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Title of the project: Mild cognitive impairment among community dwelling adults: Prevalence, associated factors, and feasibility of a multidomain intervention package for preventing cognitive decline

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2. Objectives

1. To estimate the burden of mild cognitive impairment among community dwelling adults between 50-65 years in a taluk of a South Kerala district

2. To develop a multidomain intervention package for preventing cognitive decline in those with mild cognitive impairment

2. To explore the barriers and facilitators for adherence towards multidomain intervention to prevent cognitive decline in community dwelling older adults between 50- 65 years with mild cognitive impairment in the study area

3. Summary of the proposed research (up to 150 words) indicating overall aims of the research and importance of the research proposal. Application of the work in the context of national priorities of medical research, if any, may also be mentioned.

In the context of increasing older adults, the burden of dementia is forecasted to increase in India. Interventions targeting risk factors and diseases may be the key element to counter the dementia epidemic. The state of Kerala having highest proportion of older adults and burden of lifestyle diseases causes even greater concern and hence there is need for identifying a feasible multidomain preventive intervention to be applied. First the burden of mild cognitive impairment will be determined as this information is scare from the setting. A multidomain intervention package will be developed appropriate for the setting which consists of nutritional guidance, physical exercise, cognitive training and management of metabolic and vascular risk factors. The adherence rates, and barriers and facilitators towards adherence will be assessed and if found feasible can be recommended for further clinical trials.

4. Present knowledge and relevant bibliography including full titles of articles relating to the project.

Dementia and Mild Cognitive Impairment

Dementia is an umbrella term for several diseases that are mostly progressive, affecting memory, other cognitive abilities and behavior, and that interfere significantly with a person's ability to maintain the activities of daily living (1). It is characterized by progressive cognitive decline that interferes with the ability to function independently(2,3). Symptoms of dementia are gradual, persistent and progressive. The clinical presentation of dementia varies greatly among individuals, and the cognitive deficits can present as memory loss, communication and language impairments, agnosia (inability to recognize objects), apraxia (inability to perform previously learned tasks) and impaired executive function (reasoning, judgement and planning)(4). Mild Cognitive Impairment (MCI) is an objective cognitive impairment in patients who do not meet the criteria for dementia

and have preserved function (5). The difference between MCI and Dementia is largely the ability to function independently. Individuals with MCI are at a higher risk for developing Alzheimer's Disease and other Dementia's when compared to patients without an MCI. The reported annual conversion rate ranges from 1.6% to 28% (3,6–8). Common forms of dementia include Alzheimer's disease, vascular dementia and Lewy body dementia. Dementia accounts for nearly 11.9% of Years lost due to disability due to a communicable disease(9). The Global Action Plan on the Public Health Response to Dementia was released by the WHO in 2017 and lists Dementia as a Public Health Priority(1).

Burden of Disease

According to WHO estimates, approximately 50 million people have dementia worldwide, with 10 million new diagnoses every year(10) . This accounts for nearly 5% of the global elderly population. Increasing lifespan and decreasing fertility rates have led to a marked rise in the proportion of the elderly in India. It is estimated that by 2050, 19.1% of the Indian population is likely to be elderly. There has been a steady increase in the burden of Non Communicable Diseases such as Diabetes and Hypertension leading to an epidemiological transition from Communicable to Non Communicable Diseases(11–14).

The Global Burden of Disease Study estimated that 2.93 million people in India (in a population of 1.36billion) as compared to 4.03 billion people in the United States (in a population of 322.87 million)(15). The estimate for the USA was based on several large, epidemiological studies; however, the estimate for India was extrapolated from sparse available data. There is a clear death of research in the domain of dementia in India. However the increasing burden on non – communicable disease , especially vascular disease means that the prevalence of dementia is only expected to increase(16).

Of all the states, the south Indian state has the highest proportion of elderly in the country. According to Sample Registration Survey of 2015, 16.5 % of the population in Kerala is estimated to be above the age of 60 as compared to the the national average of 10.1%(17). There have been calls for a need to strengthen Kerala's health system to strive to the ideal of "healthy ageing"(18). This would include the prevention and management of Dementia.

Risk Factors for Dementia

It has been estimated that one third of the global burden of Alzheimer's Disease can be attributed to seven risk factors – low education, midlife hypertension, midlife obesity, diabetes, physical inactivity, smoking and depression (19). Many of these risk factors are shared with Cardiovascular Disease. One commonly used score for the prediction of dementia is the CAIDE Score (20). This score attempted to quantify the risk of dementia in 20 years.

Screening for Dementia

Various instruments have been used for the early screening of dementia in the elderly. The Mini Mental State Examination is one popular tool used for screening (21).It is a short tool that can be completed in less than 10 minutes and assesses cognitive functions in various domains. The tool has been widely translated and used in different settings. However MMSE has several limitations as well including high “floor and ceiling effect”(2). There has also been reported bias when using the MMSE with populations with lower literacy(22). Questions have also been raised of validity when the tool is not in the native language of the person being tested. The Indian Council of Medical Research – Neuro-Cognitive Toolbox was developed to try to standardize dementia testing across linguistic and educational diversity (23) .

Other screening tests commonly used for the screening of Dementia include the Abbreviated Mental Test Score (AMTS)(24) , The Clock Drawing Test (25), The Mini Cog Test (26), 6-CIT Test (27). The 10/66 Dementia tool is a tool specifically developed for populations with lower levels of education and validated in Low and Middle Income countries (LMICs)(28). However, the study found that when the 10/66 tool was used prevalence of dementia in those above 65 years of age was found to be 7.5%. However, when the DSM IV criteria was used this prevalence dropped to 0.9 %. This wide variance emphasizes the need for selection of the right tool and nuanced interpretation of results.

Interventions

The larger question that was being asked of the scientific community was if early screening and detection could help prevent or slow the progression of MCI to Dementia. The Finnish Geriatric Intervention Study to prevent Cognitive Impairment and Disability (FINGER) Study was a proof-of-concept trial on the effectiveness of a 2-year multidomain intervention in at-risk elderly in preventing / slowing dementia. The hypothesis was that simultaneous change in several risk factor (even at a small magnitude) would lead to protection of cognitive function. Primary outcomes were measured using a standardized neuropsychological battery testing for cognition. The study found a significant beneficial effect from the intervention. Another multidomain interventional study done to establish the effectiveness of an intervention was the MAPT Trial (France) (29) and the PreDiva Trial (Netherlands) (30)

Even though there appears to be significant studies demonstrating the effectiveness of such interventions in the western world, adaptations and extrapolations to the Indian context are challenging. Interventions designed in the west cannot be directly implemented. Dietary recommendations such as fish, nuts, fruits and olive oil may not be accessible , affordable or culturally acceptable to the community. While tobacco cessation in the western world largely revolves around smoking cessation, Smokeless Tobacco such as nasal snuff or chewing tobacco may play a more significant role in the Indian context (16).

In this context, we propose to assess the burden of cognitive impairment, develop an intervention package and find the feasibility with respect to the adherence rates.

References

1. Global action plan on the public health response to dementia 2017–2025 [Internet]. [cited 2021 Dec 13]. Available from: https://www.who.int/publications-detail-redirect/9789241513487

2. Sheehan B. Assessment scales in dementia. Ther Adv Neurol Disord. 2012 Nov;5(6):349–58.

3. Hildreth KL, Church S. Evaluation and Management of the Elderly Patient Presenting with Cognitive Complaints. Med Clin North Am. 2015 Mar;99(2):311–35.

4. Duong S, Patel T, Chang F. Dementia. Can Pharm J CPJ. 2017 Feb 7;150(2):118–29.

5. Hildreth KL, Church S. Evaluation and Management of the Elderly Patient Presenting with Cognitive Complaints. Med Clin North Am. 2015 Mar;99(2):311–35.

6. Schmidtke K, Hermeneit S. High rate of conversion to Alzheimer's disease in a cohort of amnestic MCI patients. Int Psychogeriatr. 2008 Feb;20(1):96–108.

7. Jack CR, Shiung MM, Gunter JL, O'Brien PC, Weigand SD, Knopman DS, et al. Comparison of Different MRI Brain Atrophy Rate Measures with Clinical Disease Progression in AD. Neurology. 2004 Feb 24;62(4):591–600.

8. Artero S, Ancelin M-L, Portet F, Dupuy A, Berr C, Dartigues J-F, et al. Risk profiles for mild cognitive impairment and progression to dementia are gender specific. J Neurol Neurosurg Psychiatry. 2008 Sep;79(9):979–84.

9. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. Alzheimers Dement J Alzheimers Assoc. 2013 Jan;9(1):63-75.e2.

10. Dementia [Internet]. [cited 2021 Dec 13]. Available from: https://www.who.int/news-room/fact-sheets/detail/dementia

11. Hunter DJ, Reddy KS. Noncommunicable diseases. N Engl J Med. 2013 Oct 3;369(14):1336–43.

12. Misra A, Tandon N, Ebrahim S, Sattar N, Alam D, Shrivastava U, et al. Diabetes, cardiovascular disease, and chronic kidney disease in South Asia: current status and future directions. BMJ. 2017 Apr 11;357:j1420.

13. Dandona L, Dandona R, Kumar GA, Shukla DK, Paul VK, Balakrishnan K, et al. Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. The Lancet. 2017 Dec 2;390(10111):2437–60.

14. Arokiasamy P. India's escalating burden of non-communicable diseases. Lancet Glob Health. 2018 Dec 1;6(12):e1262–3.

15. Nichols E, Szoeke CEI, Vollset SE, Abbasi N, Abd-Allah F, Abdela J, et al. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019 Jan 1;18(1):88–106.

16. Ravindranath V, Sundarakumar JS. Changing demography and the challenge of dementia in India. Nat Rev Neurol. 2021 Dec;17(12):747–58.

17. Ministry of Statistics and Programme Management , Government of India. Elderly iN 2021.

18. Wong RY. A New Strategic Approach to Successful Aging and Healthy Aging. Geriatrics. 2018 Nov 29;3(4):86.

19. World Health Organization. Dementia: a public health priority [Internet]. World Health Organization; 2012 [cited 2021 Dec 14]. viii, 102 p. Available from: https://apps.who.int/iris/handle/10665/75263

20. Kivipelto M, Ngandu T, Laatikainen T, Winblad B, Soininen H, Tuomilehto J. Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. Lancet Neurol. 2006 Sep;5(9):735–41.

21. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975 Nov;12(3):189–98.

22. Monroe T, Carter M. Using the Folstein Mini Mental State Exam (MMSE) to explore methodological issues in cognitive aging research. Eur J Ageing. 2012 Jun 15;9(3):265–74.

23. Iyer GK, Paplikar A, Alladi S, Dutt A, Sharma M, Mekala S, et al. Standardising Dementia Diagnosis Across Linguistic and Educational Diversity: Study Design of the Indian Council of Medical Research-Neurocognitive Tool Box (ICMR-NCTB). J Int Neuropsychol Soc JINS. 2020 Feb;26(2):172–86.

24. Qureshi, Hodkinson. he Abbreviated Mental Test Score (AMTS). 1974;

25. Brodaty H, Moore CM. The Clock Drawing Test for dementia of the Alzheimer's type: A comparison of three scoring methods in a memory disorders clinic. Int J Geriatr Psychiatry. 1997 Jun;12(6):619–27.

26. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The mini-cog: a cognitive "vital signs" measure for dementia screening in multi-lingual elderly. Int J Geriatr Psychiatry. 2000 Nov;15(11):1021–7.

27. Brooke P, Bullock R. Validation of a 6 item cognitive impairment test with a view to primary care usage. Int J Geriatr Psychiatry. 1999 Nov;14(11):936–40.

28. Llibre Rodriguez JJ, Ferri CP, Acosta D, Guerra M, Huang Y, Jacob KS, et al. Prevalence of dementia in Latin America, India, and China: a population-based cross-sectional survey. Lancet Lond Engl. 2008 Aug 9;372(9637):464–74.

29. Vellas B, Carrie I, Gillette-Guyonnet S, Touchon J, Dantoine T, Dartigues JF, et al. Mapt study: a multidomain approach for preventing alzheimer's disease: design and baseline data. J Prev Alzheimers Dis. 2014 Jun;1(1):13–22.

30. Richard E, Van den Heuvel E, Moll van Charante EP, Achthoven L, Vermeulen M, Bindels PJ, et al. Prevention of dementia by intensive vascular care (PreDIVA): a cluster-randomized trial in progress. Alzheimer Dis Assoc Disord. 2009 Sep;23(3):198–204.

8. Detailed research plan. (give here the design of study, indicating the total number of cases/samples/animals to be studied, the mode of selection of subjects specially in experiments involving human beings, equipments and other materials to be used, methodology/techniques to be employed for evaluating the results including statistical methods any potential to obtain patents etc.)

Study design: Mixed-Methods study

Phase 1: Quantitative design to assess the burden of MCI

Phase 3: Qualitative design to explore the barriers and facilitators for adherence to intervention

Study setting: The study will be conducted in one of the southern districts of Kerala

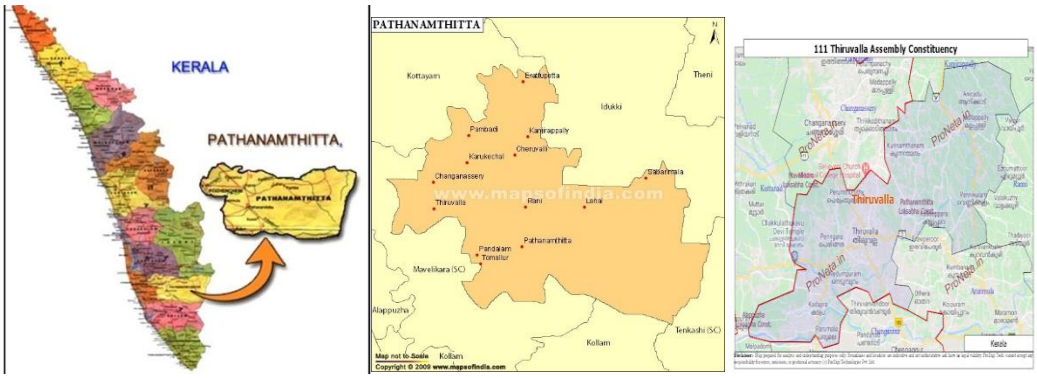

Figure 1: Study setting- Pathanamthitta district and wards

Kerala, one among 26 states in India is situated on the south-west coast, covering approximately one percent of the total area with 2.76% (33 million) of population of the country. Pathanamthitta (southern district) is one among 14 districts in Kerala with a 12, 314,12 population, 89% living in rural area and females constituting 53.1%. Under the three-tier system of panchayat in rural areas, Pathanamthitta has 6 taluks, 53 panchayaths and 70 villages. Tiruvalla taluk is further divided in to 39 rural and 15 urban wards (54 wards in total). Each ward has approximately 1500-2000 people residing in them (1, 2).

Study centre: Believers Church Medical College Hospital, Tiruvalla, Kerala

Study population: Older adults, 50-65 years of age

Study sample: Randomly selected **o**lder adults, in the age group of 50-65 years in Tiruvalla taluk of Pathanamthitta district in Kerala.

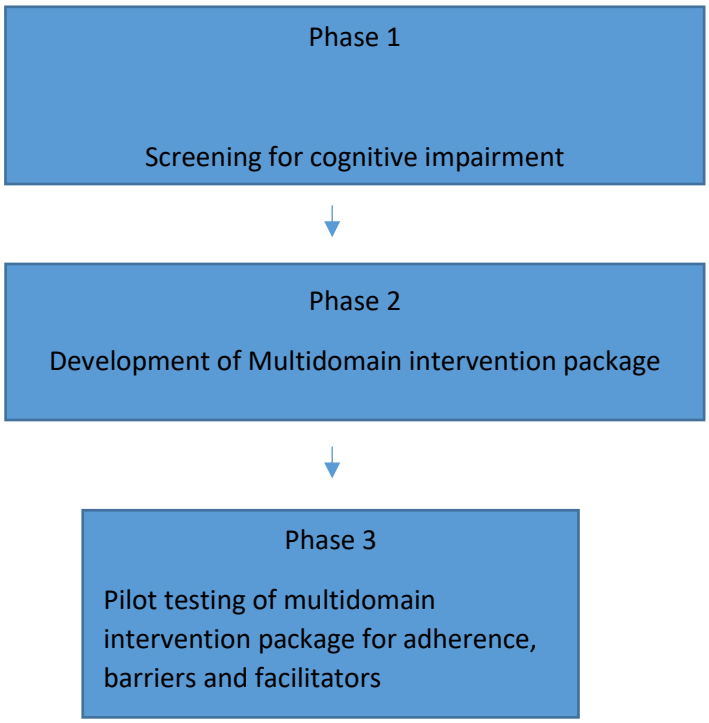

Figure 2: Phases of the study

Figure 1 illustrates the different phases of the study. Phase 1 will be the quantitative component of the study, screening for cognitive impairment. Phase 2 will be the development of the multidomain intervention package and phase 3 pilot testing of the intervention package for

adherence rates. The key barriers and facilitators for adherence will be explored using qualitative method.

Study procedure

Statutory ethical permission and institutional permissions will be obtained as required.

At the time of initiation of the project, the government officials (Health and administration) across the study site will be approached for the required approval, consent and support.

Phase 1

Sample size: The minimum required sample size was calculated as 481 based on an expected prevalence of 26%, alpha error of 5%, absolute precision of 4% (3).

Sampling procedure: Our sampling area consists of 54 wards (39 rural and 15 urban) from Tiruvalla Taluk of Pathanamthitta district. From these wards, 15 rural and 5 (total 20 wards) urban wards will be randomly picked. From each ward, 24 eligible participants will be randomly picked from all the wards, one extra person from the last ward in order to reach the sample size. Identified, consented adults (50- to 65-year-old) will be screened using the study tool to identify those with mild cognitive impairment.

All individuals (50-65yrs) consenting to participate will be included. Those who are unable to respond, critically ill will be excluded.

Outcome measures

Quantitative design: Mild cognitive impairment

Definition of mild cognitive impairment (MCI)

MCI in the study will be assessed using the European Alzheimer's Disease Consortium (4). Participants who meet all the five criteria of this definition will be defined as MCI cases. The criteria used for assessment of mild cognitive impairment has been listed in the table. Based on the cognitive features, MCI will be categorised into single-domain amnestic (only memory domain affected), multiple-domain amnestic (multiple domains affected, including memory), single-domain non-amnestic (single domain other than memory affected) and multiple-domain non-amnestic (multiple domains affected, not including memory) considering the cognitive features. Dementia will be assessed using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria (5).

Global cognition will be assessed using Addenbrooke's Cognitive Examination-III (ACE-III). It is a brief cognitive test that assesses five cognitive domains: attention, memory, verbal fluency, language and visuospatial abilities. The total score is 100 with higher scores indicating better

cognitive functioning. The Indian ACE-III (available in local language)will be used to assess cognitive function (6).

Everyday Abilities Scale for India (EASI) has twelve questions. Respondents will be asked whether the subject could (coded as 0) or could not (coded as 1) generally perform the activity. A higher total score reflects greater overall disability. If the subject could not generally perform the activity, the reason for non-performance was ascertained. Responses clearly indicative of physical or mental problems or both will be so coded. Ambiguous responses (e.g. "old age") will be probed and will be left as such when it will be obvious that no further clarification are there (4).

Table 1: European Alzheimer's Disease Consortium criteria for mild cognitive impairment (3,4)

MCI criteria used	Instrument used	Assessment cut-off adopted in the study
1. Cognitive complaints coming from the patients or their families 2. Reporting of a relative decline in cognitive functioning during the past year by the patient or informant	History from the patient or bystander	
Cognitive disorders as evidenced by clinical evaluation	Malayalam version of Addenbrooke's Cognitive Examination (m-ACE).	Score below the cut-off in at least one of the seven cognitive domains assessed. [One SD below the mean score (of that educational category) was taken as the cut-off for each domain]
Absence of major repercussions on daily life	Everyday Ability Scale for India (EASI)	95th percentile of EASI scores of subjects with no subjective or objective cognitive decline in the study sample was taken as cut-off.
Absence of dementia	Diagnostic and Statistical Manual of Mental Disorders IV criteria	Patients who do not satisfy this criteria

Independent variables

Depression, Activities of daily living, quality of life Sociodemographic factors will include age, gender, education, occupation. Education and occupation will be classified according to Kuppuswamy's classification (16). Information regarding morbidities such as hypertension, diabetes mellitus, dyslipedemia, obesity, abdominal obesity, metabolic syndrome will be collected. Dietary intake will be assessed using food records and 24 hour recall. Physical inactivity is defined as moderate intensity physical activity lasting <150 minutes per week. A current smoker will be defined as a participant who has smoked more than 100 cigarettes throughout their lifetime and smokes more than 1 cigarette each month. Social inactivity will be described as less than two social activities per week (17).

Anthropometric data will include height, weight, hip and waist measurements. Height and weight will be measured by standard procedures. Waist circumference will be taken at the level of the last rib to the nearest 0.1 inch after a normal expiration. Hip circumference will be taken at the maximum extension of the buttocks as viewed from the side. Sphygmomanometer will measure BP to the nearest millimeter of mercury in the left arm, with the individual seated after a 10-min rest and validated with a repeated periodic measure on the same individual. A third reading will be taken if the two readings were 4 mmHg apart when a mean value was determined. BMI and waist-to-hip ratio (WHR) will be calculated, and reference guidelines for Asian Indians will be used for determining obesity (18).

Phase 2: Development of multidomain intervention

An intervention package will be developed after doing a needs assessment in the study area and will be adapted to the study setting. Qualitative methods will be employed.

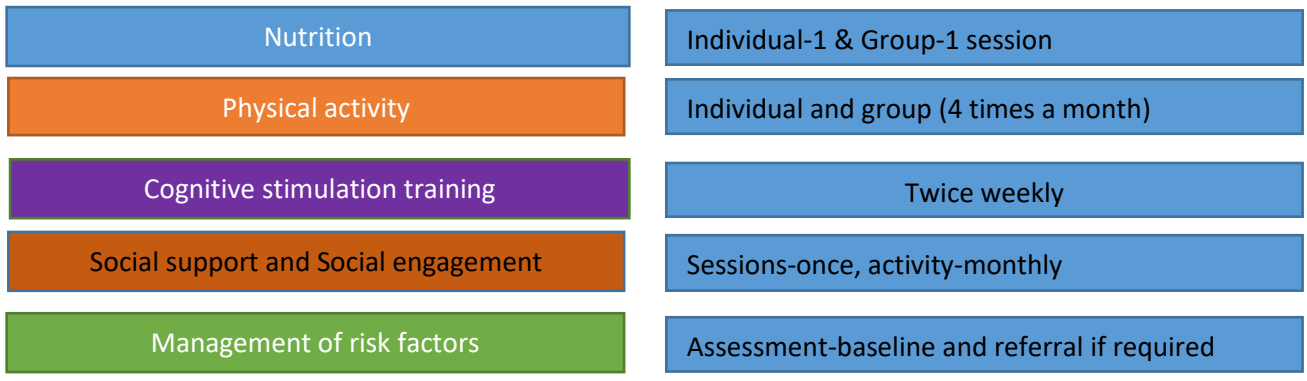

Figure 3: Multidomain intervention package

Nutritional guidance: The intervention package will begin with nutritional guidance based on National Institute of Nutrition guidelines 2020 (7). It will consist individual sessions and group sessions that will be conducted within 30 min up to 1 h over a period of 1month. Furthermore, group counselling sessions will include discussions that includes topics such as healthy plate, importance of macronutrient and fiber, making a healthy menu, and how to read nutrient information. Each session will be carried out interactively through cooking demonstration, cooking competitions, gardening (8). During individual counselling sessions, a dietitian will use A 24-h dietary recall assess diet and macronutrient consumption (carbohydrate, protein, fat, fiber, and total kilocalories) to calculate the current calorie intake and provide personalized advice to participants focusing on the intake of fiber and protein from local low-cost resources such as nutritionally rich drumstick leaves, millets, legumes/lentils, and whole grains. Discussion with family members will be done to plan a customized menu. Participants will be advised to consume a diet with 10–20% of daily energy from proteins, 25–35% daily energy from fat (<10% from saturated plus trans fatty acids, 10–20% from monounsaturated fatty acids, and 5–10% from polyunsaturated fatty acids, 45–55% daily energy from carbohydrates (<10% from refined sugar), 25–35 g/day of dietary fibre, less than 5 g/day of salt, and less than 5% daily energy from alcohol. Energy intake facilitating 5–10% reduction in bodyweight will be recommended only if necessary, after considering BMI, morbidities, age, and diet of the participant (7). Participants will set goals, action plans and self-record their activities in their program diary as a strategy to improve healthy eating (9).

Social support and engagement: Importance of health ageing will be emphasized though awareness sessions by doctors and veterans. Psychologists will conduct sessions to enable the intervention group to have healthy behavior, meaningful cross-age relationships and coping mechanism to improve their quality of life (8). These sessions will be a platform for participants and care givers to express their feelings and barriers to a healthy behaviour. health-related behaviors among older people are largely influenced by social support from family, friends, and neighbors (10). In order to overcome social loneliness, through intergenerational programmes, activities such as visit to anganwadis (government funded day care for children) will be organized to promote interactive sessions between older adults and children. Several group sessions covering all intervention domains is expected to promote social participation among the participants. Moreover, competitions in several domains will be conducted which may support and maintain healthy behaviour.

Physical activity: Training will be managed by study physiotherapists and will consist of individually tailored programmes for progressive muscle strength training (1–3 times per week) and aerobic exercise (2–5 times per week), also covering exercises to improve postural balance. The strength training programme will be adapted to include exercises for the eight main muscle groups (knee extension and flexion, abdomen and back muscles, rotation, upper back and arm muscles, and press bench for lower extremity muscles). Aerobic activities will also be planned considering the preferences of the participants (11).

Cognitive training: Cognitive stimulation therapy is an evidence-based intervention which will be implemented twice weekly for seven weeks following a diagnosis of mild to moderate dementia. Maintenance Cognitive Stimulation Therapy (MCST) requires weekly 1-2 hour sessions for people living with mild to moderate dementia. The participants will involve in meaningful and stimulating activities, which are established as strategies to maintain memory and mental functioning. The Activities include discussions, word games, quizzes, physical activities, creative and musical activities which will in addition help in building friendships (12).

Management of metabolic and vascular risk factors: Participants will be referred to the nearest primary health centre on a new diagnosis or advised to do follow up with their current physician to monitor and continue their ongoing medical interventions for existing medical conditions (8).

Phase 3: Pilot testing of multidomain intervention

The multidomain intervention will be pilot tested in 2 wards, one rural and one urban.

Inclusion for multidomain intervention

- Individuals between 50–65 years old, willing to participate and comply with all the study evaluation and intervention procedures
- Those identified to have mild cognitive impairment

Exclusion criteria for multidomain intervention

- Geriatric Depression Scale ≥ 9
- Dementia
- Disorders that may affect safe involvement in the intervention (eg, malignancy, symptomatic cardiovascular disease, Large vessel stroke in the past two years, History of transient ischemia attack (TIA) or small vessel stroke in the last 6 months, revascularization within 1 year previously, severe loss of vision, hearing, or communicative ability)
- Coincident participation in another intervention trial.
- Recent (< 3 months) bone fracture.
- History of hip fracture, joint replacement, or spinal surgery in the last 6 months

Qualitative design

Checklists will be used to estimate the adherence rates to intervention package.

In-depth interviews will be conducted with participants from urban and rural wards till saturation of information in order to identify the barriers and facilitators for adherence to multidomain intervention.

Data analysis

Quantitative analysis

Baseline characteristics of all the participants will be summarized using mean and standard deviation (SD) or median and interquartile range (IQR) for continuous variables and frequency and percentage for categorical variables. Prevalence and 95% confidence interval will be estimated. Univariate and multivariate analysis will be done to find the factors associated with mild cognitive impairment. All statistical analyses will be performed using SPSS 25 (Armonk, NY, USA) and statistical significance will be set at $p < 0.05$.

Qualitative analysis: Thematic analysis will be done to find the barriers and facilitators towards adherence to intervention

Ethical Issues

Approval from the Institutional Review Board (IRB) will be obtained. Permission will be taken from government administrative and health authorities. Prior to the data collection, written informed consent will be obtained after explaining the objectives and details of the study using a participant information sheet. Privacy and confidentiality will be assured throughout the study. Data will only be available to the investigators and disseminated only as group information. The data will be stored safely in the Department of Community Medicine, BCMCH .

Implications

1. Information on burden of cognitive impairment in the study area which will help us to plan appropriate interventions and policies.

2. A multidomain intervention package appropriate for the setting will be developed.

3. The identification of barriers and facilitators for adherence to the multidomain intervention will help in modifying the intervention and further use it for clinical trial**.**

9.Facilities in terms of equipment, etc, available at the sponsoring institution for the proposed investigation.

Believers Church Medical College Hospital, Tiruvalla, Kerala is a multidisciplinary health care institution with undergraduate, postgraduate and super specialty courses and an independent research centre. Support for all clinical investigations and consultations will be provided by the hospital. Department of Community Medicine of the institution is full-fledged with 2 professors, 2 associate professors and 3 assistant professors including epidemiologist and biostatistician. A separate medical research unit leads the research activities in the institution. The department has 2 peripheral health centres attached to it.

Timeline of the project (one year)

Activities / months	1	2	3	4	5	6	7	8	9	10	11	12
Planning and recruit staff Approvals and permissions Meetings with ASHA												
House visits and Screening for cognitive impairment												
Need assessment for developing intervention												
Development of multidomain intervention Consultation with physician Physiotherapist, psychologist, dietician												
Pilot testing of intervention Implementing intervention Individual and group meetings Follow up by ASHA												
Assessment of adherence In depth interviews												
Analysis and manuscript preparation												

References

1. Government of Kerala, Pathanamthitta. https://pathanamthitta.nic.in/en/demography1.

2. Kerala State Portal. Accessed December 10, 2021. https://kerala.gov.in/subdetail/eyJpdiI6IktcL2hlT0tcL3JMY3NiZ0pONzYwVHU0dz09IiwidmFsdWUiOiI3WWpmcjJQUXpTZVAwM2FZM1g4dk9RPT0iLCJtYWMiOiIwYzJiOTc1MDc0OWEyM2FhYWFiZDZlYTM1YzdjYTM2ZjcyZWM4YTFjM2UwOTJlMTgwMTczMmNjMTQ4ZWFkYmVjIn0=/eyJpdiI6IjJUazk4Z3NOYnFFWVEwNVlNWDFEQUE9PSIsInZhbHVlIjoiMGlZcXRuSE9SM3BQVUw3Q2J4ZnBSQT09IiwibWFjIjoiYTRjYjgzMTA1ODYwOGRmZDY2ZTQxNTcyNjU5MTNlZGIzM2JmY2YyN2YyMDJlODg5NWE0NzM0ZjU0MjQ5Y2ExYiJ9

3. Mohan D, Iype T, Varghese S, Usha A, Mohan M. A cross-sectional study to assess prevalence and factors associated with mild cognitive impairment among older adults in an urban area of Kerala, South India. BMJ Open. 2019 Mar 20;9(3):e025473.

4. Portet F, Ousset PJ, Visser PJ, Frisoni GB, Nobili F, Scheltens P, et al. Mild cognitive impairment (MCI) in medical practice: a critical review of the concept and new diagnostic procedure. Report of the MCI Working Group of the European Consortium on Alzheimer's Disease. Journal of Neurology, Neurosurgery & Psychiatry. 2006 Jun 1;77(6):714–8.

5. American Psychiatric Association. Association, AP Diagnostic and statistical manual of mental disorders. Arlington, VA, US.

6. Mekala, S., Paplikar, A., Mioshi, E., Kaul, S., Divyaraj, G., Coughlan, G., ... & Alladi, S. (2020). Dementia diagnosis in seven languages: the Addenbrooke's Cognitive Examination-III in India. Archives of Clinical Neuropsychology, 35(5), 528-538.

7. ICMR-NIN Expert group on nutrient requirement for Indian, Recommended dietary allowances and estimated average requirements (EAR)-2020 https://www.nin.res.in/RDA_short_Report_2020.html1.

8. Ponvel P, Shahar S, Singh DKA, Ludin AFM, Rajikan R, Rajab NF, et al. Multidomain Intervention for Reversal of Cognitive Frailty, Towards a Personalized Approach (AGELESS Trial): Study Design. J Alzheimers Dis. 82(2):673–87.

9. Thankappan KR, Sathish T, Tapp RJ, Shaw JE, Lotfaliany M, Wolfe R, et al. A peer-support lifestyle intervention for preventing type 2 diabetes in India: A cluster-randomized controlled trial of the Kerala Diabetes Prevention Program. PLOS Medicine. 2018 Jun 6;15(6):e1002575.

10. Thanakwang K, Soonthorndhad K (2011) Mechanisms by which social support networks influence healthy aging among Thai dwelling elderly. *J Aging Health* **23**, 1352- 1378.

11. Kivipelto M, Solomon A, Ahtiluoto S, Ngandu T, Lehtisalo J, Antikainen R, et al. The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER): Study design and progress. Alzheimer's & Dementia. 2013;9(6):657–65.

12. National Institute for Health and Care Excellence. (2018). Dementia: assessment, management and support for people living with dementia and their carers (NICE Guideline No. 97). Retrieved from https://www.nice.org.uk/guidance/ng97

13. Stephen R, Ngandu T, Liu Y, et al. Change in CAIDE Dementia Risk Score and Neuroimaging Biomarkers During a 2-Year Multidomain Lifestyle Randomized Controlled Trial: Results of a Post-Hoc Subgroup Analysis. *The Journals of Gerontology: Series A*. 2021;76(8):1407-1414.

14. Yesavage, J.A., Brink, T.L., Rose, T.L., Lum, O., Huang, V., Adey, M., & Leirer, V.O. (1982). Development and validation of a geriatric depression screening scale: A preliminary report. Journal of Psychiatric Research, 17, 37–49.

15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975 Nov;12(3):189–98.

16. Ware, J., Snow, K., Kosinski, M., & Gendek, B. (1993). RAND 36- Item Health Survey: Manual and Interpretation Guide. Boston, MA: The Health Institute, The New England Medical Center.

17. Wani RT. Socioeconomic status scales-modified Kuppuswamy and Udai Pareekh's scale updated for 2019. J Family Med Prim Care. 2019;8(6):1846-1849.

18. Park HK, Jeong JH, Moon SY, Park YK, Hong CH, Na HR, et al. South Korean Study to Prevent Cognitive Impairment and Protect Brain Health Through Lifestyle Intervention in At-Risk Elderly People: Protocol of a Multicenter, Randomized Controlled Feasibility Trial. J Clin Neurol. 2020 Apr;16(2):292–303.

19. Balagopal P, Kamalamma N, Patel TG, Misra R. A Community-Based Diabetes Prevention and Management Education Program in a Rural Village in India. Diabetes Care. 2008 Jun 1;31(6):1097–104.