Study Title: A Multidomain Intervention Program for Older People with Dementia

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A Multidomain Intervention Program for Older People with Dementia

Background

Dementia is a syndrome characterized by cognitive decline interfering with daily function. Alzheimer's disease and vascular dementia are the commonest causes of dementia separately or in combination accounting for over 80% of all dementia cases. Dementia is one of the major causes of disability and dependency among older people worldwide. The number of deaths due to dementia increased by 148% (140–157%) between 1990 and 2016. Dementia has significant social and economic implications in terms of direct medical and social care costs, and the costs of informal care. In 2020, the total global societal cost of dementia was more than 1 trillion USD.

Medications for dementia are considered to be only modestly effective.[7] The most commonly prescribed drugs are acetylcholinesterase inhibitors (AChEIs), and N-methyl-d-aspartate receptor (NMDAr) antagonists, such as memantine, may improve cognitive and behavioral outcomes, but their clinical impact remains modest and controversial. Many of these pharmacological treatments have been associated with adverse effects and greater risk of contraindications. Currently, no disease-modifying treatments has been demonstrated to be fully effective in controlling the symptoms of dementia. The effect of single-domain trials for people with dementia is still unclear. Some positive benefits have been reported for physical activity-based interventions, cognitive training. However, these benefits are of only borderline clinical relevance, and the overall quality of evidence in relation to most other outcomes was low. Many experts consider that since dementia is a complex, multifactorial disorder multidomain intervention targeting several risk factors and disease mechanisms may be more effective than single interventions to increase cognitive function, increase social activity and reduce depression, delay functional decline, while enhancing the quality of life of caregivers. The multidomain approach in many prevention trials has already proven its efficacy in chronic conditions that are associated with the development of dementia such as type 2 diabetes mellitus and cardiovascular disease. Multidomain interventions have been shown to be effective in improving cognition, reducing neuropsychiatric symptoms and delaying progression of functional impairment or disability in dementia patients in community- dwelling and nursing homes.

In Vietnam, the older adult population is increasing rapidly in both absolute and relative numbers with the average lifespan increasing by four to 75 years in the last two decades. The prevalence of cognitive symptoms of dementia in adults aged 60 years and above is relatively high in Vietnam (14.4–46.4%) with an estimated 2.4 million people living with dementia in Vietnam by 2050.[25] Advancing the mental health of older people in Vietnam is critical in the face of population growth and increased living standards resulting in longer lifespan. In the first Vietnam National Dementia Conference, dementia was recognized as a public health priority in Vietnam.[26] The number of older people living in nursing homes is increasing in Vietnam, in which the percentage of people with dementia accounts for the majority. However, there was limited evidence on multifactorial intervention program for people with dementia in nursing homes in Vietnam. In order to improve treatment effectiveness, reduce symptoms and improve the quality of life of patients with dementia and their caregivers, we plan to conduct a pilot study to investigate the feasibility of a multidomain intervention program (physical; cognitive; social and management of metabolic and vascular risk factors) for older people with dementia in nursing homes.

Objectives

Primary

To assess the feasibility of a multidomain intervention program (physical, cognitive, social and management of metabolic and vascular risk factors) for older people with dementia in nursing homes.

Secondary

To investigate the effect of a multidomain intervention program on behavioral and psychological symptoms, quality of life, functional ability, falls and sleep, frailty, global cognition and the specific cognitive domains of attention, memory, fluency and executive function; and death rate for older people with dementia.

Method

Trial Design and Participants

This is a two-armed, multicenter, randomized controlled pilot study, based in nursing homes in Hanoi, Vietnam.

Inclusion Criteria

We aim to enroll participants aged over 60 years, living in nursing homes who have a diagnosis of major neurocognitive disorder (according to DSM 5 criteria), stage mild to moderate (according

to Clinical Dementia Rating). Participants receiving pharmacological treatment for dementia must be on a stable dose for at least 3 months prior to the study. Eligible participants must be able to mobilize independently with or without a mobility aid and without physical assistance.

Exclusion Criteria are

- ✓ Acute and malignant diseases (eg, advanced cancers, end-stage chronic diseases, acute myocardial infarction, stroke)
- ✓ Symptomatic cardiovascular disease or coronary revascularization within 1 year
- ✓ Clinical evidence of schizophrenia, severe depression, psychiatric or bipolar disorder (according to DSM-V TR criteria)
- ✓ Alcoholism or substance dependence (according to DSM-5 criteria), currently, or within the past 2 years
- ✓ Severe loss of vision, hearing or communicative ability (according to the interRAI Community Health Assessment)
- ✓ Participant or family unwilling to participate in the study.

Recruitment

Participants will be recruited from November 2022 until December 2023.

Research Team

The research team consists of 5 researchers, 2 research assistants, 2 neurologists and 2 physiotherapy experts. Prior to recruiting participants, the research assistants will complete a training program in screening and data collection using the specific measures to be used in the study.

Sample Size Estimates

Assuming a standardised effect sizes (ES) of 0.2 for a pilot randomised trial, with 90% power and two-sided 5% significance, and allowing for a 10% dropout rate and 5% mortality, the final sample size to be recruited is 60 (30 per study arm).

Randomisation, Concealment, and Allocation

A concealed, computer-generated sequence of randomly permuted blocks (block size = 4), stratified by age (60–69, 70–79, 80 and over) and disease severity (mild or moderate) will be generated by a statistician not otherwise involved in the study. Randomization will occur at the completion of the entire baseline assessment.

Blinding

Participants will be informed that they will be randomly assigned to one of the two treatment groups by the research assistants. Investigators will be blinded to the intervention allocation. All outcome measures will be administered by blinded assessors.

Study Procedure

The study PI and/or researchers in the research team will contact adults aged 60 years and older in the nursing homes (Orihome, Nhan Ai, Dien Hong) to introduce the study. If they are interested in participating, the study PI and/or researchers in the research team will screen them for their eligibility. If they meet the inclusion criteria and are interested in participating, written informed consent will be obtained. Participants will be evaluated for capacity to give informed consent. If participants have the capacity to consent to the research project, they will receive a complete explanation of the purpose, risks, and procedures of the study and sign a written informed consent. Otherwise, a family member will consent for them.

A screening log will be kept to document number and reasons of participants who do not meet the inclusion criteria, decline to participate, or any other reasons.

Participants who agreed to participate in the study will be randomized into two equal groups, to receive either a multidomain intervention (intervention group) or regular health advice (control group). The intervention will include physical, cognitive, and social interventions, and management of metabolic and vascular risk factors.

The patients in the intervention group and the control group will be still participating in the usual care and activity, which were consistent across all three nursing homes in the study. The activities including quizzes and movement games will be held every 3 months. They will also be doing 15-minute morning exercise every day with light intensity. Participants in both the intervention and the control groups will be treated for dementia according to the recommendations of the Vietnam Alzheimer Disease and Neurocognitive Disorders Association.

All participants will meet the study physician to have an examination at baseline, 3 months and 6 months. At each examination, participants will undergo a physical examination, anthropometry (weight, and hip and waist circumference), blood pressure determination, pulse rate and rhythm check, assessment for cardiovascular risk factors and metabolic diseases (smoking, drinking, hypertension, coronary artery disease, dyslipidemia, atherosclerosis, diabetes) and assess blood test results (lipid profile, HbA1C and fasting glucose if patients have diabetes). Blood pressure measurements will be made on the left arm of the seated participants with a

sphygmomanometer and an appropriately sized cuff; the average of 2 physician-obtained measures constitute the examination blood pressure. Metabolic and vascular risk factors will be ascertained by self-report (or caregivers report/nursing home report). Diabetes is defined as fasting glucose >7 mmol/l or use of insulin or oral hypoglycemic medications. Hypertension is defined as a systolic blood pressure of 140 mm Hg or more, or a diastolic blood pressure of 90 mm Hg or more, or taking antihypertensive medication. Dyslipidemia is defined as having an increased level of triglycerides, total cholesterol, or low-density lipoprotein cholesterol (LDL-C) or decreased level of high-density lipoprotein cholesterol (HDL-C). Results will be provided to participants and their doctors.

Interventions

The Intervention Group

In addition to what is given to both groups, the participants in the intervention group will receive three intervention components in 6 months: (1) physical activity; (2) cognitive intervention; and (3) social intervention as well as (4) management of metabolic and vascular risk factors. Physical activity and cognitive stimulation interventions will be performed at separate sessions.

Physical Activity Intervention

Progressive resistance training (PRT) for the physical intervention will be provided at the nursing home for 45 minutes twice a week. The sessions will be organized in groups (10 patients/group) and supervised by 2 physiotherapists. Within each small group (maximum 10) participants will follow the program tailored to their individual functioning level, with constant oversight by trainers.

The exercise program consists of progressive resistance training. Participants will progress through the 6-month intervention, guided by daily ratings of perceived exertion (15–18) on the Borg Scale.

People with dementia and their care staff will be instructed to follow the prescribed PRT exercises for the rest of the week. Participants will be encouraged to exercise daily. Physiotherapists will determine progress subjectively based on the ability of the person with dementia. Training volume will be monitored by adding up the total minutes of participation during each day of the prescribed program.

Cognitive Intervention

The study subjects will receive cognitive intervention based on Cognitive Stimulation Therapy with rehabilitation experts. The intervention involves 14 sessions of themed activities, which typically run twice weekly. The sessions will be organized in groups (6-10 patients/group). Each session lasts about 45 minutes. To make sure that there is continuity between the sessions they will follow the same structure: introduction (10 minutes), main activity (25 minutes) and conclusion (10 minutes). A total set of 14 exercises will be selected including physical games, sounds, childhood, food, current affairs, word association, being creative, categorising objects, orientation, using money, number game, word games, team quiz, which will be culturally adapted in Vietnam. Necessary activities related to daily lives will also be included. People with dementia and their care staff will be instructed on how to practice the various activities at their nursing home for the rest of the week in a separate room. Training volume (multiplying the number of repetitions performed/day by the number of days) will be monitored using a training diary.

Social Intervention

Social intervention will be combined with physical and cognitive interventions through doing these interventions in a group, ie, playing group games during exercises (eg, dancing, throwing ball to each other) or doing cognitive stimulation therapy in a group.

Management of Metabolic and Vascular Risk Factors

In the intervention group, metabolic and vascular risk factors will be evaluated by cardiologists and endocrinologists in the study.

Study physicians will assess change in blood pressure, weight and BMI, and hip and waist circumference, blood tests (glucose, lipid parameters, fasting glucose and HbA1C if the person with dementia has diabetes) at 3 and 6 months.

Participants in the intervention group will be provided with information on the importance of reducing risk factors, guidance on lifestyle changes and prescribing treatment if necessary by the cardiologists and endocrinologists. The target for blood pressure is less than 120/90 mmHg and the target for HbA1c is less than 8%.

The Control Group

The control group will receive general health advice every 3 months based on their physical examination and blood findings. They will be provided usual care plus health education materials.

Outcome Measurements

- Primary Outcome

The primary outcome of the study is the feasibility of the intervention which will be assessed via the adherence and retention in intervention group.

Adherence: a count of sessions (percentage) attended out of the total planned

Retention: the number (percentage) of participants in each group who did not discontinue the study.

- Secondary Outcomes

Cognitive Function

Global cognition will be measured by Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog), the Clinical Dementia Rating scale (CDR); executive function by the Clock test; and attention by digit span forward and digit span backward

Behavioral and Psychological Symptoms of Dementia (BPSD)

Researchers will interview care staff using the Neuropsychiatric Inventory (NPI) questionnaire. Higher scores indicating greater severity

Functional ability will be assessed by using the Activities of Daily Living Scale (ADL), the Instrumental Activities of Daily Living Scale (IADL), handgrip strength and a 30 s chair stand test (30 s CST). The 30 s CST consists of counting the number of sit-stand-sit cycles completed during the 30 s test

Falls

Falls will be assessed by the fall incident report at baseline and during the study period.

Sleep Problem

Sleep Problem will be assessed with the Pittsburgh Sleep Quality Index. A global PSQI score over 5 indicates poor sleep

Health-Related Quality of Life

Health-related quality of life will be assessed with the Quality of Life in Alzheimer's Disease scale (QoL-AD). Total scores range from 13 to 52 with higher scores indicating higher quality of life.

Death

Death will be assessed through caregiver reports or nursing home records.

Ethical Approval and Consent

Ethical approval has been performed in accordance with the Declaration of Helsinki and have been approved from the National Geriatric Hospital (1139/IRB) on October 7, 2022. Participants will be evaluated for capacity to give informed consent. If participants have the capacity to consent

to the research project, they will receive a complete explanation of the purpose, risks, and procedures of the study and sign a written informed consent. Otherwise, a family member will consent for them. The trial is registered with ClinicalTrials.gov identifier: NCT04948450 registered on 02/07/2021.