**Supplementary Information 1**

**Article title:** Validation of the CogDrisk instrument as predictive of dementia in four general community-dwelling populations

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**PART A:**

**eTable 1: Study characteristics of the validation cohorts, number and age of study participants, follow-up visits, criteria for diagnosing dementia or AD, and number of participants excluded from the analysis.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study cohorts** | **Study Characteristics**  | **Number and age of participants at baseline or year at which the dementia sub-study was initiated** | **Mean age and percentage of males at baseline or year at which the dementia sub study was initiated**  | **Year of baseline examination or year at which the dementia sub study was initiated** | **No of years participants were followed up or year of follow-up** | **Diagnosis of dementia and AD**  |
| The Rush Memory and Aging Project (MAP) | The MAP study is a longitudinal, epidemiological study of common chronic conditions of aging with a focus on decline in cognitive function and risk of AD. For study design and details of dementia diagnosis refer 1,2.  | 2,184 participants aged 60 years and older | 80 years and 26.5% males  | 1997-1998 | 22 years and still ongoing | The diagnosis of dementia and AD were established by experienced physicians using the National Institute of Neurological and Communicative Diseases and Stroke- Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRA) criteria as previously reported 3. |
| The Health and Retirement Study - Aging, Demographics and Memory Study (HRS-ADAMS) | The HRS-ADAMS was a supplementary study in the HRS 4 that conducted in person clinical assessments to gather information on cognitive status. The study design and methods for the ADAMS are described in detail in Langa et al. 5. | 856 participants aged 70 years and above | 81.6 years and 41.5% males |  2001-2003 | Participants followed in 2002-2005, 2006-2008 and 2008-2009.  | Dementia and AD diagnosis was based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R and the DSM-IV), the NINCDS- ADRDA criteria and a consensus expert panel of physicians made the final diagnosis 5,6. |
| The Cardiovascular Health Study Cognition study (CHS-CS) | The CHS-CS was an ancillary study of the main Cardiovascular Health Study. In 1998-1999, CHS-CS was initiated with 3,602 participants who had a cerebral MRI and Modified MMSE in 1991-1994 and were followed up from baseline until dementia onset, loss to follow-up, or administrative censoring in 1999-2000 7. | 3,602 participants aged 65 years and above | 74.8 years and 40.9% were males | 1998-1999 | Cerebral MRI and Modified MMSE were carried out in 1991-1994 and followed up till 1998-1999. | Diagnosis of dementia was ascertained as a progressive or static cognitive deficit of sufficient severity to affect the participants daily activities and a history of normal intellectual function before onset of cognitive abnormalities. Patients were required to have impairments in two cognitive domains, which did not necessarily include memory. Classifications of dementia were based on DSM-IV or NINCDS-ADRDA, the State of California Alzheimer’s disease Diagnostic and Treatment Centres (ADDTC) and NINDS-AIREN criteria as previously reported 7. |
| The Swedish National study on Aging and Care in Kungsholmen (SNAC-K)  | SNAC-K was initiated in 2001-2004 as a continuation of the Kungsholmen Project (KP) that was carried out from 1987-1989 to 1999-2000 8. | 3,363 participants aged 60 years and above.  | 74.7 years and 35.2% were males | 2001-2004 | Follow up performed every 6 years for younger cohorts (60-78 years) and every 3 years for older cohorts (aged 78+ years).  | Dementia was diagnosed according to the DSM-IV criteria, and a 3-step diagnostic procedure was followed. AD was diagnosed following the NINCDS-ADRDA criteria 9-11. |

**PART B:**

**Data harmonization of variables for CogDrisk**

Summary of all the predictors is available below in Table 1. Education was categorised into three categories: less than secondary, upper secondary and vocational training, and tertiary (see Table 2). Height and weight were used for calculating body mass index (BMI), which was further classified into underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (≥30) using the WHO definitions13. Midlife high cholesterol was measured using a cut-off 240 mg/dl or 6.5 mmol/litre of total cholesterol. Self-reported measures of history for diabetes, TBI (with loss of consciousness), atrial fibrillation, and stroke were included. Severe symptoms of insomnia were considered present if a participant indicated that they had at least two of the three symptoms i.e., difficulty falling asleep, waking up several times during the night and trouble staying asleep (see table 16). Depressive symptoms were measured using either Composite International Diagnostic Interview -Short Form (CIDI-SF), Centre for Epidemiological Studies Depression CES-D (10 items) or self-reported question on current depression. For behavioural and lifestyle predictors, a few adjustments were made to the variables included due to the different measurement methods relative to the methods used in the CogDrisk tool. For physical activity, we calculated total MET (metabolic equivalent of task) minutes per week for each study. A total of >500 MET minutes would be equivalent to the international guidelines 14 of 150 minutes of moderate to vigorous physical activity per week which would be used to classify individuals as physically active. For cognitive activity, we computed a summary score by taking the average of time spent in the last year reading books/newspaper, writing including letters and playing board games and puzzles. This was further categorised as ‘low, ‘moderate’ and ‘high’ cognitive activity (refer table 7). Social isolation was measured by subjective loneliness. Low fish intake was calculated if individuals consumed no more than one serving of fish per week. Pesticide exposure was not available in the validation cohorts and could not be included in the CogDrisk-AD tool.

**eTable 1. A summary of risk and protective factors in the five cohorts.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Risk/protective factor**  | **MAP** | **HRS ADAMS** | **CHS-CS** | **SNAC-K** | **CogDrisk** |
| Age and sex | Self-report | Self-report | Self-report | Self-report | Self-report |
| Education  | Number of years categorised to less than secondary, upper secondary and vocational training, tertiary education. | Categorisation of grades/number of years into less than secondary, upper secondary and vocational training, tertiary education. | Categorisation of grades and qualifications into less than secondary, upper secondary and vocational training, tertiary education. | Categorisation of participants last finished level of education into less than secondary, upper secondary and vocational training, tertiary education. | Question created with highest qualification |
| Mid-life Obesity | NA  | NA  | BMI categorised as normal, underweight, overweight, and obese | NA | BMI categorised as normal, underweight, overweight, and obese |
| Mid-life high cholesterol | Total cholesterol (yes, if more than 240 mg/dl) | NA | Total cholesterol (Yes, if high (>240 mg/dl) and no if Borderline high (200-239 mg/dl) or desirable (<200 mg/dl)) | Total cholesterol (Yes, if above 6.5 mmol/litre) | History of high cholesterol |
| Diabetes | History of diabetes  | History of diabetes  | History of diabetes | History of diabetes | History of diabetes  |
| TBI | Self-reported history of head injury with loss of consciousness  | History of a blow to the head, or head trauma that was severe enough to cause loss of consciousness or memory loss for a period of time | Self-reported head injury that resulted in loss of consciousness | Self-reported head trauma with loss of consciousness/syncope | History of head injury  |
| Mid-life hypertension  | History of hypertension  | History of hypertension | Derived variable for hypertension status | History of hypertension | History of hypertension |
| Atrial fibrillation  | NA | NA | History of atrial fibrillation by ECG | History of Atrial fibrillation | History of Atrial fibrillation  |
| Stroke  | History of stroke  | History of stroke | History of stroke | History of stroke | History of stroke  |
| Insomnia | NA | Insomnia based on ICD-9 code  | Questions on trouble falling asleep, waking at night, and waking too early | Questions on trouble falling asleep, waking at night, and waking too early | Insomnia as measured by the Morin Insomnia Severity Index  |
| Depression  | NA | Measured by CIDI-SF, self-administered | CES-D (10 items) | Self-reported question on current depression | CES-D (10 items) 8 was used as cut-off |
| Physical activity | Minnesota Leisure Time Physical Activity Questionnaire: categories were calculated using MET | NA | Kilocalories expended in all physical activity questions.  | Questions on light exercise and moderate to intense exercise in last 12 months to categorise individuals performing low and moderate to intense physical activity.  | International Physical Activity Questionnaire - Short form |
| Cognitive activity | A structured interview focussed on cognitive activities in late life  | NA | NA | A structured interview on engagement in leisure activities.  | Adapted the questions used in the MAP study |
| Social engagement | Social isolation as measured by the modified version of the de Jong-Gierveld Loneliness Scale (cut-off 3.2) | NA | Question on having people to talk to when feeling lonely. | Self-reported question on ever feeling lonely | Loneliness measured by the 3-item UCLA loneliness scale |
| Fish consumption  | Fish (not fried) as categorised in the publication (MIND diet slows cognitive decline with aging) | NA | Fish related questions from the food frequency questionnaire | Fish related questions from the food frequency questionnaire | MIND diet questionnaire which includes fish intake  |
| Smoking | Questions for smoking status (current, former, and never smoking) | History of smoking and current status of smoking | Question on smoking status (current, former, never) | Question on smoking status (current, former, never) | Questions for smoking status (current, former, and never) |

Abbreviations:

NA: Not Available

TBI: Traumatic brain injury

BMI: Body mass index

ECG: Electrocardiogram

CES-D: Centre for epidemiological studies depression

CIDI-SF: Composite international diagnostic interview -short form

MET: Metabolic equivalent of task

UCLA: University of California, Los Angeles

MIND: Mediterranean-DASH intervention for neurodegenerative delay

**eTable 2- Education**

* Effect size measure for CogDrisk – Number of years of education from ANU ADRI (<8 years, 8-11 years, >11 years).
* Decision - We have three categories for education.

1. less than secondary

2. upper secondary and vocational training

3. tertiary education

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study cohorts** | **Less than secondary** | **Upper secondary and vocational training**  | **Tertiary**  | **Others** |
| HRS ADAMS | 1-8. Grades | 9-11. Grades12. High School | 13-15. Some college16. College graduate17. Post College (17+ years) | 99. Not ascertained |
| CHS-CS | 1. Grade 8 or less | 2. Some high school3. High school grad or GED | 4. Tech college or some college5. 4-year college grad6. graduate or professional |  |
| MAP- years of education is based on number of years of regular school.  | 0 to 8 years | 8.1 to 11.0 years | 11.1 to 30.0 years |  |
| SNAC-K | 1. Unfinished primary education2. Primary school (6 years)3. Elementary school/secondary girls’ school | 4. High school/ Upper secondary5.Folk high school/Vocational/Trade school | 6. Education of at least one year after high school graduation 7. College/University degree8. Researcher (licentiate/PhD) | 88. No response9. Don’t know |

**eTable 3- Obesity**

* Effect size measure from systematic review- Underweight, normal, overweight, and obese
* Decision- We will have 4 categories from the body mass index (BMI) measured-
1. Underweight (BMI <18.5)
2. Normal (BMI 18.5-24.9)
3. Overweight and (BMI 25-29.9)
4. Obese (BMI >30)

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Variable** | **Approach** |
| HRS ADAMS | ABWEIGHT ABHEIGHT1 | Calculate BMI by formula and then divide into 4 groups |
| CHS-CS | BMI (interval scale) | Divide into 4 categories  |
|  |  |  |
| MAP | BMI | Divide into 4 categories  |
| SNAC-K | Height and weight  | Calculate BMI and divide into 4 categories. |

**eTable 4- High cholesterol**

* Effect size measure from systematic review- 6.5mmol/litre as a cut off for high cholesterol.
* Decision- Yes or no for high cholesterol.

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Variable** | **Answer option** |
| HRS ADAMS | Lifetime medical history of high cholesterol | Yes or no |
| CHS-CS | Total cholesterol | Yes, if high (>240mg/dl) and No, if Borderline high (200-239mg/dl) or desirable (<200mg/dl) |
| MAP | Total cholesterol | Yes, if more than 240mg/dl |
| SNAC-K | Lab results of total cholesterol  | Yes, if above 6.5mmol/litre |

**eTable 5- Symptoms of depression**

* Effect size measure from systematic review- Score of 20/21 out of 60, CES-D 20 item
* Decision- Yes or no for current depression

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Scale** | **Cut-off/decision** |
| HRS ADAMS | CIDI measured | Diagnostic instrument for depression (we will use the CIDI-SF and the cut-off for major depressive episode will be 5 out of 8 symptoms) |
| CHS-CS | CES-D 10 item scale | Each item is scored 0-3, for a maximum of 30 points. Depression scores were dichotomised at each visit with a cut-off > equal to 8; low (CES-D<8) and high (CES-D> equal to 8). The cut off 8 on the short version of CES-D corresponds to cut off >16 on 20 item CES-D. |
| MAP | CES-D 10 item scale | Yes or no answer options, total score 10. One of their studies have used 4 as a cut-off. |
| SNAC-K  | Depression (current)  | Yes, no, no response, don’t know |

**eTable 6- Physical activity**

* Effect size measure from systematic review**-** We decided to use150 minutes of moderate to vigorous physical activity per week according to international guidelines of physical activity.
* Decision-
1. Calculate total metabolic equivalent of task (MET) minutes per week, if the total time >500MET mins then the individual meets the international guidelines of 150 minutes of moderate to vigorous physical activity per week.

|  |  |
| --- | --- |
| **Study cohorts** | **Definitions** |
| CHS-CS | KCAL- kilocalories expended in all physical activities. Since 1 MET=1kcal/kg/hr we could use the kcals as MET.mins without further calculation.  |
| MAP | Calculate total MET time/week by summing the 5 physical activities along with the other activity question.  |
| SNAC-K | Questions on light exercise and moderate to intense exercise in last 12 months. |

**eTable 7- Cognitive engagement**

* Effect size measure from systematic review- Participating in cognitively stimulating activities. We decided to use the effect size from ANU-ADRI as that is divided by level of participation: lowest, middle and highest. The variable in ANU-ADRI is computed by considering **reading newspapers** (read about special subjects), **write letters** (written business letters, typed papers/letters for self or others, written letters to friend), **museum/edtv** (followed science shows on TV or radio), **attend concerts plays musicals/culture** (gone to/acted in plays, gone to recitals, concerts, musicals), **Reading books** (read literature**), reading magazines** (read scientific books/magazines**), games** (checkers or other board games, cards, puzzles, word games, mind teasers, or any other similar games- including online games)- solved maths/chess puzzles.
* Decision- As across the datasets we do not have all the variables that was used in ANU-ADRI we are computing cognitive activity variable= reading books/newspaper + writing/write letters + board games/puzzles.

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Measures**  | **Answer options** |
| MAP | 1. Read newspaper/magazine/books(last year) |  | Everyday/ almost everyday | Several times a week | Several times a month  | Several times a year | Once a year |
|  | 2. Write letters(last year)  |  | Everyday/ almost everyday | Several times a week | Several times a month  | Several times a year | Once a year |
|  | 3. Play games like checkers, or other board games cards puzzles(last year) |  | Everyday/ almost everyday | Several times a week | Several times a month  | Several times a year | Once a year |
| SNAC-K  | 1. Read newspaper, magazine or journal, read books (last year) | Never, don’t know  |  | Every week |  | Every month | Less frequent |
|  | 3. Play chess, internet or play computer games (last year) | Never, don’t know  |  | Every week |  | Every month | Less frequent |

**eTable 8- Social engagement**

* Effect size measure from systematic review- Measure of loneliness.
* Decision- We decided to measure social isolation by measuring subjective loneliness (yes or no).

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Loneliness questions** | **Answer options** |
| CHS-CS | When I feel lonely there are several people, I can talk to | False | True |
| MAP  | 1. I experience a general sense of emptiness.2. I miss having people around.3. I feel like I don’t have enough friends.4. I often feel abandoned.5. I miss having a really close friend. | 4. Agree5. Strongly agree | 1. strongly disagree2. disagree3. Neutral |
| SNAC-K | Do you ever feel lonely? | 1. Yes, often2. Yes, sometimes | 3. No, rarely4. No, never5. No, never. Wishes to get more time alone8. No response9. Don’t know |

**eTable 9- Fish intake**

* Effect size measure from systematic review- More than one serving of fish per week.
* Decision- fish serving more than once per week

|  |  |  |  |
| --- | --- | --- | --- |
| **Study cohorts** | **Question**  | **More than once per week** | **No, other responses**  |
| CHS-CS | how often have you eaten this food over the past 12 months?-Fried fish/fish sandwich, -tuna fish/tuna salad/tuna casserole, -shellfish,-other fish  |  |  |
| MAP | -tuna sandwich-fish sticks, cakes, or sandwich- fresh fish as a main dish- shrimp, lobster, scallops | Servings per week  |  |
| SNAC-K | -low fat fish (perch, cod, pollock), -oily fish (herring, whitefish, salmon, mackerel, eel),-pickled fish (salted herring, pickled herring), shellfish (shrimp, mussels, crayfish),-fish casserole | 5= 2-3 times per week, 6= 4-6 times per week,7= once a day, 8= 2-3 times per day, 9= 4 times a day or more | 1= never,2= a few times a year, 3= 1-3 times per month4= once a week, 88= no response0= several options checked  |

**eTable 10- Smoking**

* Effect size measure from systematic review- Current versus never smoking.
* Decision- Current versus never smoking.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study cohorts** | **Notes/ variables or questions** | **Current smoker** | **Former smoker** | **Never smoker** |
| HRS ADAMS | Joining two questions from medical history. | Yes, s/he still smoking cigarettes or cigars. | Ever smoked cigarettes or cigars but not current smoker. | Never smoked cigarettes or cigars |
| CHS-CS | Current smoke status | 3= current smoker | 2= former smoker | 1= never smoked |
| MAP | Smoking status at baseline – do you smoke cigarettes now? | 2= current smoker | 1= former smoker (does not currently smoke) | 0=never smoked  |
| SNAC-K  | Are you, or have you been a smoker? | 1= yes, smoke regularly2= yes, smoke sometimes | 3= no, quit smoking  | 4= no, never smoked8. No response9. Don’t know |
|  |  |  |  |  |

**eTable 11- Diabetes**

* Effect size measure from systematic review- History of diabetes
* Decision- Diabetes (yes or no)

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Variable / Question**  | **Answer options** |
| HRS ADAMS | Has (s/he) ever been told by a doctor that (s/he) has diabetes? | 1. yes  | 2. no 7. refused 8. don’t know |
| CHS-CS | Have you been told by a doctor that you currently have any of the following conditions?Another question, ever had any of the following? | Yes, for diabetes |  |
| MAP | Have you ever been told by a doctor, nurse or therapist that you had diabetes, or sugar in the urine or high blood sugar?Has a doctor, nurse or therapist ever told you to take insulin or injections for your high blood sugar?Has a doctor, nurse or therapist ever told you to take medicine by mouth for your blood sugar? | 1= history of diabetes – answered yes to one or more questions or participants was taking diabetes medication prior to or in the given cycle.  | 0= no history of diabetes- answered no or suspect or possible to all questions in all cycles and no diabetes medication inspected.  |
| SNAC-K  | Diabetes type 2 (adult -onset, not necessary insulin dependent) | 1. Yes  | 2. No 8. No response9. Don’t know |

**eTable 12- Hypertension**

* Effect size measure from systematic review- History of hypertension
* Decision- Hypertension (yes or no)

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Variable/Question**  | **Answer options** |
| HRS ADAMS | Has (s/he) ever been told by a doctor that (s/he) had high blood pressure or hypertension? | 1. Yes  | 2. No 7. Refused8. Don’t know |
| CHS-CS | Calculated hypertension status (calculated variable) | 1= borderline (seated blood pressure average systolic =140-159mmHG, or seated blood pressure average diastolic =90-94mm HG 2= hypertensive Seated blood pressure average systolic =160mmHG OR seated blood pressure average diastolic =95mmHG, OR history of hypertension = Yes and participant takes hypertensive medication.  | 0= Normotensive/ normal  |
| MAP | History of hypertension – self report. At baseline interview, have you ever been told by a doctor, nurse or therapist that you had high blood pressure? | 1= History of hypertension (reported prior to or in the given cycle) | 0= No history of hypertension |
| SNAC-K  | Hypertension (current)(if no) previous hypertension? | Yes  | No |

**eTable 13- Atrial Fibrillation**

* Effect size measure from systematic review- AF without stroke versus no AF
* Decision- Atrial fibrillation (yes or no)

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Variable**  | **Answer options** |
| HRS ADAMS | History of atrial fibrillation from the medical history record form. | 1= Yes  | 2= No, 8= don’t know |
| CHS-CS | Atrial fib by ECG -calculated from 12-lead ECG dataor had atrial fibrillation? (self-reported- collected as part of phone follow up)  | 1= YesIf Minnesota code= otherwise1= Yes  | 0= NoIf Minnesota Code =8-30= No |
| SNAC-K  | Atrial fibrillation  | 1. Yes | 2. No |

**eTable 14- Stroke**

* Effect size measure from systematic review- History of stroke for AD
* Decision- Stroke (yes or no)

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Questions**  | **Answer options** |
| HRS ADAMS | Has (NAME) ever been told by a doctor or nurse that (s/he) had a stroke? | 1. Yes  | 2. No 7. Refused8. Don’t know |
| CHS-CS | Stroke status at baseline- self report | 1. = definite Hx | 0= no history2= possible Hx3= Silent/unreported |
| MAP | History of stroke | 1= History of stroke -diagnosis of highly probable or probable in at least one cycle prior to or in the given cycle. | 0= No history of stroke – diagnosis of possible or not present in all cycles  |
| SNAC-K | Stroke | 1. Yes  | 2. No 8. No response9. Don’t know |

**eTable 15- TBI loss of consciousness**

* Effect size measure from systematic review- Prior TBI – yes or no (effect size of head injury with and without status of consciousness)
* Decision- TBI (yes or no)

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Questions**  | **Answer options** |
| HRS ADAMS | Has (NAME) ever had a blow to the head, a head injury or head trauma thatwas severe enough to require medical attention, to cause loss of consciousness or memory loss for a period of time? | 1. Yes  | 2. No 7. refused8. don’t know  |
| CHS-CS | Have you ever had an injury that resulted in loss of consciousness? | 1= Yes  | 0= No  |
| MAP | Q1: Have you ever had a head injury?If yes, then:Q2: Have you ever lost consciousness because of a head injury? | 1= History of head injury with loss of consciousness- reported at baseline | 0= No history of head injury- no head injury reported or reported head injury without loss of consciousness (includes suspect or possible loss of consciousness) |
| SNAC-K | Head trauma with loss of consciousness/syncope | 1. Yes  | 2. No 8. No response9. Don’t know |

**eTable 16- Insomnia**

* Effect size measure from systematic review- Clinical insomnia
* Decision- We decided to use the Morin Insomnia Severity as it is a validated scale (which have the 3 standard questions – difficulty falling asleep, wake up several times and trouble staying asleep along with personal questions on how the sleep affects your life). As we do not have the personal questions, we are scoring only on the three standard questions, and we are scoring for severe symptoms of insomnia which would mean they say ‘yes’ for at least 2 out of the 3 questions.

|  |  |  |
| --- | --- | --- |
| **Study cohorts** | **Questions**  | **Answer options** |
| HRS ADAMS | Lifetime medical history – record at the condition level based on ICD-9 code  | 780.52= Insomnia |  |
| CHS-CS | Do you usually have trouble falling asleep?Do you usually wake up several times at night?Do you usually wake up far too early? | 1. Yes1. Yes1. Yes | 2. No2. No2. No |
| SNAC-K | Do you have trouble falling asleep?Do you wake up during the night? Are you unable to fall back asleep if you wake up during the night? | 1. Yes1. Yes1. Yes | 2. No 8. No response2. No 8. No response2. No 8. No response |

**eTable 17- Dementia diagnosis**

* Decision – Clinical diagnosis for dementia

|  |  |  |  |
| --- | --- | --- | --- |
| **Study cohorts** | **Questions**  | **Dementia** | **No dementia**  |
| HRS ADAMS | Dementia – whether overall DSM IV criteria met (based on checklist) Wave D Final primary diagnosis (consensus dementia diagnosis) | 1. Yes 1=probable AD2= possible AD3= probable vascular dementia4= possible VaD5= Parkinson’s 6= Huntington’s and many more options  | 2. No   |
| CHS-CS | Dementia type | 1= AD only2= Mixed3= VaD only4=Unknown | 0= Normal |
| MAP | Clinical diagnosis of cognitive status (AD, other dementia, MCI or no impairment) | 4 AD: Alzheimer’s disease, no other condition contributing to CI (NINCDS/ADRDA probable AD)5. AD+: Alzheimer’s disease AND other condition contributing to CI (NINCDS/ADRDA possible AD)6. Other dementia: other primary cause of dementia, no clinical evidence of AD | 1. No cognitive impairment (no dementia or no cognitive impairment)2. MCI: Mild cognitive impairment, no other condition contributing to cog impairment3.MCI: Mild cognitive impairment and another condition contributing to Cog impairment. |
| SNAC-K | Dementia  | 1. Yes  | 2. No 8. No response9. Don’t know |

**PART C:**

**eTable 1- Selection of covariates from various waves of the studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Covariates** | **MAP** | **HRS ADAMS** | **CHS-CS** | **SNAC-K** |
| Age | Baseline | Baseline | Baseline2 | Baseline |
| Gender | Baseline | Baseline | Baseline2 | Baseline |
| Education | Baseline | Baseline | CHS enrolment | Baseline |
| Obesity | Baseline | Baseline |  | Baseline |
| Diabetes | Baseline | Baseline | Baseline2 | Baseline |
| Stroke | Baseline | Baseline | Baseline2 | Baseline |
| TBI | Baseline | Baseline | NA | Baseline |
| Hypertension | Baseline | Baseline | Baseline2 | Baseline |
| Smoke | Baseline | Baseline | Baseline2 | Baseline |
| Depression | Baseline | Baseline | Baseline2 | Baseline |
| Loneliness | Baseline | NA | Baseline2 | Baseline |
| Physical activity | Baseline | NA | Baseline2 | Baseline |
| Cognitive activity | Baseline | Baseline | Baseline2 | Baseline |
| Cholesterol | Baseline | Baseline | CHS year2 visit | Baseline |
| Fish intake | Wave 2 to 101 | NA | CHS year2 visit | Baseline |
| Atrial Fibrillation | NA | Baseline | Baseline2 | Baseline |
| Insomnia | NA | Baseline | CHS year2 and Year 4-6 | Baseline |

1 Missing values in earlier waves were replaced by available values from the subsequent waves.

2 Baseline was defined at first MRI, which was during Years 4-6 of CHS enrolment.

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