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CHI study: protocol for an observational cohort study on ageing and mental health in community-dwelling older adults

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Title

CHI study: protocol for an observational cohort study on ageing and mental health in community-dwelling older adults

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ABSTRACT

Introduction: Ageing is associated with a multitude of healthcare issues including dementia, depression, frailty, morbidity associated with chronic disease and, high healthcare high utilization. With Singapore's population projected to age significantly over the next two decade, it has become increasingly important to understand the disease burden and etiological process among older adults. The Community Health and Intergenerational (CHI) study aims to holistically examine aging in place by investigating the mental resilience and vulnerability factors of the aging process in the biological, psychological and social domains within the environment.

Methods and analysis: Using a cohort multiple randomized controlled trial (cmRCT) design, comprehensive health profiles of community-dwelling older adults will be collected. The objective is to recruit 1000 participants (aged 60 to 99 years old) living in the western region of Singapore within a period of three years (2018-2020). Assessments include basic sociodemographic, physical health and function (cardiac, oral, and blood profiles as well as visual function), cognitive functioning, daily functioning, physical fitness, emotional state, free-flowing speech, sleep quality, social connectedness, caregiver burden, intergenerational communication, quality of life, life satisfaction, attitudes to ageing, gratitude and compassion. Results from the cohort will enable future studies to identify at-risk groups and develop interventions to improve the physical and mental health, and quality of life of older adults.

Ethics and dissemination: Approval of the cohort study by the National University of Singapore Institutional Review Board (NUS-IRB Reference code: H-17-047) was obtained on 12 October 2017. Written consent will be obtained from all participants. Findings from the cohort study will be disseminated by publication of peer-reviewed manuscripts, presentations at scientific meetings and conferences with local stakeholders.

Keywords: Ageing, biopsychosocial risk factors, older adults, community cohort

ARTICLE SUMMARY

Strengths and limitations of this study

- This ongoing study will be among the first few cohort studies that comprehensively investigates the health profiles of older adults in Singapore.
- Results of this study may contribute to better understanding of vulnerability and resiliency factors of aging and provide new health-related estimates.
- Use of the cmRCT design will enable future interventions to identify at-risk individuals and test the feasibility of clinical interventions and community programmes.
- Having data collected in only one region of Singapore may affect the generalisability of results; however, the in-depth findings from this study will provide further evidence and identify suitable interventions for older adults.

INTRODUCTION

Background

The World Health Organization (WHO) estimates that the global population of older adults aged 60 years and above will rise from 900 million in 2015 to 2 billion in 2050[1]. In Singapore, the proportion of residents aged above 65 years old nearly doubled from 8.8% in 2009 to 14.4% in 2019 and is projected to be 25% by 2030[2]. This poses as a challenge as ageing is associated with a plethora of healthcare issues and high healthcare utilization. Over the years, researchers have conducted nation-wide studies in Singapore to understand age-related diseases[3, 4] and modifiable factors to promote healthy ageing[5, 6]. Previous research has adopted a multidimensional framework (e.g., WHO's definition of health) to better understand the ageing process and healthcare related needs[7]. Using a similar framework, the Community Health and Intergenerational study adopts Engel's[8] Biopsychosocial Model of health and disease to holistically examine ageing in place by collecting comprehensive health profiles of older adults in Singapore.

To date, there are a few cohort studies that used a holistic framework to observe ageing and health in the community. The Healthy Older People Everyday (HOPE) study (n = 1051) is one such study that sought to assess physical and mental health amongst community-dwelling older adults (aged ≥ 65 years) through basic health screening as well as a health survey[9]. Although the study used objective screening tools (e.g., Mini-Mental State Exam and physical fitness tests), it comprised mostly of self-reported measurement. The authors also suggested the need for more robust and comprehensive tools to be considered such as the Geriatric Depression Scale. The Well-being of the Singapore Elderly (WiSE) study (n = 2565) was another comprehensive study that included face-to-face interviews and physical examination; however it lacked laboratory measurements and did not assess cardiovascular risk[10, 11]. Further research using objective measures to determine physical (e.g., blood

markers or echocardiography) and cognitive (e.g., neurocognitive assessments) health status is needed to complement self-reported data. In terms of oral health, there appears to be an association between dental disease, tooth loss and onset of frailty[12]. It is plausible that this may be mediated through triggering of inflammatory processes by pathogens from periodontal tissues, but there is a lack of longitudinal data to confirm this hypothesis.

There have been a few cross-sectional cohort studies carried out on older adults in the local context, these include the Singapore Longitudinal Ageing Study (SLAS) and the Diet and Healthy Ageing (DaHA) cohort. Conceived in 2003, the SLAS (n = 6183) aimed to provide a community-based cohort of older adults (aged 55 years and above) for subsequent clinical-based interventions[7]. Results from the ongoing study found new prevalence rates[13] and associations[6, 14]. Participants from SLAS were also identified to join subsequent intervention studies such as a computer training RCT that was found to improve cognitive functioning[15]. On the other hand, the DaHA (cohort) study placed emphasis on dietary factors and its association with healthy ageing and reduced risk of age-related medical conditions[5]. For instance, the bioactive compounds found in mushroom and long-term tea consumption was associated with delay in cognitive impairment and reduced depression/anxiety symptoms respectively[5, 16]. The cohort study later invited suitable subjects to participate in subsequent non-pharmacological RCTs that aimed to improve cognitive and psychological health— art therapy and music reminiscence activity[17], mindfulness awareness program[18], and horticultural therapy[19].

Although the aforementioned community studies in Singapore documented valuable findings, many of them did not incorporate other important measures of health the older adult such as detailed oral health examination, cardiovascular assessments, olfactory measures or speech analysis. More observational studies using in-depth and holistic assessments of older adults are needed. This calls for greater integration of health, psychosocial and environmental

resources through close collaborations among clinicians, researchers and community partners.

Research aims

The primary goal is to examine the health profiles of older adults based on the following:

1a) Biological factors such as the physical health condition (e.g., cardiac, oral, blood profiles, vital signs and visual function), physical fitness/ function, medical history and medication use, and nutritional status;

1b) Psychological factors such as the cognition, emotional state (anxiety and depression), sleep quality, attitudes, values, satisfaction with life and quality of life;

1c) Social factors such as social support, intergenerational relationships and the impact on family members.

Once interventions are developed, each study (e.g., feasibility or full-scale trial) will use the cohort data to help identify at-risk groups or normal ageing participants eligible for pharmacological and psychosocial interventions.

METHODS AND ANALYSIS

Study design

The CHI study adopts a cohort multiple randomized controlled trial (cmRCT) design, whereby the cohort provides capacity for multiple randomised controlled trials over time[20]. Using a cmRCT design may increase efficiency in trial recruitment and potentially lower attrition rates[21]. Hence, the cmRCT design is adopted to determine biopsychosocial factors involved in the ageing process and subsequently introduce interventions that can mitigate ageing-related issues such as cognitive and psychological health, diet, medication adherence, speech impairments, oral hygiene. The ongoing CHI study has started data collection on 1st February 2018. It will be conducted in two phases. Phase I comprises of a cross-sectional

cohort study (baseline) detailed in this paper. Participants enrolling for the CHI cohort will be given the option of allowing their data to be used for analyses and in identifying them for future research interventions (i.e., Phase II), or for comparison purposes for intervention trials. Details of the Phase II interventions will be published in full manuscripts separately.

Study sample

This 3-year cohort study targets to recruit 1000 community-dwelling older adults in Singapore. Participants aged between 60 to 99 years of any gender and ethnic group will be eligible for the study. Illiterate participants are also eligible for the study; however, they will be excused from the Cambridge Neuropsychological Test Automated Battery (CANTAB). Assessments will be conducted in languages such as English, Mandarin, Malay and Chinese dialect (e.g., Hokkien), depending on the assessors' preference.

In collaboration with Presbyterian Community Services (PCS), the main study site will be held at a local seniors activity centre, Hannah Seniors Activity Centre (HSAC), located within the community in the central west district of Singapore. Confirmation of the sociodemographic data of over 3000 older adults in the Anak Bukit area (i.e., a subzone of the central west district) has been verified through Department of Statistics Singapore[22]. Data from PCS also indicated an estimate of 1000 older adults within a 20-block radius from Toh Yi drive. Recruitment is restricted to the central west district of Singapore that may affect generalisability of results. However, the in-depth findings from this study will provide further evidence and identify suitable interventions for older adults.

Patient and public involvement

Participants in this study were not involved in the development of the study design or objectives. The research design and objectives were developed by the investigators of this study and underwent review by a board of academic advisors affiliated to National University of Singapore Mind-Science Centre (NUS MSC). PCS, a community partner, provided the

study site (e.g., quiet rooms in HSAC). In addition, information about the study procedures and recruitment process were shared with staff from PCS prior to data collection.

Procedure

Older adults will be recruited from residences via door-to-door visits by research nurses and research assistants in the Toh Yi, Anak Bukit area and other areas within the district encompassed by a 10km radius from the HSAC. Eligible individuals will also be recruited onsite from HSAC, community centres, resident corners, senior activity centres and residences within the recruitment area – advertisement flyers will be made available for visitors to the respective centres and word of mouth. Interested individuals will be invited to HSAC at their convenience. Non-ambulant individuals who are keen to participate in the study will have their consent taken in their own homes. A member of the research team will explain the study in detail and time will be given for individual to consider before written consent is given.

Participants will be invited to complete up to six separate visits, estimating to a total of 11 hours; they will be scheduled to complete five visits to HSAC and one to NUS Cardiovascular Imaging Core Lab (CICL) at their earliest convenience. Data will be obtained through semi-structured face-to-face interviews (visit 1 and 2), neuropsychological assessments (visit 3 and 4), biological specimen collection (blood and dental samples), dental examination (visit 5), and cardiovascular examination (visit 6), details of which are given in Table 1. Non-ambulant participants will be assessed in their own homes and will only have to complete visit 1 to 3. Trained research assistants and certified nurses will conduct visit 1 to 4 and blood venepuncture, while certified dentists and medical sonographers will conduct visits 5 and 6 respectively. Moreover, experts will provide referral letters to participants for further follow-up should incidental findings arise from assessments such as neuropsychological tests,

depression/anxiety screening, oral health examination, blood tests and/or cardiovascular examination.

Outcome measures

A wide range of data, spanning across several health domains, will be collected. Instruments and physical examinations were introduced by the investigators of this study that comprises of experts in psychiatry, cardiology, dentistry, otolaryngology, sociology, pharmacy, family and population research, linguistics, public health, orthopaedics, and ophthalmology. Table 1 provides an overview of the measures to be collected.

Table 1 Outcome measures

Variables	Instrument/scale	Visit
Socio-demographic		
Age	Age will be measured based on the date of birth stated on the National Registration Identification Card (NRIC) or Long-term visit pass.	1
Sex	Male or female stated on NRIC or visit pass.	1
Language Use	Measured by language of interview, languages participant is able to speak, and common language spoken at home.	1
Marital Status	Self-report of marital status; single, married, widowed or divorced/separated.	1
Ethnicity	Ethnicity as recorded in NRIC or self-report; categorised as Chinese, Malay, Indian or others.	1
Religion	Religion will be classified as Taoism/Buddhism, Christianity/Catholicism, Hinduism, Islam, or others. Participants will also be asked, "How important is your religion to you?" via a 4-point Likert scale response.	1
Citizenship	Based on citizenship recorded on NRIC or visit pass, which will be categorized into Singapore citizen, Permanent Resident (PR) or others. For PRs, previous citizenship and year of PR status will be collected.	1
Education	Measured by years of formal schooling and highest education level, which will be categorized as none, primary, secondary/technical education, pre-university/polytechnic, or university.	1
Employment status	Determined by self-reported employment status; categorised as retired, housewife, full-time, part-time, or self-employed. Participants will also be asked to state their previous and current occupation.	1
Living arrangement and family support	Questions from previous surveys centred on older adults and their children's living arrangement, and sources of support and care will be used[24].	1
Financial status	Financial status is determined by housing type, current gross personal monthly income, current gross household income, insurance coverage, and expenditure on medical expenses per month. Participants will also be asked if their income/allowances are adequate to cover their monthly expenses, reasons if it is	1

Variables	Instrument/scale	Visit
	not adequate and if their financial resources are adequate to meet their future needs. Various sources of support will be recorded, such as private savings, borrowing money from relatives/friends etc.	
Spouse demographic	Spouse's age, ethnicity, education, citizenship, and employment will also be collected.	1
Medical history	The medical history of participants and their family will be collected using the self-reported questionnaire from the Diet and Health Aging study[5]. Medical conditions such as hypertension, stroke, diabetes, hyperlipidaemia, cancer, cataracts, mental health illnesses and many more will be recorded.	1
Biological factors		
Body measures	Blood pressure, pulse rate, height, weight, neck circumference and abdominal girth will be measured. In addition, body mass index (BMI) will be calculated.	1
Visual function	Visual acuity will be measured using a standardized Tumbling E distance vision chart of 3-meteres[25], while colour blindness is measured using the Ishihara 38-plate colour test[26]. To measure visual functioning, five items were selected from the original 25-item National Eye Institute Visual Functioning Questionnaire[27]. One item was selected from five subscales on general vision, near vision, distance vision, social function and driving, and will be scored on a 3-point Likert scale (good, acceptable or poor).	1
Speech	Participants will be asked to speak freely about their life story and experiences for 15 to 20 minutes using a language of their choice. Their speech will be recorded using an audio recorder and they will be instructed to remain anonymous in the recording.	1
Functional status	Barthel's Index of Activities of Daily Living[28] and Lawton's[29] Instrumental Activities of Daily Living scale (iADL) are common scales used in Singapore to assess older adults' ability to perform basic and complex self-care tasks independently. This study adapts five items (bowels, bladder, grooming, toilet use and feeding) from the 10-item Barthel Index and the original 8-item iADL scale. Both scales are scored on a 3-point ordinal scale (independent, some help required or dependent).	1
Medication use/adherence	Participants will be asked to bring along any prescribed medication, supplements and/or over-the-counter medication. Name of medication, dosage form, dosing instructions, frequency of use, duration used, purpose and source of medication will be recorded.	1
Physical fitness	Physical fitness is determined by results from five tasks; hand grip test using a calibrated Jamar dynamometer[30], modified functional reach test[31], 30-seconds chair stand[32], timed up and go[33, 34], 6 meters fast gait speed test[35]. These tests will assess grip strength, balance, lower extremity strength, functional mobility and gait speed respectively. In addition, levels of physical activity will be measured by the 4-item international physical activity (short form) questionnaire[36].	2

Variables	Instrument/scale	Visit
Blood profile*	23.5ml of blood will be obtained through venepuncture performed by certified nurses. 13.5ml of blood will be tested for general health markers; alkaline phosphatase, alanine aminotransferase, phosphate, calcium, uric acid, full blood count panel without erythrocyte sedimentation rate, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, fasting blood glucose, glycated haemoglobin A1c, free thyroxine (T4), thyroid-stimulating hormone, thyroid peroxidase antibody, intact parathyroid hormone, 25-hydroxyvitamin D, sodium, potassium, chloride, urea, creatinine, estimated glomerular filtration rate. The remaining 10ml of blood will be used for near-term assays of candidate cardiovascular biomarkers that includes (but not limited to) N-terminal-proB- type natriuretic peptide, high-sensitivity cardiac troponin, growth differentiation factor-15 and ST2 protein.	2/3/4/5
Olfactory status	Using a recently developed olfactory test kit, participants will be tasked to smell nine locally developed scents (almond, lemon, orange, pineapple, banana, coconut, rose, cinnamon and mushroom). They will then be asked to identify the scent and rate the intensity and pleasantness of the scent scored on a 5-point likert scale.	2/3/4/5
Oral health status	Participants will receive intra-oral and extra-oral clinical examinations by three calibrated dentists. Similar to previous studies, the oral health examination includes examining and recording of oral mucosa status, periodontal status, tooth (coronal and root) status and treatment needs, tooth wear, occlusal contacts, and prosthodontic status[37-39]. In addition, oral samples (dental plaque and saliva) will be collected for DNA extraction and microbiome analyses. Specifically, supragingival plaque will be removed with sterile cotton pellets and dried prior to sampling of subgingival plaque. Full mouth subgingival plaque will be removed using a sterile curette and resuspended in a microcentrifuge tube containing 500 µl of sterile saline. Participants will then be asked to chew a paraffin gum to transfer bacteria from teeth to saliva and subsequently drool intro a receptacle.	5
Nutritional status	The widely used Mini Nutritional Assessment – Short Form (MNA-SF) will be used to assess nutritional status[13, 40]. It consists of six items; appetite, weight loss, mobility, psychological stress or current illness, BMI and neuropsychological problems. Total weighted screening scores ranges from 0 to 14 points.	5
Cardiovascular status	Six non-invasive cardiovascular procedures will be performed; (1) echocardiography (ultrasound scanning) will be conducted to assess the morphology and function of the heart using a scanning transducer lightly applied to the chest, (2) echocardiography of the carotid and femoral arteries, and modified applanation tonometry at the radial artery of the wrist will also be used to determine carotid intima-media thickness and arterial stiffness properties, (3) skin autofluorescence scanning to detect dermal deposition of Advanced Glycation End Products (AGEs) will be measured by an AGE Reader SU device, which requires participants to place their forearm on the reader, (4)	6

Variables	Instrument/scale	Visit
	echocardiography of flow-mediated dilation (FMD) at the brachial artery will be conducted using a 10MHz linear array probe, steadied by a stereotactic clamp to image the brachial artery and position electronic tracking gates at the media-adventitia interface of opposing arterial walls as well as the use of the E20 rapid cuff inflator, to induce reactive hyperaemia by inflation of a pneumatic cuff placed around the participant's proximal forearm to a pressure of 50 mmHg above the systolic blood pressure for 5 minutes, (5) electrocardiogram (ECG) will also be performed so as to record the electrical activity of the participant's heart at resting state using electrodes with adhesive pads attached to the chest, arms and legs, and lastly (6) ambulatory ECG (Holter) monitoring will be conducted to detect arrhythmias, including atrial fibrillation, assess heart rate variability and heart rate complexity using a portable monitor attached by wires to electrode patches placed on the chest for 24 hours. During the 24-hour monitoring, participants will also be tasked to fill in a diary sheet (i.e., type of activities and heart-related symptoms experienced) as accurately as possible. These cardiovascular procedures will adhere to strict local standards and reports will be reviewed by cardiologists.	
Psychological factors		
Psychiatric symptoms	Depressive and anxiety symptoms are assessed using the 15-item Geriatric Depression Scale[41], and the 20-item Geriatric Anxiety Inventory[42] respectively. Both scales have been validated in the local context and shown good psychometric properties in older adult populations[43, 44].	1
Lifestyle factors	Lifestyle factors is assessed by a previously developed lifestyle questionnaire[45]. In addition, participants will be asked about the type of leisure activity that have participated before and number of hours spent per week participating in; mindfulness, art work, exercise, social activities, musical activities or others (same as previous work[46]).	1
Perceived oral health and QoL	A self-developed 15-item Oral Health Attitudes Questionnaire[47] assesses attitudes to oral health, while oral health related quality of life will be assessed using the short form Oral Health Impact Profile – 14 items[48].	1
Subjective cognitive decline (SCD)	The 20-item Perceived Deficits Questionnaire (PDQ) is part of the Multiple Sclerosis Quality of Life Inventory that assesses self-perceived cognitive decline[49]. PDQ has also been used to measure SCD in a Singapore cohort[50].	1
Cognitive functioning	Measures of cognitive functioning include: (1) A locally modified and validated 30-point Mini-Mental State Examination (MMSE) with stratified education and ethnic cut-offs to assess global cognitive function[51, 52]; (2) the 5-point Clinical Dementia Rating (CDR;[53]) to measure subjective and/or informant complaints as well as cognitive and functional performance; (3) a neurocognitive battery assessing verbal and learning memory (Rey Auditory Verbal Learning Test) attention and working memory (Digit Span Forward and Backward Task), divided attention and sequencing (Colour Trails Test), visual-spatial abilities (Wechsler's Block Design) and verbal fluency (Semantic Verbal Fluency – Animals);	3

Variables	Instrument/scale	Visit
	(4) Eight computerized language-independent cognitive tests of the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge, UK[54]) will be administered: Motor Screening Task (sensorimotor), Paired Associates Learning – 12 patterns (visual memory and learning), Verbal Recognition Memory – immediate and delayed recall (verbal memory), Stockings of Cambridge (spatial planning), Emotion Recognition Test – short (social cognition), Rapid Information Visual Processing – 3 targets (sustained attention), Spatial Span – forward and reverse (visuospatial working memory), and Multitasking Test (executive function). Participants will be diagnosed as either cognitively normal, having mild cognitive impairment or dementia by a 3-member expert panel of psychiatrists who will review scores from the MMSE, CDR and neurocognitive battery based on Petersen's[55] mild cognitive impairment criteria and the DSM-V for dementia criteria[56].	4**
Caregiver burden	The widely used 22-item Zarit Burden Interview[57] will measure caregiver burden and will be conducted through a phone interview with participants' caregiver/family member.	3
Quality of life	Quality of life (QoL) will be determined by the 13-item World Health Organization QoL assessment for older adults[58] scored on a 5-point Likert scale, with higher scores indicating higher QoL.	2
Sleep quality	Sleep quality will be assessed by locally validated 19-item Pittsburgh Sleep Quality Index[59, 60]. Used in both clinical and general population, the STOP-Bang questionnaire[61] will also be used to screen for obstructive sleep apnea.	2
Life satisfaction	Life satisfaction will be measured by a 5-item Satisfaction With Life Scale[62] scored on a 7-point Likert response scale as well as extended questions on nine different areas of life such as health, financial situation, community elderly service, government elderly policy, friendships, spouse, children, leisure activities and current work status.	2
Perceived health state	Perceived health state will be assessed by EQ-5D-3L that was developed by EuroQol Group[63]; (1) the EQ-5D descriptive system that measures five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and (2) the EQ visual analogue scale where participants indicate their health state ranging from 0 (worse imaginable health) to 100 (best imaginable health).	2
Attitudes to ageing	The 24-item Attitudes to Ageing Questionnaire[64] will be used to measure older adults' attitudes to the process of ageing using a 5-point Likert scale.	2
Gratitude	Dispositional gratitude will be determined by the 6-item Gratitude Questionnaire[65] scored on a 7-point Likert scale (strongly disagree to strongly agree).	2
Compassion	The 10-item Compassion Scale[66] is used to measure five dimensions of compassion: generosity, hospitality, objectivity, sensitivity and tolerance across social networks and relationships using a 1 (none) to 7 (all) response scale.	2
Social factors		

Variables	Instrument/scale	Visit
Parenting style	A self-developed 13-item Personal and Parents' Parenting Style Scale[67] is used to examine the relationship between participants' parenting strategies and how they were parented as children, scored on a 1 (Never) to 5 (Always) scale.	1
Social connectedness	Social connectedness/isolation will be measured by the 6-item Friendship Scale[68] scored on a 5-point Likert Scale, whereby higher scores indicate higher level of connectedness ($\alpha = 0.83$).	2
Perceived Social support	Perceived social support is determined by a self-developed scale that consists of an open-ended question ("How many close friends/relatives do you have?") and 7 items on perceived social support scored on a 5-point Likert scale.	2
Intergenerational communication	The Perceptions of Intergenerational Communication Scale[69] will be used to measure perceived communication between generations scored on a 7-point Likert-type scale, ranging from 1 (strongly disagree) to 7 (strongly agree).	2

* Venipuncture procedure will be scheduled in conjunction with another visit
** Available to the first 300 literate participants only as the test was added in at a later stage of the study.

Data storage and analysis

Participants will be assigned a subject identification number (SID). Their corresponding data including questionnaire responses, audio recording, assessment records and biological samples will be kept anonymous and coded with the same assigned SID for consistency. All hardcopy data responses will be checked by two personnel to minimize missing data. Hardcopy coded data collected will be entered and stored on a standalone computer and softcopy data will be password protected. Furthermore, all hardcopy data will be stored in a designated secured and locked space, accessible only to selected personnel.

Demographic variables will be presented as descriptive summaries such as mean±SD, median, percentages for continuous variables and proportions for categorical variables. Univariate and multivariate linear regression analyses will be conducted to determine associations between continuous outcomes; logistic regressions will be used for dichotomous outcomes. Cox regression models/survival analyses will be conducted for predicting time to events where applicable. Prediction modelling will be attempted utilizing the new covariates under study (e.g., attitudes to ageing and intergenerational influence). P values of <0.05 will be considered statistically significant.

ETHICS AND DISSEMINATION

The CHI study will be conducted in accordance with the principles of Good Clinical Practice and adhere to the Human Biomedical Research Act which provides a legal framework for researchers in Singapore to conduct research and the use of human tissue[23].

Written informed consent will be obtained from all participants after objectives and procedures of the research are fully explained to them by a member of the research team. Participants will also be informed that they can withdraw from the research at any time without giving any reasons. In addition, participants will be given the option of (1) providing their coded human biological materials and data for use in future research, (2) being recorded for the free flow speech segment, (3) being contacted for future intervention studies, incidental findings, changes to the research and follow-up appointment for memory concerns. Participants with dementia will also be asked to invite their legally acceptable representatives to the consent-taking process and data collection. The research team will ascertain that any persons making a decision on behalf of the participant with dementia, acts in the best interest of the participant and takes into account of the participant's wishes and feelings.

Results from the cohort study will be disseminated by publication of peer-reviewed manuscripts, presentations at scientific meetings and/or conferences with local stakeholders. The researchers may also communicate aggregated results to members of the public and clinical professionals through ad hoc meetings/events or mass media releases.

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Contributors

RM, KEH and IR made significant contribution to the conception of the study and implementation of the protocol. FL, PFA, LLH, BZ, WDY, TLL, YKZ, FQ, LJK, LCT and TN participated in the design of the study. RM initiated and conducted the study with a team of researchers (including PFA, LLH & RZYL), and is the primary author of the manuscript. RM, RZYL and YJ prepared the first draft of the manuscript. RZYL, BZ and PFA made revisions to the manuscript. All authors read and approved the final version of the manuscript.

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Competing interests

None.

Ethics approval

This study is approved by National University of Singapore Institutional Review Board, reference number H-17-047.

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1 & 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-2
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls ***Cross-sectional study***—Give the eligibility criteria, and the sources and methods of selection of participants	8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N.A.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10-15 (Table 1)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10-15 (Table 1)
Bias	9	Describe any efforts to address potential sources of bias	N.A.
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N.A.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	15
		(*b*) Describe any methods used to examine subgroups and interactions	15
		(*c*) Explain how missing data were addressed	15
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	15

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	Nil
Results			N.A. (Protocol paper)
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	-
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	-
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	-
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	-
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			N.A. (Protocol paper)
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

CHI study: protocol for an observational cohort study on ageing and mental health in community-dwelling older adults

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Primary Subject	Epidemiology

Heading:	
Secondary Subject Heading:	Public health, Cardiovascular medicine, Dentistry and oral medicine, Geriatric medicine, Mental health
Keywords:	EPIDEMIOLOGY, GERIATRIC MEDICINE, Old age psychiatry < PSYCHIATRY, PUBLIC HEALTH, Cardiac Epidemiology < CARDIOLOGY, MENTAL HEALTH

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Title

CHI study: protocol for an observational cohort study on ageing and mental health in community-dwelling older adults

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ABSTRACT

Introduction: Ageing is associated with a multitude of healthcare issues including dementia, depression, frailty, morbidity associated with chronic disease and, high healthcare utilization. With Singapore's population projected to age significantly over the next two decades, it has become increasingly important to understand the disease burden and etiological process among older adults. The Community Health and Intergenerational (CHI) study aims to holistically examine ageing in place by investigating the resilience and vulnerability factors of the ageing process in the biological, psychological and social domains within the environment.

Methods and analysis: Using a cohort multiple randomized controlled trial (cmRCT) design, comprehensive health profiles of community-dwelling older adults will be collected. The objective is to recruit 1000 participants (aged 60 to 99 years old) living in the western region of Singapore within a period of three years (2018-2020). Assessments include basic sociodemographic, physical health and function (cardiac, oral, and blood profiles, and visual function), cognitive functioning, daily functioning, physical fitness, emotional state, free-flowing speech, sleep quality, social connectedness, caregiver burden, intergenerational communication, quality of life, life satisfaction, attitudes to ageing, and gratitude and compassion. Results from the cohort will enable future studies to identify at-risk groups and develop interventions to improve the physical and mental health, and quality of life of older adults.

Ethics and dissemination: Approval of the cohort study by the National University of Singapore Institutional Review Board (NUS-IRB Reference code: H-17-047) was obtained on 12 October 2017. Written consent will be obtained from all participants. Findings from the cohort study will be disseminated by publication of peer-reviewed manuscripts, presentations at scientific meetings and conferences with local stakeholders.

Keywords: Ageing, biopsychosocial risk factors, older adults, community cohort

ARTICLE SUMMARY

Strengths and limitations of this study

- This ongoing study will be among the first few cohort studies that comprehensively investigates the health profiles of older adults in Singapore.
- Results of this study may contribute to better understanding of vulnerability and resiliency factors of ageing.
- Using a cmRCT design will enable subsequent interventional studies to identify at-risk groups and test the feasibility of clinical interventions and community programmes that aim to improve health outcomes in older adults.
- Due to sample size and cost considerations, the study lacks other in-depth measures; while restricted recruitment limits generalisability of results.
- The extensive range of findings from this study will provide useful health information about older adults that is relevant to clinicians, researchers and policy makers in Singapore.

INTRODUCTION

Background

The World Health Organization (WHO) estimates that the global population of older adults aged 60 years and above will rise from 900 million in 2015 to 2 billion in 2050[1]. In Singapore, the proportion of residents aged above 65 years old nearly doubled from 8.8% in 2009 to 14.4% in 2019 and is projected to be 25% by 2030[2]. This poses a challenge as ageing is associated with a plethora of healthcare issues and high healthcare utilization. Over the years, researchers have conducted nation-wide studies in Singapore to understand age-related diseases[3, 4] and modifiable factors to promote healthy ageing[5, 6]. Previous research has adopted a multidimensional framework (e.g., WHO's definition of health) to better understand the ageing process and healthcare related needs[7]. Using a similar framework, the Community Health and Intergenerational (CHI) study adopts Engel's[8] Biopsychosocial Model of health and disease to holistically examine ageing in place by collecting comprehensive health profiles of older adults in Singapore.

To date, cohort studies are shifting towards using holistic frameworks to observe ageing and health in the community. The Healthy Older People Everyday (HOPE) study (n = 1051) is one such study that sought to assess physical and mental health amongst community-dwelling older adults (aged ≥ 65 years) through basic health screening as well as a health survey[9]. Although the study used objective screening tools (e.g., Mini-Mental State Exam and physical fitness tests), it comprised mostly of self-reported measurement. The authors also suggested the need for more robust and comprehensive tools to be considered such as the Geriatric Depression Scale. Although other larger age-related cohort studies such as the Australian Imaging Biomarkers and Lifestyle study[10] and Alzheimer's Disease Neuroimaging Initiative[11] are notable studies that have collected a wide range of measures (e.g., clinical, cognitive, neuroimaging, lifestyle and genetic data), nonetheless the focus was

largely on the treatment and progression of Alzheimer's Disease (AD). Further research is needed to assess other health-related determinants of older adults in the healthy ageing spectrum such as oral health assessments, cardiovascular investigations, speech analysis and olfactory measures. The Well-being of the Singapore Elderly (WiSE) study (n = 2565) was another comprehensive study that included face-to-face interviews and physical examination; however it lacked laboratory measurements and did not assess cardiovascular and other physical health risks[12, 13]. Research using objective measures to determine physical (e.g., blood markers or echocardiography) and cognitive (e.g., neurocognitive assessments) health status is needed to complement self-reported data. In terms of oral health, there appears to be an association between dental disease, tooth loss and onset of frailty[14]. It is plausible that this may be mediated through triggering of inflammatory processes by pathogens from periodontal tissues, but there is a lack of longitudinal data to confirm this hypothesis.

There have been a few cross-sectional cohort studies carried out on older adults in the local context; these include the Singapore Longitudinal Ageing Study (SLAS) and the Diet and Healthy Ageing (DaHA) cohort. Conceived in 2003, the SLAS (n = 6183) aimed to provide a community-based cohort of older adults (aged 55 years and above) for subsequent clinical-based interventions[7]. Results from the ongoing study found new prevalence rates[15] and associations[6, 16]. Participants from SLAS were also identified to join subsequent intervention studies such as a computer training RCT that was found to improve cognitive functioning[17]. On the other hand, the DaHA (cohort) study placed emphasis on dietary factors and its association with healthy ageing and reduced risk of age-related medical conditions[5]. For instance, the bioactive compounds found in mushroom and long-term tea consumption was associated with delay in cognitive impairment and reduced depression/anxiety symptoms respectively[5, 18]. The cohort study later invited suitable subjects to participate in subsequent non-pharmacological RCTs that aimed to improve

cognitive and psychological health— art therapy and music reminiscence activity[19], mindfulness awareness program[20], and horticultural therapy[21].

Although the aforementioned studies on older adults documented valuable findings, some of them mainly focused on the treatment and progression of AD, while most studies did not incorporate other important measures of health such as detailed oral health examination, cardiovascular assessments and biomarkers, olfactory measures or speech analysis. More observational studies using in-depth and culturally relevant assessments of older adults in the healthy ageing spectrum are needed. This calls for greater integration of health, psychosocial and environmental resources through close collaborations among clinicians, researchers and community partners. Thus, the CHI study aims to holistically investigate factors associated to healthy ageing in a community setting using a broad range of health-related measures.

Research aims

The primary goal is to examine the health profiles of older adults and form meaningful associations based on the following:

1a) Biological factors such as the physical health condition (e.g., cardiac, oral, blood profiles, vital signs and visual function), physical fitness/ function, medical history and medication use, and nutritional status;

1b) Psychological factors such as the cognition, emotional state (anxiety and depression symptoms), sleep quality, attitudes, values, satisfaction with life and quality of life;

1c) Social factors such as social support, intergenerational relationships and the impact on family members.

Secondly, this study also acts as a recruitment platform for future interventional studies (e.g., feasibility or full-scale trial) to identify at-risk groups or normal ageing participants. The cohort data will enable the development and evaluation of pharmacological and psychosocial interventions targeted at improving health outcomes for older adults. Specifically, data will

be used to identify at-risk groups such as (but not limited to) older adults with subsyndromal depression or anxiety, mild cognitive impairment, medical conditions (e.g., Hyperlipidemia, Diabetes, Hypertension), at-risk of cardiovascular diseases, oral diseases, speech impairment, or sleep apnea. Other future sub-studies will also explore culturally relevant psychosocial factors related to healthy ageing such as intergenerational communication, attitudes to ageing, social networks, satisfaction with life and many more.

METHODS AND ANALYSIS

Study design

The CHI study adopts a cohort multiple randomized controlled trial (cmRCT) design, whereby the cohort provides capacity for multiple randomised controlled trials over time[22]. Using a cmRCT design may increase efficiency in trial recruitment and potentially lower attrition rates[23]. Hence, the cmRCT design is adopted to determine biopsychosocial factors involved in the ageing process and subsequently introduce interventions that can mitigate ageing-related issues such as cognitive and psychological health, diet, medication adherence, speech impairments, oral hygiene. The ongoing CHI study has started data collection on 1st February 2018. It will be conducted in two phases. Phase I comprises of a cross-sectional cohort study (baseline) detailed in this paper. Participants enrolling for the CHI cohort will be given the option of allowing their data to be used for analyses and in identifying them for future research interventions (i.e., Phase II), or for comparison purposes for intervention trials. Details of the Phase II interventions will be published in full manuscripts separately.

Study sample

This 3-year cohort study targets to recruit 1000 community-dwelling older adults in Singapore. Participants aged between 60 to 99 years of any gender and ethnic group will be eligible for the study. Illiterate participants are also eligible for the study; however, they will be excused from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Assessments will be conducted in languages such as English, Mandarin, Malay and Chinese dialect (e.g., Hokkien), depending on the subject's preference.

In collaboration with Presbyterian Community Services (PCS), the main study site will be held at a local seniors activity centre, Hannah Seniors Activity Centre (HSAC), located within the community in the central west district of Singapore. Confirmation of the sociodemographic data of over 3000 older adults in the Anak Bukit area (i.e., a subzone of the central west district) has been verified through Department of Statistics Singapore[24]. Data from PCS also indicated an estimate of 1000 older adults within a 20-block radius from the activity centre at Toh Yi. Recruitment is restricted to the central west district of Singapore.

Patient and public involvement

Participants in this study were not involved in the development of the study design or objectives. The research design and objectives were developed by the investigators of this study and underwent review by a board of academic advisors affiliated to National University of Singapore Mind-Science Centre (NUS MSC). PCS, a community partner, provided the study site (e.g., quiet rooms in HSAC). In addition, information about the study procedures and recruitment process were shared with staff from PCS prior to data collection.

Procedure

Older adults will be recruited from residences via door-to-door visits by research nurses and research assistants in the Toh Yi, Anak Bukit area and other areas within the district encompassed by a 10km radius from the HSAC. Eligible individuals will also be recruited onsite from HSAC, community centres, resident corners, senior activity centres and residences within the recruitment area – advertisement flyers will be made available for visitors to the respective centres and word of mouth. Interested individuals will be invited to HSAC at their convenience. Non-ambulant individuals who are keen to participate in the

study will have their consent taken in their own homes. A member of the research team will explain the study in detail and time will be given for individual to consider before written consent is given.

Participants will be invited to complete up to six separate visits, estimating to a total of 11 hours; they will be scheduled to complete five visits to HSAC and one to NUS Cardiovascular Imaging Core Lab (CICL) at their earliest convenience. Data will be obtained through semi-structured face-to-face interviews (visit 1 and 2), neuropsychological assessments (visit 3 and 4), biological specimen collection (blood and dental samples), and dental examination (visit 5), and cardiovascular examination (visit 6), details of which are given in Table 1. Non-ambulant participants will be assessed in their own homes and will only have to complete visit 1 to 3. Trained research assistants and certified nurses will conduct visit 1 to 4 and blood venepuncture, while certified dentists and medical sonographers will conduct visits 5 and 6 respectively. Moreover, experts will provide referral letters to participants for further follow-up should incidental findings arise from assessments such as neuropsychological tests, depression/anxiety screening, oral health examination, blood tests and/or cardiovascular examination.

Outcome measures

A wide range of data, spanning across several health domains, will be collected. Instruments and physical examinations were introduced by the investigators of this study that comprises of experts in psychiatry, cardiology, dentistry, otolaryngology, sociology, pharmacy, family and population research, linguistics, public health, orthopaedics, and ophthalmology. These measures have been validated in the local context[15, 25-42]. It also comprises novel scales that will be used to test for validity in this sample. Table 1 provides an overview of the measures to be collected.

Table 1 Outcome measures

Variables	Instrument/scale	Visit

Variables	Instrument/scale	Visit
Socio-demographic		
Age	Age will be measured based on the date of birth stated on the National Registration Identification Card (NRIC) or Long-term visit pass.	1
Sex	Male or female stated on NRIC or visit pass.	1
Language Use	Measured by language of interview, languages participant is able to speak, and common language spoken at home.	1
Marital Status	Self-report of marital status; single, married, widowed or divorced/separated.	1
Ethnicity	Ethnicity as recorded in NRIC or self-report; categorised as Chinese, Malay, Indian or others.	1
Religion	Religion will be classified as Taoism/Buddhism, Christianity/Catholicism, Hinduism, Islam, or others. Participants will also be asked, "How important is your religion to you?" via a 4-point Likert scale response.	1
Citizenship	Based on citizenship recorded on NRIC or visit pass, which will be categorized into Singapore citizen, Permanent Resident (PR) or others. For PRs, previous citizenship and year of PR status will be collected.	1
Education	Measured by years of formal schooling and highest education level, which will be categorized as none, primary, secondary/technical education, pre-university/polytechnic, or university.	1
Employment status	Determined by self-reported employment status; categorised as retired, housewife, full-time, part-time, or self-employed. Participants will also be asked to state their previous and current occupation.	1
Living arrangement and family support	Questions from previous surveys centred on older adults and their children's living arrangement, and sources of support and care will be used[43].	1
Financial status	Financial status is determined by housing type, current gross personal monthly income, current gross household income, insurance coverage, and expenditure on medical expenses per month. Participants will also be asked if their income/allowances are adequate to cover their monthly expenses, reasons if it is not adequate and if their financial resources are adequate to meet their future needs. Various sources of support will be recorded, such as private savings, borrowing money from relatives/friends etc.	1
Spouse demographic	Spouse's age, ethnicity, education, citizenship, and employment will also be collected.	1
Medical history	The medical history of participants and their family will be collected using the self-reported questionnaire from the Diet and Health Aging study[5]. Medical conditions such as hypertension, stroke, diabetes, hyperlipidaemia, cancer, cataracts, mental health illnesses and many more will be recorded.	1
Biological factors		
Body measures	Blood pressure, pulse rate, height, weight, neck circumference and abdominal girth will be measured. In addition, body mass index (BMI) will be calculated.	1
Visual function	Visual acuity will be measured using a standardized Tumbling E distance vision chart of 3-meteres[44], while colour blindness is measured using the Ishihara 38-	1

Variables	Instrument/scale	Visit
	plate colour test[45]. To measure visual functioning, five items were selected from the original 25-item National Eye Institute Visual Functioning Questionnaire[46]. One item was selected from five subscales on general vision, near vision, distance vision, social function and driving, and will be scored on a 3-point Likert scale (good, acceptable or poor).	
Speech	Participants will be asked to speak freely about their life story and experiences for 15 to 20 minutes using a language of their choice. Their speech will be recorded using an audio recorder and they will be instructed to remain anonymous in the recording.	1
Functional status	Barthel's Index of Activities of Daily Living[47] and Lawton's[48] Instrumental Activities of Daily Living scale (iADL) are common scales used in Singapore to assess older adults' ability to perform basic and complex self-care tasks independently[25]. This study adapts five items (bowels, bladder, grooming, toilet use and feeding) from the 10-item Barthel Index and the original 8-item iADL scale. Both scales are scored on a 3-point ordinal scale (independent, some help required or dependent).	1
Medication use/adherence	Participants will be asked to bring along any prescribed medication, supplements and/or over-the-counter medication. Name of medication, dosage form, dosing instructions, frequency of use, duration used, purpose and source of medication will be recorded.	1
Physical fitness	Physical fitness is determined by results from five tasks; hand grip test using a calibrated Jamar dynamometer[49], modified functional reach test[50], 30-seconds chair stand[51], timed up and go[52, 53], 6 meters fast gait speed test[54]. These tests will assess grip strength, balance, lower extremity strength, functional mobility and gait speed respectively. In addition, levels of physical activity will be measured by the 4-item international physical activity (short form) questionnaire[26, 55].	2
Blood profile*	23.5ml of blood will be obtained through venepuncture performed by certified nurses. 13.5ml of blood will be tested for general health markers; alkaline phosphatase, alanine aminotransferase, phosphate, calcium, uric acid, full blood count panel without erythrocyte sedimentation rate, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, fasting blood glucose, glycated haemoglobin A1c, free thyroxine (T4), thyroid-stimulating hormone, thyroid peroxidase antibody, intact parathyroid hormone, 25-hydroxyvitamin D, sodium, potassium, chloride, urea, creatinine, estimated glomerular filtration rate. The remaining 10ml of blood will be used for near-term assays of candidate cardiovascular biomarkers that includes (but not limited to) N-terminal-proB- type natriuretic peptide, high-sensitivity cardiac troponin, growth differentiation factor-15 and ST2 protein.	2/3/4/5
Olfactory status	Using a recently developed olfactory test kit, participants will be tasked to smell nine locally developed scents (almond, lemon, orange, pineapple, banana, coconut, rose, cinnamon and mushroom). They will then be asked to identify the	2/3/4/5

Variables	Instrument/scale	Visit
	scent and rate the intensity and pleasantness of the scent scored on a 5-point likert scale.	
Oral health status	Participants will receive intra-oral and extra-oral clinical examinations by three calibrated dentists. Similar to previous studies, the oral health examination includes examining and recording of oral mucosa status, periodontal status, tooth (coronal and root) status and treatment needs, tooth wear, occlusal contacts, and prosthodontic status[27, 28, 56]. In addition, oral samples (dental plaque and saliva) will be collected for DNA extraction and microbiome analyses. Specifically, supragingival plaque will be removed with sterile cotton pellets and dried prior to sampling of subgingival plaque. Full mouth subgingival plaque will be removed using a sterile curette and resuspended in a microcentrifuge tube containing 500 µl of sterile saline. Participants will then be asked to chew a paraffin gum to transfer bacteria from teeth to saliva and subsequently drool intro a receptacle.	5
Nutritional status	The widely used Mini Nutritional Assessment – Short Form (MNA-SF) will be used to assess nutritional status[15, 57]. It consists of six items; appetite, weight loss, mobility, psychological stress or current illness, BMI and neuropsychological problems. Total weighted screening scores ranges from 0 to 14 points.	5
Cardiovascular status	Six non-invasive cardiovascular procedures will be performed; (1) echocardiography (ultrasound scanning) will be conducted to assess the morphology and function of the heart using a scanning transducer lightly applied to the chest, (2) echocardiography of the carotid and femoral arteries, and modified applanation tonometry at the radial artery of the wrist will also be used to determine carotid intima-media thickness and arterial stiffness properties, (3) skin autofluorescence scanning to detect dermal deposition of Advanced Glycation End Products (AGEs) will be measured by an AGE Reader SU device, which requires participants to place their forearm on the reader, (4) echocardiography of flow-mediated dilation (FMD) at the brachial artery will be conducted using a 10MHz linear array probe, steadied by a stereotactic clamp to image the brachial artery and position electronic tracking gates at the media-adventitia interface of opposing arterial walls as well as the use of the E20 rapid cuff inflator, to induce reactive hyperaemia by inflation of a pneumatic cuff placed around the participant's proximal forearm to a pressure of 50 mmHg above the systolic blood pressure for 5 minutes, (5) electrocardiogram (ECG) will also be performed so as to record the electrical activity of the participant's heart at resting state using electrodes with adhesive pads attached to the chest, arms and legs, and lastly (6) ambulatory ECG (Holter) monitoring will be conducted to detect arrhythmias, including atrial fibrillation, assess heart rate variability and heart rate complexity using a portable monitor attached by wires to electrode patches placed on the chest for 24 hours. During the 24-hour monitoring, participants will also be tasked to fill in a diary sheet (i.e., type of activities and	6

Variables	Instrument/scale	Visit
	heart-related symptoms experienced) as accurately as possible. These cardiovascular procedures will adhere to strict local standards and reports will be reviewed by cardiologists.	
Psychological factors		
Psychiatric symptoms	Depressive and anxiety symptoms are assessed using the 15-item Geriatric Depression Scale[58], and the 20-item Geriatric Anxiety Inventory[59] respectively. Both scales have been validated in the local context and shown good psychometric properties in older adult populations[29, 30]. Participants with scores above the local cut-off point that signifies risk of depression and anxiety will undergo an assessment by a psychiatrist and referred for follow-up.	1
Lifestyle factors	Lifestyle factors is assessed by a previously developed lifestyle questionnaire[31]. In addition, participants will be asked about the type of leisure activity that have participated before and number of hours spent per week participating in; mindfulness, art work, exercise, social activities, musical activities or others (same as previous work[60]).	1
Perceived oral health and QoL	The 15-item Oral Health Attitudes Questionnaire[32] will assess attitudes to oral health, while oral health related quality of life will be assessed using the short form Oral Health Impact Profile – 14 items[61].	1
Subjective cognitive decline (SCD)	The 20-item Perceived Deficits Questionnaire (PDQ) is part of the Multiple Sclerosis Quality of Life Inventory that assesses self-perceived cognitive decline[62]. PDQ has also been used to measure SCD in a Singapore cohort[33].	1
Cognitive functioning	Measures of cognitive functioning include: (1) A locally modified and validated 30-point Mini-Mental State Examination (MMSE) with stratified education and ethnic cut-offs to assess global cognitive function[34, 35]; (2) the 5-point Clinical Dementia Rating (CDR;[63]) to measure subjective and/or informant complaints as well as cognitive and functional performance; (3) a previously validated neurocognitive battery[36, 60] assessing verbal and learning memory (Rey Auditory Verbal Learning Test) attention and working memory (Digit Span Forward and Backward Task), divided attention and sequencing (Colour Trails Test), visual-spatial abilities (Wechsler's Block Design) and verbal fluency (Semantic Verbal Fluency – Animals);	3
	(4) Eight computerized language-independent cognitive tests of the Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge, UK[64]) will be administered: Motor Screening Task (sensorimotor), Paired Associates Learning – 12 patterns (visual memory and learning), Verbal Recognition Memory – immediate and delayed recall (verbal memory), Stockings of Cambridge (spatial planning), Emotion Recognition Test – short (social cognition), Rapid Information Visual Processing – 3 targets (sustained attention), Spatial Span – forward and reverse (visuospatial working memory), and Multitasking Test (executive function). Participants will be diagnosed as either cognitively normal, having mild cognitive impairment or dementia by a 3-member expert panel of psychiatrists who will review scores from the MMSE,	4**

Variables	Instrument/scale	Visit
	CDR and neurocognitive battery based on Petersen's[65] mild cognitive impairment criteria and the DSM-V for dementia criteria[66].	
Caregiver burden	The widely used 22-item Zarit Burden Interview[37, 67] will measure caregiver burden and will be conducted through a phone interview with participants' caregiver/family member.	3
Quality of life	Quality of life (QoL) will be determined by the 13-item World Health Organization QoL assessment for older adults (WHOQOL-AGE[68]) scored on a 5-point Likert scale, with higher scores indicating higher QoL.	2
Sleep quality	Sleep quality will be assessed by locally validated 19-item Pittsburgh Sleep Quality Index[38, 69]. Used in both clinical and general population, the STOP-Bang questionnaire[39, 70] will also be used to screen for obstructive sleep apnea.	2
Life satisfaction	Life satisfaction will be measured by a 5-item Satisfaction With Life Scale[40, 71] scored on a 7-point Likert response scale as well as extended questions on nine different areas of life such as health, financial situation, community elderly service, government elderly policy, friendships, spouse, children, leisure activities and current work status.	2
Perceived health state	Perceived health state will be assessed by EQ-5D-3L that was developed by EuroQol Group[41, 72]; (1) the EQ-5D descriptive system that measures five dimensions of health (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) and (2) the EQ visual analogue scale where participants indicate their health state ranging from 0 (worse imaginable health) to 100 (best imaginable health).	2
Attitudes to ageing	The 24-item Attitudes to Ageing Questionnaire[73] will be used to measure older adults' attitudes to the ageing process using a 5-point Likert scale.	2
Gratitude	Dispositional gratitude will be determined by the 6-item Gratitude Questionnaire[74] scored on a 7-point Likert scale (strongly disagree to strongly agree).	2
Compassion	The 10-item Compassion Scale[75] is used to measure five dimensions of compassion: generosity, hospitality, objectivity, sensitivity and tolerance across social networks and relationships using a 1 (none) to 7 (all) response scale.	2
Social factors		
Parenting style	A self-developed 13-item Personal and Parents' Parenting Style Scale[42] is used to examine the relationship between participants' parenting strategies and how they were parented as children, scored on a 1 (Never) to 5 (Always) scale.	1
Social connectedness	Social connectedness/isolation will be measured by the 6-item Friendship Scale[21, 76] scored on a 5-point Likert Scale, whereby higher scores indicate higher level of connectedness ($\alpha = 0.83$).	2
Perceived Social support	Perceived social support is determined by a self-developed scale that consists of an open-ended question ("How many close friends/relatives do you have?") and 7 items on perceived social support scored on a 5-point Likert scale.	2
Intergenerational communication	The Perceptions of Intergenerational Communication Scale[77] will be used to measure perceived communication between generations scored on a 7-point	2

Variables	Instrument/scale	Visit
	Likert-type scale, ranging from 1 (strongly disagree) to 7 (strongly agree).	

* Venipuncture procedure will be scheduled in conjunction with another visit
** Available to the first 300 literate participants only as the test was added in at a later stage of the study.

Data storage and analysis

Participants will be assigned a subject identification number (SID). Their corresponding data including questionnaire responses, audio recording, assessment records and biological samples will be kept anonymous and coded with the same assigned SID for consistency. All hardcopy data responses will be checked by two personnel to minimize missing data. Hardcopy coded data collected will be entered and stored on a standalone computer and softcopy data will be password protected. Furthermore, all hardcopy data will be stored in a designated secured and locked space, accessible only to selected personnel.

In general, demographic variables will be presented as descriptive summaries such as mean±SD, median, percentages for continuous variables and proportions for categorical variables. Univariate and multivariate linear regression analyses will be conducted to determine associations between continuous outcomes; logistic regressions will be used for dichotomous outcomes. Specifically, group differences (between cognitive diagnoses or self-reported medical conditions) will be analysed using independent-samples t-tests and analysis of variance (ANOVAs). Relationships between physical and mental health, psychosocial and demographic variables will be analysed using multiple regressions and structural equation models. In addition, mixture models will be used to identify subgroups of participants based on their psychosocial, physical and mental health characteristics. Prediction modelling will also be attempted utilizing the new covariates under study (e.g., attitudes to ageing and intergenerational influence). P values of <0.05 will be considered statistically significant.

ETHICS AND DISSEMINATION

Ethics approval from the National University of Singapore Institutional Review Board (NUS-IRB Reference code: H-17-047) was obtained on 12 October 2017. The CHI study will be conducted in accordance with the principles of Good Clinical Practice and adhere to the Human Biomedical Research Act which provides a legal framework for researchers in Singapore to conduct research and the use of human tissue[78].

Written informed consent will be obtained from all participants after objectives and procedures of the research are fully explained to them by a member of the research team. Participants will also be informed that they can withdraw from the research at any time without giving any reasons. In addition, participants will be given the option of (1) providing their coded human biological materials and data for use in future research, (2) being recorded for the free flow speech segment, (3) being contacted for future intervention studies, incidental findings, changes to the research and follow-up appointment for memory concerns. Participants with dementia will also be asked to invite their legally acceptable representatives to the consent-taking process and data collection. The research team will ascertain that any persons making a decision on behalf of the participant with dementia, acts in the best interest of the participant and takes into account of the participant's wishes and feelings.

Results from the cohort study will be disseminated by publication of peer-reviewed manuscripts, presentations at scientific meetings and/or conferences with local stakeholders. The researchers may also communicate aggregated results to members of the public and clinical professionals through ad hoc meetings/events or mass media releases.

DISCUSSION

Using a cmRCT design, the CHI study seeks to explore vulnerability and resiliency factors associated with ageing with subsequent clinical trials of interventions and community programs that could potentially hold translational significance. The study intends to recruit a thousand older adults and collect a comprehensive set of biological, psychological and social

data. Meaningful associations between outcomes measures found will provide significant information on the physical and mental health of older adults in Singapore. Results will also help identify at-risk groups of older adults and test out subsequent interventions targeted at improving health outcomes. In addition, having an interdisciplinary team of investigators enables the introduction of in-depth and novel health assessments such as oral examination, cardiovascular investigations, olfactory test and speech analysis. Given the limited sample size and cost considerations, this study excluded genetic and other in-depth measures (e.g., neuroimaging and Structured Clinical Interview for DSM-5) which could have added value to findings. Moreover, several ageing cohort studies in Singapore[79-81] have previously collected the above-mentioned data; hence due to limited resources, these measures were excluded in favour of other novel measures. Recruitment of participants in a confined area may also affect generalisability of results. Nevertheless, the CHI cohort is culturally relevant and will provide clinicians, researchers, and policy makers with information on improving the physical and mental health of older adults in Singapore.

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Contributors

RM, KEH and IR made significant contribution to the conception of the study and implementation of the protocol. FL, PFA, LLH, BZ, WDY, TLL, YKZ, FQ, LJK, LCT and TN participated in the design of the study. RM initiated and conducted the study with a team of researchers (including PFA, LLH & RZYL), and is the primary author of the manuscript. RM, RZYL and YJ prepared the first draft of the manuscript. RM, YJ, RZYL, BZ and PFA made revisions to the manuscript. All authors read and approved the final version of the manuscript.

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Competing interests

None.

Ethics approval

This study is approved by National University of Singapore Institutional Review Board, reference number H-17-047.

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1 & 3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1-2
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-9
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls ***Cross-sectional study***—Give the eligibility criteria, and the sources and methods of selection of participants	8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N.A.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	10-15 (Table 1)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	10-15 (Table 1)
Bias	9	Describe any efforts to address potential sources of bias	N.A.
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	N.A.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	15
		(*b*) Describe any methods used to examine subgroups and interactions	15
		(*c*) Explain how missing data were addressed	15
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	15

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	Nil
Results			N.A. (Protocol paper)
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	-
		(b) Give reasons for non-participation at each stage	-
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	-
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	-
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	-
		Cross-sectional study—Report numbers of outcome events or summary measures	-
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	-
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			N.A. (Protocol paper)
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.