baseline and post-intervention assessments were included in the final analysis; dropout participants were excluded from the analysis. Repeated measures analysis of covariance (ANCOVA) with the covariate of age was used to analyze the completed cases. Age was used as a covariate, because the ages were significantly different between the two groups (Table 1). The interaction was examined to assess the differential effect between the intervention and control groups, and post-hoc "within subjects" analysis was carried out with Bonferroni correction. Regarding the measures where significant

interaction was shown, intention-to-treat analysis was also carried out; the participants who received the intervention but did not claim Long-Term Care Insurance for three consecutive months were included in the intention-to-treat analysis. A significant difference was set as $P < 0.05$.

Results

Demographic data of the participants are shown in Table 1. Analysis of 158 participants in the intervention group and 54 in the control group was carried out (Fig. 1). The number of participants who took donepezil during the intervention/observation period was two in both groups ($P = 0.269$, χ^2-test).

Cognitive tests

Participants in the intervention group showed significant improvement in HDS-R score compared with those in the control group (interaction F[1, 196] = 5.190, $P = 0.024$; post-hoc intra-subject analysis: intervention group, $P = 0.001$, control group $P = 0.480$). There were no significant differences observed in MMSE (Table 2).

Questionnaire

The intervention group showed significant improvement compared with the control group in DBD[13] (F[1,197] = 4.506, $P = 0.035$; post-hoc intra-subject analysis: intervention group, $P = 0.004$, control group $P = 0.413$) and NM Scale (F[1,198] = 9.550, $P = 0.002$; post-hoc intra-subject analysis: intervention group, $P < 0.001$, control group $P = 0.380$). Regarding the sub-items of the NM Scale, significant differences in interaction were observed for social interaction (F[1,198] = 15.736, $P < 0.001$), memory (F[1,198] = 7.635, $P = 0.006$) and orientation (F[1,198] = 4.220, $P = 0.041$).

Although the interaction was not significant, comparison between pre- and post-intervention showed significant improvement in ADL (Barthel Index), Social Activity Scale, motivation (Vitality Index) and mood (GDS) only in the intervention group after multiple correction (Table 2).

Intention-to-treat analysis

Significant differences remained in the intention-to-treat analysis in the HDS-R and NM Scale; HDS-R, interaction (F[1, 230] = 4.466, $P = 0.036$), post-hoc analysis within subjects: intervention group $P < 0.001$, control group $P = 0.585$; NM Scale, interaction (F[1, 236) = 8.113, $P = 0.005$), post-hoc analysis: intervention

Table 2 Outcome of intensive cognitive rehabilitation

	Intervention group Pre mean ± SD	Intervention group Post mean ± SD	n	Control group Pre mean ± SD	Control group Post mean ± SD	n	Interaction F (DF)	P	Intra-subject[†] Intervention	Intra-subject[†] Control
Cognitive test										
MMSE	19.1 ± 4.5	19.4 ± 5.5	100	19.5 ± 4.9	18.2 ± 7.4	13	1.780 (1,110)	0.185	0.542	0.234
HDS-R	16.9 ± 5.7	17.9 ± 6.5	149	17.0 ± 5.9	16.7 ± 6.3	50	5.190 (1,196)	0.024*	0.001**	0.480
Questionnaire										
NM	30.4 ± 9.1	32.1 ± 9.5	149	31.4 ± 9.8	30.7 ± 10.9	52	9.550 (1,198)	0.002**	$P < 0.001$***	0.380
ADL	16.4 ± 7.1	17.3 ± 7.1	152	15.7 ± 7.0	15.9 ± 6.9	53	1.448 (1,202)	0.230	0.001**	0.621
Activity	8.6 ± 3.3	8.8 ± 3.4	150	8.5 ± 3.1	8.6 ± 3.2	53	1.169 (1,200)	0.281	0.038*	0.972
Vitality	8.0 ± 1.7	8.2 ± 1.6	149	8.1 ± 1.8	8.2 ± 1.8	53	1.792 (1,199)	0.182	0.004**	0.864
DBD	4.5 ± 5.1	4.0 ± 4.1	150	4.5 ± 4.2	4.8 ± 4.7	50	4.506 (1,197)	0.035*	0.004**	0.413
GDS	2.5 ± 1.8	2.4 ± 1.9	148	2.3 ± 1.5	2.4 ± 1.5	51	2.048 (1,196)	0.154	0.042*	0.634

[†]Intra-subject: post-hoc analysis of intra-subject (comparison between pre- and post-intervention analysis). *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. Activity, Original Activity Scale; ADL, Activities of daily living; DBD, Dementia Behavior Disturbance Scale; DF, degree of freedom; GDS, Geriatric Depression Scale; HDS-R, Hasegawa Dementia Scale revised; MMSE, Mini-Mental State Examination; NM, N-Memory Scale; Post, post-intervention assessment; Pre, pre-intervention assessment; Vitality, Vitality Index.

group $P < 0.001$, control group $P = 0.410$. The interaction of DBD was marginal; interaction ($F[1, 232] = 3.717$, $P = 0.055$), post-hoc analysis: intervention group $P = 0.007$, control group $P = 0.439$.

Discussion

Significant improvement by the intervention was shown in multiple domains; therefore, the intensive rehabilitation for dementia was beneficial for the individuals with dementia and also their caregivers. Pharmacological effects were thought to be negligible, as just two participants in both groups took donepezil during the intervention/observation period.

Regarding cognitive function, the effects of intensive rehabilitation for dementia were shown in both a cognitive test and observational evaluation of memory and orientation measured by NM Scale. In the symptomatic treatment of dementia, amelioration in daily living rather than in neuropsychological factors should be the therapeutic objectives, and thus the emphasis would be laid on improving performance in everyday life rather than on scores of cognitive tests.[16] Besides, it is often pointed out that scores of cognitive tests cannot always be generalized to daily living, although cognitive tests are moderately predictive of functional status in everyday life.[17] Therefore, mere enhancement of cognitive test scores is not sufficient, and beneficial changes in daily living are required. In the present study, cognitive improvement was shown in observational evaluation, in addition to a cognitive test. Cognitive enhancement is also beneficial for caregivers, because the severity of cognitive impairment could be a predictor of burden, in addition to BPSD.[18,19] The effects of non-pharmacological approaches on cognitive function have not yet been established,[16,19] and the present study could provide additional evidence for their benefit.

Amelioration of BPSD was also attained in the present study. Care for demented individuals requires allocation of longer times than for care of the elderly suffering from physical diseases. In particular, the presence of BPSD might induce more stress than do medical problems,[4,20–23] and could result in depression or strain in caregivers.[24] Consequently, caregivers' burden is associated with an increased risk of institutionalization.[25] However, institutionalization could not solve caregivers' distress; a year after institutionalization, distress still persisted in caregivers.[26] In contrast, treatment of BPSD could help diminish caregiver burden.[27] Thus, it is beneficial both for individuals with dementia and their caregivers to reduce BPSD by rehabilitation in intermediate facilities between hospital and home.

In addition to enhancement of cognitive function and reduction of BPSD, improvement of social functioning and quality of life (QOL) should be the main outcomes of rehabilitation for dementia.[16]

Social isolation is associated with increased risk of mental decline,[28] whereas a rich social network and interaction might protect against mental decline.[29,30] In demented individuals, symptoms of depression were a consistent predictor of QOL.[31] In the present study, the intervention group showed improvement of social functioning measured by the Social Activity Scale, and amelioration of depressive mood measured by GDS.

Regarding the intervention, individualized tailor-made therapies were carried out, because the aim of the present study was to enhance each participant's ability to meet their individual needs, and not to show the efficacy of any specific method. Personally-relevant goals were identified, and the therapist worked with the individuals with dementia to devise strategies to cope with difficulties in their everyday lives by building on the person's strengths and developing ways of compensating for impairment.[15] Personal selection was considered an essential therapeutic element to enhance the motivation and optimize the emotional impact of the training. Changing and combining methods were allowed during the intervention period.

The present study showed that intensive rehabilitation should be beneficial for both individuals with dementia and caregivers. To promote community-based care and dehospitalization, continuity of rehabilitation is desirable to maintain function after returning home; another mission of Roken is to offer community-based rehabilitation and various care services to support home-based care.

As a limitation, the participants were not randomized. By data cleaning, data including missing values were excluded so that the numbers of valid data were different among assessments. Finally, for evaluation of the effects on dehospitalization, a longitudinal follow-up study is required.

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Disclosure statement

The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Twelve-week physical and leisure activity programme improved cognitive function in community-dwelling elderly subjects: a randomized controlled trial

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Abstract

Background: Japan is one of the most rapidly ageing societies in the world. A number of municipalities have started services for the prevention of cognitive decline for community-dwelling elderly individuals, but the effectiveness of these services is currently insufficient. Our study explored the efficacy of a comprehensive intervention programme consisting of physical and leisure activities to prevent cognitive decline in community-dwelling elderly subjects.

Method: We administered a 12-week intervention programme consisting of physical and leisure activities aimed at enhancing participants' motivation to participate and support one another by providing a pleasant atmosphere, empathetic communication, praise, and errorless support. This programme for the prevention of cognitive decline was conducted as a service by the city of Maebashi. All participants underwent the Five-Cog test, which evaluated the cognitive domains of attention, memory, visuospatial function, language, and reasoning. Executive function was evaluated by the Wechsler Digit Symbol Substitution Test and Yamaguchi Kanji-Symbol Substitution Test. Subjective health status, level of social support, functional capacity, subjective quality of life, and depressive symptoms were assessed with a questionnaire. Grip strength test, timed up-and-go test, 5-m maximum walking times test, and functional reach test were performed to evaluate physical function. Fifty-two participants were randomly allocated to intervention (n = 26) and control (n = 26) groups. Twenty-six participants, aged between 65–87 years, received intervention once a week at a community centre. The programme was conducted by health-care professionals, with the help of senior citizen volunteers.

Results: The intervention group (n = 19) showed significant improvement on the analogy task of the Five-Cog test ($F_{1,38}$ = 4.242, P = 0.046) and improved quality of life ($F_{1,38}$ = 4.773, P = 0.035) as compared to the control group (n = 24).

Conclusion: A community-based 12-week intervention programme that aimed to enhance motivation to participate in activities resulted in improvements in some aspects of cognitive function and quality of life. Senior citizens who volunteered in the present intervention enabled the smooth implementation of the programme and alleviated the burden on professional staff.

INTRODUCTION

Japan is one of the most rapidly ageing societies in the world. The number of demented elderly people who need nursing care is predicted to be 3.5 million by 2015 and 4.7 million by 2025.[1] Since Japan's long-term care insurance system was revised in 2008 to emphasize the importance of preventing the need for long-term care, a number of municipalities have started services to help prevent cognitive decline in community-dwelling elderly individuals. The services focus on maintaining and improving the cognitive functions of those who do not need care at present. However, the effectiveness of these services is currently insufficient, and such public services still need to demonstrate their effectiveness in preventing cognitive decline.

Physical exercise intervention has been suggested as an efficient strategy to reduce the risk of cognitive decline. A meta-analysis that focused on elderly subjects with dementia and related cognitive impairments suggested that physical exercise increases fitness, physical function, cognitive function, and positive behaviour.[2] The results of a more recent meta-analysis showed that non-demented subjects who performed physical activity had a significantly reduced risk of cognitive decline.[3] Also, recent randomized intervention studies reported that physical activity helps improve cognitive function of elderly patients.[4-6]

Participation in leisure activities is associated with a reduced risk of dementia by increasing cognitive reserve.[7-9] Frequent participation in cognitively stimulating activities, such as playing games, is associated with a reduced risk of Alzheimer's disease.[10] Previous randomized intervention studies have suggested that cognitively stimulating training or activity improves some aspects of cognitive ability in elderly subjects.[11,12]

Physical and leisure activities in a pleasant atmosphere can be effective for the prevention of cognitive decline. It has been shown in an animal study that exercise in enriched environments has a suppressive effect on the accumulation of amyloid-β protein.[13] We have proposed the efficacy of intervention conducted in a pleasant atmosphere with an emphasis on communication.[14] Therefore, it could be meaningful to facilitate a pleasant atmosphere between participants and form a group in which participants enjoy mutual communication.

We performed a randomized controlled trial of a comprehensive intervention programme consisting of physical and leisure activities for prevention of cognitive decline in community-dwelling elderly subjects. The programme was conducted as a service of the city of Maebashi, Japan, and it was administered by the city's staff of health-care professionals along with senior citizen volunteers. In the intervention, a pleasant atmosphere, empathetic communication, praising each other, and errorless support were emphasized to enhance the participants' motivation to participate and support one another according to five principles of brain-activating rehabilitation.[14]

Our study explored the efficacy of this service for preventing cognitive decline in elderly residents.

METHOD

Participants

The intervention programme was carried out as a service of the municipality of Maebashi in 2012. The service for the prevention of cognitive decline targeted elderly subjects aged 65 years and older residing in Maebashi. Participants were recruited through a lecture on the prevention of cognitive decline for community residents, leaflets that went to 2986 households, and door-to-door visits by public health nurses, local welfare commissioners, and senior citizen volunteers to invite elderly residents to the programme.

The Medical Ethics Committee of Gunma University (Maebashi, Japan) approved this study (21–47), and written informed consent was obtained from all participants.

Initial screening

Participants ($n = 58$) were screened by a questionnaire and medical interview (Fig. 1). They were examined by a clinician who specialized in dementia. Those who were diagnosed as having dementia according to the criteria of International Statistical Classification of Diseases and Related Health Problems 10th Revision or who had a medical condition that made them unable to engage in physical activity were excluded. After screening and exclusion, 52 participants remained.

Participants who were excluded from the study were still able to participate in the intervention programme, as it was conducted as a community service available to all community dwellers.

Amnesic mild cognitive impairment was diagnosed according to the following criteria:[15] reported memory
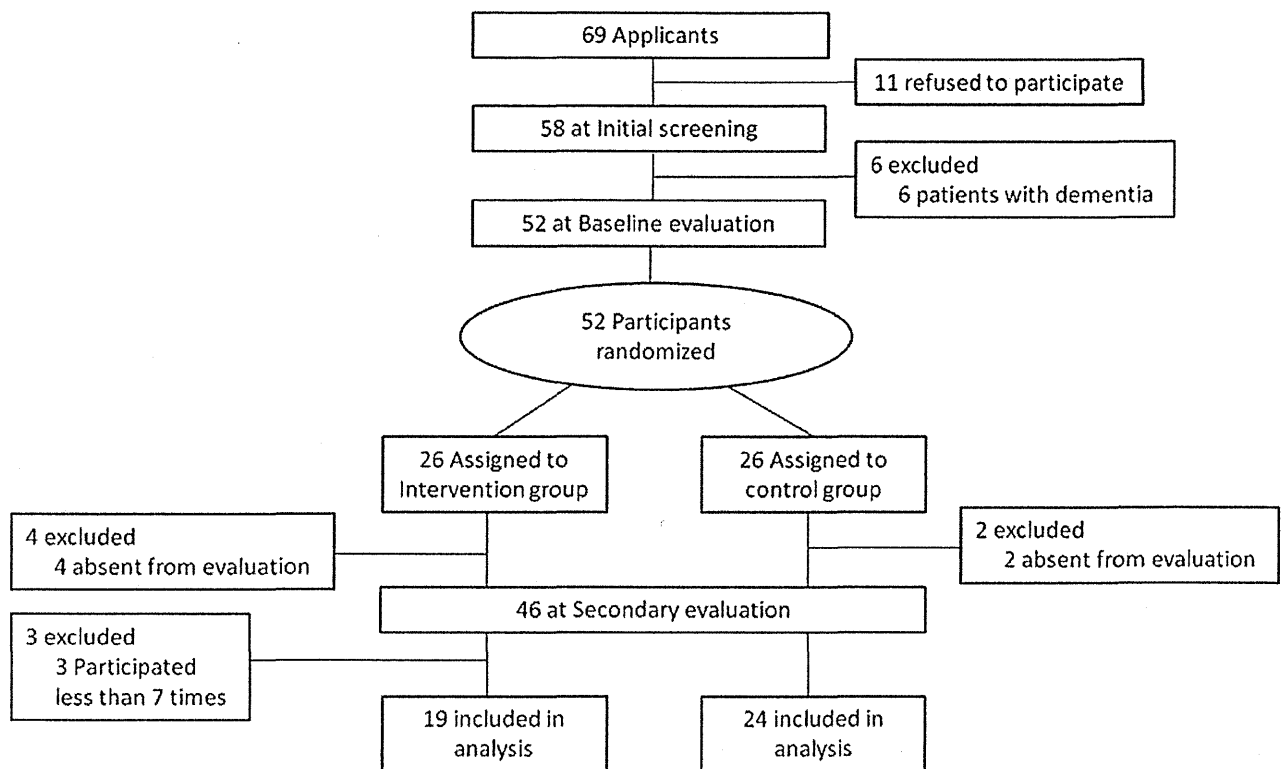
Figure 1 Flow of participants through the study.

complaint; objective memory impairment for age; essentially preserved general cognitive function; largely intact functional activities; and not demented. Reported memory complaint was examined based on information provided in the questionnaire administered at the baseline evaluation. Objective memory impairment for age was evaluated based on the score of the three-word delayed recall task of the Mini-Mental State Examination and questions about recent events or news by a clinician. Essentially preserved general cognitive function was evaluated based on the Mini-Mental State Examination score. Whether functional activities were largely intact was evaluated based on the score of Tokyo Metropolitan Institute of Gerontology Index of Competence.

Evaluation

Change in cognitive function was evaluated using the Five-Cog test, which evaluates attention, memory, visuospatial function, language, and reasoning. The Five-Cog test consists of five items: character position referencing task to evaluate attention, category

cued recall task to evaluate memory, clock drawing task to evaluate visuospatial function, animal name listing task to evaluate language ability, and analogy task to evaluate abstract reasoning ability.[16,17] Participants were also evaluated using the Wechsler Digit Symbol Substitution Test and Yamaguchi Kanji-Symbol Substitution Test,[18] which evaluate executive function.

To evaluate the physical function of each participant, a grip strength test, timed up-and-go test, 5-m maximum walking times test, and functional reach test were performed.

Participants were required to complete a questionnaire consisting of questions regarding age, sex, education, and previous/current medical history. Their subjective health status was evaluated with the question 'How is your health in general?' and scored using a rating scale from 1 (excellent) to 4 (poor). The level of social support was evaluated with the Lubben Social Network Scale Revised, which gauges social isolation in older adults by measuring the perceived social support from family, friends, and neighbours.[19]

Functional capacity was determined using the Tokyo Metropolitan Institute of Gerontology Index of Competence,[20] which is a multidimensional 13-item index of competence comprising three dimensions: instrumental self-maintenance, intellectual activity, and social role. The index was designed to measure higher level competence in community-dwelling elderly subjects.[20,21] The Satisfaction in Daily Life, a simple measurement of subjective quality of life (QOL), was used to evaluate the life satisfaction of participants.[22,23] The Satisfaction in Daily Life consists of 11 items: physical health, mental health, self-care, gait, housework, house facilities, partner and family relationships, hobby and leisure activities, social intercourse, economic state and social security, and having a job. Each item was rated from 1 (dissatisfied) to 5 (satisfied). The 15-item short version of the Geriatric Depression Scale was used to evaluate depressive symptoms.[24]

Randomization

After receiving the initial screening and baseline evaluation, 52 eligible participants were randomly allocated to the intervention group or control group.

Intervention

A comprehensive intervention programme consisting of physical and leisure activities was designed. The physical activity programme was the primary content of the programme. The exercise programme included muscle-stretching exercise in a sitting position (17 items), muscle-strengthening exercise in a sitting position (3 items), muscle-strengthening exercise in a standing position (7 items), and aerobic exercise (3 items). These exercises require comprehensive abilities in physical activity involving body flexibility, muscle-strength, balance and endurance. The mean duration of the exercise programme was 45 min. Participants were encouraged to perform exercises based on the programme at home. Walking was recommended to participants as a regular exercise. Leisure activities, such as cooking, handcrafts, and competitive games, were included in the programme to stimulate participant's cognitive function. All participants allocated to the intervention group attended a weekly 2-h programme at a community centre located in the district where they resided for 12 weeks.

The programme was presented by health-care professionals, including a physical therapist, occupational therapist, and public health nurse. Each session was conducted by three health-care professionals and three to five senior citizen volunteers. Maebashi has promoted elderly participation in volunteer activities, particularly those focusing on long-term care prevention in the community. In the present intervention, 32 senior citizens participated as volunteers. They received training on brain-activating rehabilitation. In each programme, three to seven volunteers participated in assisting the professional staff. Their roles were to assist the professional staff in conducting the physical and leisure activities, support participants who needed assistance engaging in the programmes, facilitate communication among the participants and help maintain a pleasant atmosphere. Participants in the control group did not attend a programme during this period.

Statistical analysis

Statistical analysis was performed using the Japanese version of SPSS v. 17.0 (IBM, Armonk, NY, USA). For baseline comparison between the intervention and control groups, a χ^2 test was conducted in categorical data, and two-sample t-tests were conducted in continuous variables. No significant differences were observed between the two groups at baseline. Changes from baseline were analyzed by repeated measures ANCOVA, with covariance of age, sex, and years of education. Post-hoc analysis was conducted using Bonferroni correction. $P < 0.05$ indicated significance.

RESULTS

Flow of participants through the study

Figure 1 shows the flow of participants through the study. Fifty-two participants were randomized to the intervention ($n = 26$) and control ($n = 26$) groups. The attendance rate during the intervention was 77.6%. Nine were excluded from the analysis: seven in the intervention group attended the programme less than eight times and two in the control group were absent from the second evaluation. Finally, 43 subjects were included in analysis. Table 1 shows the demographic and clinical characteristics of the participants. Changes from baseline were investigated