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Protocol Title: Reducing Dementia Risk by Identifying and Promoting Social Determinants: A Multi-Site and Multi-Method Study
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Summary
This is a study that has two main aim to test the exploratory effect of environmental influences modifications on practices toward dementia prevention in older adults. Community-dwelling people 60 years or older living in Chile and without dementia will be invited to participate. The study will be conducted with older adults and health professionals participating and working in community day care centers in Chile, respectively. Community day care centers will be randomly assigned to two conditions: 1) control group (n: 4 centers), 2) health professional training and educational material/nudges about dementia risk reduction (n: 4 centers). Older adult participants attending the eight centers will receive a survey about dementia risk reduction attitudes, knowledge, and practices, and cognitive performance at baseline, and 6 months after enrollment. The two groups will be compared in terms of participants' dementia risk reduction attitudes, knowledge, and practices, and cognitive performance after receiving education. In addition, health professionals of the eight centers will be interviewed about their dementia risk reduction attitudes, knowledge, and practices at baseline and after 6 months.

CHOOSE YOUR CATEGORY(IES) OF EXEMPTION FROM FULL IRB REVIEW

(*Category 2*) 45 CFR 46.104(d)(2) Research not regulated by the FDA that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met: (Please indicate which criteria applies)

> ☒(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;
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> ☐(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or
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> ☐(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination.

This exemption category applies to research with minors ONLY if the research involves educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.

1) **Describe the purpose of the study.**
This study has the aim to test the exploratory effect of environmental influences modifications on practices toward dementia prevention in older adults.

2) **Describe the target population.**

Target population in the study: a) community-dwelling people 60 years or older, b) participants of community day care centers of the National Service of Older Adults (SENAMA) in Chile, c) no diagnosis of dementia (according to self-report, medical records, or cognitive evaluation Montreal Cognitive Assessment Method -MOCA- ≥ 21/30 pts.) or no evidence of cognitive impairment that could interfere with their voluntary participation and interview, d) no sensory or speech impairment that could exclude them from participating in an interview, and e) attending the community day care center for the next six months after the baseline interview. We will recruit healthcare professionals as a secondary sample. Secondary sample must be: a) healthcare professionals working directly with older adults in community day care centers of SENAMA; b) being in working functions in the center for the next three months (e.g., no interruption for vacations); and c) availability to participate in four online training sessions in a period of one month.

3) **Describe the location of the study.**

The study will be conducted in Chile, with support of the National Service of Older Adults (SENAMA).

   a. **Does this study include an international location?** ☒ Yes ☐ No
   If yes, specify location: Chile

4) **Describe the procedures that will be used to recruit subjects.**

People will be recruited in the community daycare centers from the National Service of Older Adults in Chile (SENAMA): there exist 108 community centers throughout Chile with capacities from 30 to 90 older people per center. These centers attend to older adults belonging to the 60% most socially vulnerable group of the population and that present mild dependency in daily life activities (difficulties performing two instrumental activities of daily living or one basic activity of daily living) and no dementia. People attend these centers one to two times per week for six months approx. People participate in leisure, physical and social activities guided by a health professional team constituted of physical therapist, occupational therapist, psychologist, and nurse. Participants for this study will be recruited from eight community day care centers. To invite people to participate in our study, we will work with the personnel of the community day care centers to select days for going to the community day care centers in person, introduce ourselves with the older adults' and/or health professional participants, and invite participants to voluntarily participate in our study.

5) **Describe how subjects will provide consent (and/or research authorization) to participate in the study.**

Participants will be invited to participate through in-person contact in the facilities of day care centers. We will check the inclusion criteria through a brief 5-minute interview with the participants. As participation in the study will require only the response to surveys, we will provide a study information document explaining all the study procedures and contact information of the principal investigator to all the participants interested in participating (see submitted form). People meeting inclusion criteria will be invited to provide research authorization to participate in a follow-up survey of 45 minutes survey. After people provide research authorization, the interview will be conducted immediately after accepting participation or ideally a day in the same week in the facilities of the day care center. Day

care centers will provide a private space to facilitate the study details explanation, acceptance or rejection of study participation, and data collection (survey).

In the case of health and social professionals working in the community day care centers, participants will be invited to participate through in-person contact in the facilities of day care centers or by phone call. As participation in the study will require the response to surveys and may imply or not the participation in a four-session health education training program, we will provide an informed consent document explaining all the study procedures and contact information of the principal investigator to all the participants interested in participating (see submitted form). People will be invited to provide research authorization by signing the consent form to participate in a follow-up survey of 30 minutes survey and four-week health education training. After people provide research authorization, the interview will be conducted immediately after accepting participation or ideally a day in the same week in the facilities of the day care center. Day care centers will provide a private space to facilitate the study details explanation, acceptance or rejection of study participation, and data collection (survey).

6) **Describe the procedures that will be used to conduct the research.** ***(NOTE - If using enumerators, include the name of the agency, training provided to individuals at the agency, and the specific role in this research. If using a survey platform, name the platform.)***

To test the exploratory effect of environmental influences modifications on practices toward dementia prevention in older adults.

We will recruit people from eight different community day care centers for older adults in Chile. Eight-day care centers with similar populations and physical characteristics will be selected by the national Director of community day care centers for older adults of the National Service of Older Adults (SENAMA). We will randomly assign the eight centers using a computer-generated system (SPSS software) on a 1:1 basis to four different conditions:

Condition 1 - Usual care (n: 2 centers): people attending the center in the usual care group will receive one to two times per week of participation in group leisure, physical and social activities in the facilities of the community daycare center. These activities are conducted by health professionals' staff as part of the regular intervention in the community daycare centers. Therefore, we will not incorporate education material or any intervention in this group. We will only apply questionnaires and surveys to this group.

Condition 2 - Environmental stimulus (ES) + Health professionals training (HPT) (social and psychical environment modifications – n: 2 centers): Participants in this group will be exposed to both environmental stimuli (educational material/nudges), and health professional training.

Health professionals training (HPT) (social environment modifications – n: 2 centers): In this condition, health professionals (n~5-9 per center) who work with older adults in these community day care centers will participate in an online educational program about dementia risk reduction of four one-hour sessions over four weeks. The program seeks to train professionals about myths and facts about cognition in older adults and causes of dementia (session 1); identification of modifiable/non-modifiable risk factors and social determinants of dementia risk reduction (session 2); interventions for dementia prevention, available resources in the public health network for referral and management of risk factors, and strategies for promoting behavioral change modifications using cognitive and behavioral influences (session 3-4). Throughout all the sessions, participants will be exposed to positive views about aging through the terms and language used by the trainers to portray aging, older adults, and dementia risk reduction, and the use of images, words, and implicit stimulus in the educational material of the training. The content of the training will be based on the WHO Guidelines

'Risk Reduction of Cognitive Decline and Dementia,' and the 'Accelerate Risk Reduction and Promote Cognitive Health' core areas from the Alzheimer's Association. The training will be imparted by two health professionals (one geriatrician and one occupational therapist) with previous experience training Chilean health professionals on topics of dementia and lifestyles in older adults. We will use theoretical content, activities such as case studies, capsules, readings, and surveys. The training and educational material will be developed with a group of designers as part of the research, incorporating opinions and feedback of the research team and health professionals.

Environmental stimulus (ES) (psychical environment modifications – n: 2 centers): This group will be exposed to educational material/nudges (e.g., posters, flyers, information sheets) promoting dementia risk reduction with positive aging framing messaging, located in strategic places of the community day care centers' facilities (e.g., walls, tables, hallways). For example, the printed material will describe exercises for promoting brain health including illustrations of proximal histories of people achieving healthy brain behaviors, and positive aging messaging. The material will be developed with a group of designers and tailored to users' characteristics. The material will be developed as part of the research project.

Randomization and blinding

Once participants from all included centers are assessed for baseline information, senior centers will be randomized to control or experimental centers using simple randomization with computer-generated random numbers (SPSS). The evaluation team will be external to senior centers and was not aware of the campaign, study hypothesis, or assignment of senior centers to groups. All assessments will be conducted in locations and rooms with no exposure to campaign materials.

Sample size calculation

We estimated the sample size considering this is a clustered intervention trial (senior centers). If we consider f= 0.35 as a small-to-medium effect size difference and assume the standard deviation in the population is 0.5, an α of 0.05, power 0.8, and two intervention groups, a total sample size of 81 people is necessary. If we consider cluster sizes of ~30 people per senior center, assuming within-cluster correlation ρ= 0.05, we estimate a total necessary sample size of 180 people (90 per group) to detect a small-to-medium effect size difference (f= 0.31) between control and experimental centers. Accounting for a 15% loss to follow-up, we recruited a sample of 200 older adults (100 people per group).

Data collection

This is a 45 minutes survey that will include: sociodemographic information (e.g., age, gender, area of residence -rural/urban-, marital status, Race/Ethnicity group, current occupation, years of education), perceptions about attributions to memory loss in older adults, dementia risk reduction attitudes, dementia risk reduction knowledge, dementia risk reduction practices, and cognitive performance evaluation (MOCA test) to all the participants enrolled in the eight community day care centers (n: 220 older adults approximately). For this study, all the older adults will be interviewed in person in the facilities of the day care centers by a researcher using the Qualtrics® survey platform. In addition, photographs will be taken with the previous authorization of participants. A unique ID number will be assigned to every participant to protect their identity. The information collected will be stored in a private web-based repository where only the research team will have access through

private password. The survey will be applied at baseline, and week 23 to 25 after baseline. In the groups of older adult participants of centers who received educational material and/or health professionals' training, we will invite older adults to respond to a survey about the acceptability and usefulness of the educational material provided at the end of the follow up period.

In parallel, a survey including sociodemographic information, dementia risk reduction attitudes and knowledge, age beliefs, and dementia risk reduction prescriptions (e.g., referral to cardiovascular care, or referral to vision or audition evaluation) will be applied to health professionals working in the eight community day care centers at baseline and at the end of the educational program. if data allows, we will measure the numbers of referrals made by community day care centers' healthcare professionals to other programs and services available in the public health network related to the management of individual risk factors of dementia (e.g., cardiovascular management, hearing aids, physical rehabilitation, social activities, social services). For this, we will ask health and social professionals working in the community day care centers to register for every participant the type and number of referrals made to other medical and social services in the last three months. Then, health professionals will facilitate a data registry with that information. We will assign the same ID number to every participant to protect their personal information. This data will be handled and kept in Chile, in the facilities of the community day care centers, and will not be moved to U.S.

For the health professionals who received the educational training (HPT), we will add a survey evaluating the acceptability and feasibility of the educational material and training received. We will also take photographs, audio and video recordings of the health professionals participating in the educational training program for analysis and training purposes. We will ask participants for their consent to use this information.

Data management

All the information collected in the study will be stored in a private web-based repository with exclusive access to the research team using a private password. Once all the information is collected, we will compare the two conditions (eight centers) in terms of the older adult's dementia risk reduction practices, attitudes, and knowledge before and after receiving the educational intervention using the data analysis software Python, SAS, and R. The information about older adults' participants' referrals to other services available in the public health network will be analyzed and stored in Chile.

Outcomes

Cognitive healthy behaviors

Cognitive healthy behaviors will be measured with a previously validated composite measure comprised of an average of six z-scores of lifestyles factors related to dementia risk: physical activity, social activity, diet, cardiovascular care, smoking, and alcohol intake. The specific components of the composite measure are listed below.

Physical activity level will be measured using the Rapid Assessment of Physical Activity for Older Adults (RAPA), a 1-to-7 scale classifying people according to the frequency and intensity of physical activity performed in the last month.

Social activity participation will be measured with 5 items from the Social Activities Scale for Community-Dwelling Older People Requiring Support (SASOS), a five-point Likert scale that measures engagement in social activities in community-dwelling older adults.

Adherence to a healthy brain diet will be measured using the Mediterranean diet and the DASH diet (MIND diet) score, a 0-to-15-point scale that measures the frequency of weekly consumption of several healthy and unhealthy foods for cognitive and cardiovascular health.

A cardiovascular care score from 0 to 9 points will be calculated based on questions derived from the Home-Based Cardiac Rehabilitation Self-Management Scale, asking people about blood pressure control, sugar levels, and weight management practices.

Smoking will be measured using adapted questions based on the World Health Organization definition from the National Health Insurance Service of Korea (NHIS), covering the time and frequency of smoking.

Alcohol intake will be measured using the Australian National University-Alzheimer's Disease Risk Index (ANU-ADRI) scale which assesses frequency and type of alcohol intake in a regular week.

Healthcare providers dementia prevention practices
To assess healthcare providers' practices toward dementia prevention, we will ask older adults participants if a healthcare provider has talked with them about ways to prevent AD or dementia (Yes, No/I don't know) and if a healthcare provider have referred them to at least one of six different dementia risk factor management recommendations in the last six months (hypertension, weight or diet, cholesterol, hearing loss, depression, sleeping problems, or memory complaints management).

Older adults' cognition
Participants' cognition will be measured for memory and executive functioning. Memory was measured using the MIS (Memory Impairment Screen) scale that measures delayed free- and cued-recall. Executive functioning will be measured using an alternative trail making test, visuoconstruction skills (cube and clock drawing tests), verbal fluency (number of words in a minute), and abstraction (word-pairing). A composite memory and executive functioning score will be constructed in the same fashion as the primary outcome. In addition, we will compare the number of people before and after the intervention that had a MOCA score ≤ 21 pts., validated cut-off point for mild-to-moderate cognitive impairment in the Chilean population.

Secondary outcomes
Secondary outcomes will be dementia prevention beliefs (10 items, five-point Liker scale, higher score reflecting more positive beliefs), if they knew ways to prevent AD or dementia (Yes, No/I don't know), and if they had asked a healthcare provider about ways to prevent AD or dementia (Yes, No).

Recognition of the campaign material will be measured at the end of the trial by asking all participants about the sources from which they learned something new about AD or dementia prevention in the last few months. Usability and acceptability will be measured by asking healthcare providers if they used the campaign material with patients, measuring satisfaction and usability of campaigns and its components.

Statistical analysis plan
We will compared baseline characteristics between control and experimental centers members using linear and logistic multivariate regressions to account for the senior centers' random effect. To establish a conservative analysis aligned with real-life clinical practice estimates, we will conduct an

intention-to-treat analysis including all the variables and participants regardless of their adherence to the study protocol.

For the continuous outcomes including the dementia prevention behavior score and cognitive score outcomes, treatment effects will be estimated using linear mixed models for the changes from baseline to follow-up (6 months), considering within-participant correlation of the repeated measures and senior centers as random effects.

For binary outcomes, including healthcare providers' practices and secondary outcomes, generalized estimating equations logistic models with robust standard errors clustered on participants and senior centers will be used.

In two sensitivity analyses to assess whether the intervention influences those with greater dementia risk at baseline, first we will assess the primary outcome excluding people in the highest 30% in the cognitive healthy behaviors score at baseline; then, we will include only people with mild-to-moderate cognitive impairment (MOCA score $\leq$ 21 pts.) at baseline. In a third sensitivity analysis, we will adjust for age, sex, education level, number of dementia risk factors, baseline cognition, and time attending the senior center.

Data management will be performed with Python (version 3.9.6) and data analyses were conducted using R (version 4.4.1). All analyses will follow a significance level of <0.05 and 95% confidence interval (CI).

Safety considerations

This study involved no procedures, medication, or direct behavioral manipulation. Participants were passively exposed to dementia prevention educational materials (e.g., posters, brochures, and a website) in their usual senior center setting. As such, there were no anticipated physical, psychological, or social risks to participants.

As part of the study, we will record in the follow-up survey any health events experienced by the participants during the six months of the study. We will discuss with the healthcare providers working in the centers, the person, and the research team events that may be related or not to the intervention.

7) **If subjects' identity can be readily ascertained directly or through identifiers linked to them, could any disclosure of their responses outside the research reasonably place them at risk of criminal or civil liability or be damaging to their financial standing, employability, educational advancement, or reputation? ☐ Yes ☒ No ☐ NA**

8) **If you are from Yale School of Medicine, School of Nursing, or another HIPAA covered entity (such as Psychology clinics) and wish to collect PHI without obtaining written HIPAA authorization, – a HIPAA waiver must be obtained. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data:**

Not applicable to this research.

Informed consent forms and other materials upon request to the principal investigator: Jose Miguel Aravena (jose.aravena@yale.edu).