

# The Brain Aging National Cohort-PUMC: study design and baseline characteristics

## Article history:

Received: 11-11-2022

Revised: 06-03-2023

Accepted: 15-03-2023

Published: 25-03-2023

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## ABSTRACT

**Objectives:** To describe the study design and baseline characteristics of the Brain Aging National Cohort (BANC)-Peking Union Medical College (PUMC), a study aiming to identify risk and protective factors that contribute to brain aging and age-related neurological diseases.

**Methods:** The BANC-PUMC is a longitudinal study established in 2017 in the city of Beijing, enrolling participants who agreed to donate their bodies and brains for medical research. Participants received face-to-face clinical evaluations including questionnaires, physical examinations, and comprehensive cognitive assessments. Biological samples and brain magnetic resonance images were collected. Neuropathological evaluation of the autopsied brain is performed.

**Results:** Among the 885 participants, 43.3% were men, and the mean age of the cohort was  $71.3 \pm 8.2$  years. The participants were predominantly equipped with high-level education, and they had an average of 12 years (SD 3.6) of education. The most common chronic disease of participants was hypertension (61.4%). The proportion of Mini-Mental State Examination scores below 24 was 4.3%. The cohort has been followed up annually.

**Conclusions:** The BANC-PUMC study has the potential to unravel the causes and consequences of age-related neurological diseases via a clinicopathological correlation study. The program will continue and allow further follow-up and extension of current investigations

**KEYWORDS:** Aging; Cohort study; Willed donation; Study design; Clinicopathological correlation.

## INTRODUCTION

The aging demographic presents a significant worldwide dilemma and challenge (Prince *et al.*, 2015). The ever-increasing weight of neurodegenerative and cerebrovascular maladies, brought on by societal advancement and elongated life expectancies, creates substantial obstacles for China's healthcare infrastructure (Yang *et al.*, 2013). The establishment of well-designed volunteer cohort studies and subsequent clinicopathological investigations are crucial in determining the factors that impact aging, both positively and negatively. The collection of clinical data from body donors during the time frame between the submission of a body donation request and the completion of brain

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procurement constitutes a vital strategy in aiding researchers in obtaining a thorough comprehension of both healthy aging and age-related neurological diseases. Given that China boasts the largest population of a single ethnicity globally, a prospective cohort study that incorporates thorough clinical assessments and brain sample collection in this population is imperative.

Population-based prospective clinicopathological studies (Au *et al.*, 2012; Brayne *et al.*, 2009; Brenowitz *et al.*, 2017; White & Launer, 2006; Zaccari, Ince, & Brayne, 2006) and cohort studies focusing on certain selected populations or a defined population (Arnold *et al.*, 2010; Mortimer, 2012; Santa Cruz *et al.*, 2011) were initiated in the last century, which have revealed extensive findings concerning dementia and healthy aging. Unfortunately, these types of studies are absent in China due to cultural differences, as body donation has scarcely been accepted by Chinese society since ancient times. Only in recent decades, the transition slowly happened and considerable volunteers signed donation agreements at Peking Union Medical College, which is the most famous medical school in China.

The Brain Aging National Cohort (BANC)-Peking Union Medical College (PUMC) is a longitudinal study that enrolls a large and well-defined cohort of participants who have agreed to donate their bodies for medical education and research purposes. The study collects clinical, biological, and imaging data. The BANC-PUMC study endeavors to examine the interplay between risk factors from early life and declines in cognitive and physical capacity, incidence of dementia, and results of neuropathological autopsy examination, while also exploring the role of vascular factors in the advancement of neurodegenerative diseases. This paper describes the design of the BANC-PUMC study, and presents baseline demographic characteristics and clinical information on the first 885 participants of the volunteer cohorts.

## METHODS

### Brief description of PUMC willed body donation program

The Body Contribution Plan of PUMC was established in May 1999 (H. Zhang *et al.*, 2018; H. Zhang *et al.*, 2022). People living in Beijing can submit a request for body donation to the PUMC plan, except

for those with Type A and B communicable illnesses according to China's Communicable Disease Prevention and Control Law. The Body Contribution Plan of PUMC is optional and does not provide payment, and every donor and their family must give written consent for the use of the donated body parts for medical education and research purposes. Prospective donors can either obtain the application form online (<http://anatomy.sbm.pumc.edu.cn/bone.asp>) or request paper copies from the donation office. In Beijing, body and organ donation programs are administered by different organizations, with the latter usually excluding participation in the former.

### Study design and target population

The BANC-PUMC is a longitudinal study established in 2017, enrolling participants who agreed to donate their bodies and brains for medical education and research. BANC-PUMC study aimed at identifying risk and protective factors of brain aging and investigating links between cardiovascular disease and neurodegenerative disease.

Subjects in the BANC-PUMC study were enrolled in the PUMC willed body donation program. The criteria for inclusion were: (I) Beijing, China residents who had applied for willed body donation to the PUMC program; (II) readiness for prolonged monitoring; (III) agreeable to approve. The reasons for disqualification were: (I) rejection of participation in the research and (II) incapacity, either physical or cognitive, to finish the survey discussions and evaluations.

This research was executed in conformity with the Declaration of Helsinki. The Ethical Committee of Peking Union Medical College Hospital approved the study and informed consent was procured from all participants or their legally authorized representatives.

### Data collection

In-person interviews, bodily check-ups, procurement of blood and urine specimens, and evaluations of cognitive and motor abilities were carried out at the clinic of PUMC hospital. Heart and blood vessel assessments, including electrocardiogram and transthoracic echocardiography, were conducted during the interview session. Magnetic Resonance Imaging (MRI) was performed at PUMC Hospital from the years 2017 to 2020.

## STRUCTURED INTERVIEW

### Demographics and lifestyle

A survey utilizing standardized questionnaires was performed through personal interviews conducted by instructed interviewers. The questionnaires comprised the following assessments: (1) individual demographic information, encompassing date of birth, gender, marital status, educational attainment, and yearly household income; (2) upbringing surroundings, including sibling count and birth weight; (3) way of life, including employment history, physical activity, smoking of cigarettes, exposure to secondhand smoke, alcohol intake, tea consumption, and dietary practices. The behavior of cigarette smoking is characterized by the number of cigarette packs smoked with the duration of smoking in years. Alcohol consumption is quantified as units daily as well as the age when beginning (and if ceased) alcohol consumption was recorded. The objective of the food frequency questionnaire was to obtain information on the intake of vital nutrients and specific types of Chinese cuisine, including salted foods, fermented foods, and soy-based foods.

### Vascular risk factors and cardiovascular disease

Each participant was given a structured questionnaire to gather information on their history of conditions such as hypertension, diabetes, atrial fibrillation, transient ischemic attack, stroke, myocardial infarction, coronary bypass, percutaneous coronary angiography, carotid endarterectomy, and migraine. The family history of cerebrovascular disease and myocardial infarction among their relatives was also recorded.

### Medication use

As part of the examination, a complete list of all medications taken in the past month was compiled. The names of the medications were recorded and classified following the Chinese translation of the Anatomical Therapeutic Chemical (ATC) Classification System (WHO, WHO Collaborating Centre for Drug Statistics and Methodology, <http://www.whocc.no/atcddd/>)

## Assessments of other variables

A comprehensive structured questionnaire, previously employed in extensive epidemiological research, was utilized to examine the history of restless legs syndrome, movement disorders, peripheral nerve diseases, and sleep disorders. Assessments of falls and urinary dysfunction were also administered with the aid of standardized questionnaires.

## PHYSICAL EXAMINATION

### Anthropometric measurement

Weight and height were assessed with the participant barefoot and wearing lightweight clothing. The Body Mass Index (BMI) was calculated as the weight divided by the square of height (in meters). The maximum waist circumference was measured in a standing position, taken at the level between the bottom rib and the iliac crest during normal expiration. Blood pressure and heart rates were measured three times after a 5-minute rest period, and the average values were utilized for analysis.

### Neurological examination

The biceps, hand grip, hip flexor, thigh, and foot extensor muscles' power on both sides was determined. The existence of the space between the eyebrows, nose, and grip reflexes, the clapping gesture, and the response of the sole were noted. Sensory capability was evaluated in a semi-quantitative fashion utilizing a tuning fork that vibrates on both big toes and both inner ankle bones.

### Assessment of motor performance

Motor capabilities were assessed by various performance checks, that are extensively applied in past research on people living in communities, those with cerebral small vessels, or Parkinson's disease. The thorough examination sets, which measured both upper and lower limb abilities, included the Short Physical Performance Battery (Guralnik *et al.*, 1994), Assessment and Rating of Ataxia (Schmitz-Hubsch *et al.*, 2006), Tinetti Performance-Oriented Assessment of Mobility (Tinetti, 1986), Timed Up and Go test (Podsiadlo & Richardson, 1991), and Unified Parkinson's Disease Rating Scale (Goetz *et al.*, 2008). To measure walking pace, subjects have to walk for three meters at their normal speed. All

motor performance tests were carried out in front of a Kinect-based system that was custom-built. The system automatically identified the participant, and separated the walking segments, to obtain quantitative walking measurements with an integrated movement recognition model. With this system, we captured comprehensive motion pictures of the participant's posture and limb movements and measured their motor performances.

### Assessment of cognition

A comprehensive neuropsychological (NP) assessment was performed to assess overall cognitive abilities and specific cognitive domains, such as memory, attention, and executive functions, which are in line with other major epidemiological studies (de Groot *et al.*, 2000; Group, 2003; van Norden *et al.*, 2011). The adaptations of the MMSE and Montreal Cognitive Assessment were applied for screening ("The application of Montreal cognitive assessment in urban Chinese residents of Beijing,"; "The mini-mental state examination in the Chinese residents population aged 55 years and over in the urban and rural areas of Beijing "). NP assessments were carried out among consenting individuals, including the Fuld Object Memory Test, the Chinese version of the 12-word Philadelphia Verbal Learning Test, the Rapid Verbal Retrieval Test, Block Design, Digit Span, and the Trail Making Test in their Chinese versions (M. Zhang *et al.*, 1998). If a participant's MMSE score was  $\leq 24$  or they reported challenges in cognitive functions, further tests were conducted using the Clinical Dementia Rating Scale (Lim, Chong, & Sahadevan, 2007; Morris, 1993). All subjects underwent a Hamilton Rating Scale for screening of depression (Hamilton, 1960) and the neuropsychiatric inventory-aphathy subscale for apathy screening (Cummings *et al.*, 1994).

### Assessment of activities of daily living

The Barthel Index was utilized to indicate incapacitation (Leung, Chan, & Shah, 2007). The evaluation of daily life activities was performed through the Alzheimer's Disease Cooperative Study-Activities of Daily Living scale (Galasko *et al.*, 1997), Katz Index of self-sufficiency in daily life activities (Shelkey & Wallace, 1999), and the Lawton-Brody Instrumental Activity of Daily Living scale (Lawton & Brody, 1969). The general wellness status (life satisfaction) was gauged using the Short Form Health Survey 36 (Ware & Sherbourne, 1992).

### Biological data and blood bank specimens

Samples of blood and urine were acquired after a fast in the night before. The central labs measured various biological markers, including blood sugar, lipid levels, homocysteine, C-reactive protein, albumin in blood/urine, and creatinine. Blood bank specimens (serum, plasma, free circulating nucleic acids, ribonucleic acid, deoxyribonucleic acid [DNA]), were saved for further examination in a freezer at  $-80^{\circ}\text{C}$  or in nitrogen liquid containers.

### Magnetic resonance imaging examination

A single 3T Skyra scanner was applied to acquire 3D T1-weighted, T2-weighted, fluid-attenuated inversion recovery, and susceptibility-weighted imaging scans. The parameters for each MRI sequence were uniform with those of the previously published Shunyi study (Han *et al.*, 2020).

### Electrocardiogram and Echocardiography

A standard 12-lead electrocardiogram was captured after a minimum rest period of 5 minutes. A seasoned cardiologist evaluated the ECG using a standardized technique and documented numerous aspects, such as frequency, heart rhythm, PQ, QRS, and QTC intervals, conduction problems, left ventricular hypertrophy, repolarization abnormalities, infarction, pathological Q waves, and acute ischemia. The final categorization of the diagnosis ranged from normal to abnormal with clinical implications, an abnormal ECG with significant impact, or a pathological ECG that necessitated immediate consultation with a specialist if needed.

Transthoracic echocardiography was carried out utilizing commercially accessible equipment (Vivid I; GE Vingmed Ultrasound, Horten, Norway). Structural as well as functional data have been assessed using ultrasound measurements following the Guidelines of the American Society of Echocardiography (Lang *et al.*, 2015; Nagueh *et al.*, 2016).

### Yearly monitoring as well as follow-up in the longer timeframe

The cohort was monitored on an annual basis since 2017 through telephonic communication and correspondence. For participants who reported incidence events, medical records provided supplementary

data during the subsequent examination. Commencing 2022, a secondary in-person interview was initiated. Health information, evaluations of primary cardiovascular risk elements, neurological evaluations, cognitive assessments, and A brain MRI were done using the same method as the original, as part of the follow-up process.

### Neuropathological assessment

Death certificates were procured to acquire information about the location and cause of death. Standardized protocols and systematic management were established to secure human brain specimens of acceptable quality for neuroscience research. The duration between death and receipt of the brain varied greatly depending on whether the death occurred at our center or elsewhere.

Neuropathological examination of autopsied brains was performed by expert neuropathologists who did not possess any prior knowledge of the individual's clinical information. The brains were obtained fresh, and the macroscopic neuropathological observations were documented. The quantification of Alzheimer's disease lesions and vascular/microvascular lesions was performed using standardized protocols (Au *et al.*, 2012).

### Statistical analysis

The demographics and characteristics of the participants are depicted through descriptive statistical examinations. Continuous variables are shown as mean (standard deviation), and categorical data are represented as frequency (percentage). The t-test (for means), Wilcoxon rank-sum test (for medians), and chi-square test (for ratios) were employed to compare data between groups. The relationship between baseline features and outcomes was evaluated through multivariate regression models.

All probabilities and 95% confidence intervals were computed with a two-tailed approach. Significance was considered at a probability of  $p \leq 0.05$ . The data underwent analysis utilizing SPSS 24.0 (SPSS Inc., Illinois, USA).

## RESULTS

### The BANC-PUMC Study Population

From January 2017 to December 2019, we carried out in-person interviews and clinical evaluations

on 885 participants. Table 1 presents the baseline demographic features of the BANC-PUMC population. Among the 885 participants, 43.3% (383) were male, with a mean age of  $71.3 \pm 8.2$  years (52-95 years). The vast majority (75.1%) were married, with 24.6% currently living alone. Participants had an average education of  $12 \pm 3.6$  years, with 74.2% having completed high school or higher. Most participants had an annual family income of 10,000 to 50,000 CNY (35%) or 50,000 to 100,000 CNY (44.1%).

### Alcohol and Tobacco Consumption

The fraction of current smokers was 9.6% (male: 20.8%, female: 1.2%); 50.7% of males and 97.1% of females had never smoked. The proportion of current alcohol drinkers was 15.9% (men: 32.4%, women: 4.4%); 58.6% of men and 94.5% of women had never drunk. Regular consumption of Chinese Baijiu (13.6%) was more common than that of beer (3.8%) and wine (3.3%), and 8.5% of the participants drank Chinese Baijiu daily.

### Medical History

At baseline, the incidence of major vascular risk elements was 61.4% for hypertension, 21.7% for diabetes mellitus, and 39.1% for hyperlipidemia. Forty percent of the participants used antihypertensive drugs, 33.1% used lipid-lowering agents and 22.6% used antiplatelet or anticoagulant medication. Baseline frequencies of past or present self-reported history of stroke, coronary artery disease, osteoporosis, fractures, thyroid disorders, prostate diseases, and cancer are given in Table 2.

As shown in Table 2, the average BMI of participants was  $23.9 \pm 3.5$  kg/m<sup>2</sup>, and the average waist-to-hip ratio was  $0.87 \pm 0.07$ . The average systolic and diastolic blood pressures measured on the interview day were  $135.4 \pm 17.1$  mmHg and  $70.9 \pm 9.9$  mmHg. Blood samples were collected from 857 (96.8%) subjects, and baseline levels of blood glucose and lipid profiles are shown in Table 2.

### Cognitive Assessment

The average MMSE score was 27.8 (SD=2.7), which, as anticipated, rose with elevated education and younger age. The proportion of MMSE scores below 24 rose from 3.3% in the age group under 85 years to 14.3% in individuals aged 85 and above.

Other cognitive evaluations displayed comparable relationships with education and age as the MMSE.

### Follow-up

The cohort has been monitored by telephone and letters annually since 2017. A second-round on-site interview follow-up has been initiated in 2022. As of October 2022, we have had a total of 15 deaths in the BANC-PUMC participants, all of whom had donated their whole bodies, including brain samples. Detailed neuropathology reports are available for all cases.

### DISCUSSION

This prospective cohort in the well-defined population was designed specifically to study aging and age-related neurological diseases. The BANC-PUMC is a clinicopathological study conducted on willed body donors of China with a similar design for research, methods, and pathological diagnostic standards to most previous autopsy cohort studies. This study, consisting of volunteer participants, stands out for its comprehensive evaluations that included neurological, neuroimaging, neuropsychological, and epidemiological assessments, positioning it as a rare example of a prospective cohort study. Our examination endeavors to bridge the data shortfall present in the Chinese demographic. The study's design and reasoning are outlined here.

Dementia research utilizing human brain specimens encompasses a range from the observation of chosen individuals' pathology to probe the molecular dynamics of dementia, to population-based investigations aimed at comprehending the demographics, geographic, and causative factors of dementia disorders. Most neuropathological studies have drawn on cases from prospective community-based cohorts, brain donation volunteer cohorts, or clinic patients of dementia. These investigations employed standardized neuropathologic techniques, enabling the examination of clinicopathological correlations and diagnosis validation, and investigating the associations between neuropathological burden and risk factors. The core information for the representative studies is shown in Table 3.

Community-based neuropathological studies included the Hisayama study in Japan, the Cognitive Function and Ageing Study (<http://www.cfas.ac.uk>) (Foltnie, Matthews, Ishihara, Brayne, & Mrc, 2006) and the Cambridge City over -75s

Cohort Study (<http://www.cc75c.group.cam.ac.uk>) (Brayne *et al.*, 2009) in UK, the Honolulu-Asia Aging Study (Stephan *et al.*, 2022; White *et al.*, 2002) and the Cache County Study on Memory and Aging (Tschanz *et al.*, 2005) in the US. Studies among community-dwellings provided unique insights in dementia, but still face challenges in keeping longitudinal follow-up and increasing tissue donation rate. Studies conducted in brain donation volunteer cohorts, including the Nun Study (Mortimer, 2012; Riley, Snowdon, & Markesbery, 2002; Santa Cruz *et al.*, 2011), the Religious Orders Study (Bennett, Schneider, Arvanitakis, & Wilson, 2012) and the Rush Memory and Aging Project (Bennett, Schneider, Buchman, *et al.*, 2012; Bennett *et al.*, 2005; Oveisgharan *et al.*, 2022), enrolled individuals of Catholic sisters, priests, and brothers with high follow-up rates and autopsy rates. The Framingham Brain Donation Program was embedded within the prospective Framingham Heart Study (Au *et al.*, 2012), therefore, comprehensive lifestyle and hazard factor information has been collected throughout the adult life of all individuals, and the majority also possess pre-death imaging, neurological, and neuropsychological evaluation data. However, studies conducted in volunteer cohorts may be less representative of the whole population due to sample selection bias. The Alzheimer's Disease Neuroimaging Initiative Neuropathology Core (ADNI-NPC) was embedded within the ADNI (<https://adni.loni.usc.edu/>), investigating neuropathological correlates in demented patients (Franklin *et al.*, 2015). Founded in 2007, it aimed to encourage brain donation among ADNI participants, streamline the procurement of brain specimens upon autopsies, carry out a standardized neuropathologic evaluation, and establish a brain repository consisting of both fixed and frozen tissues to advance dementia research.

The BANC-PUMC study will contribute Chinese population data to this field. The strong point of the BANC-PUMC study is that it tends to hold complete and extensive information about the participants, and prospective longitudinal investigations are essential to identify risk and protective factors that influence the aging process. There is a higher rate of autopsy in the willed donation cohort compared to the population-based neuropathological study, opening opportunities for clinicopathological correlation studies and making the post-mortem-confirmed diagnosis possible. However, as a volunteer cohort, the BANC-PUMC study is composed of willed-body donors who differ from

the general population, which may lead to sample selection bias. Therefore, the significance of specific maladies or the connections between maladies and hazard elements may not be transferable to the senior demographic in its entirety. One potential result of the sample's inadequate representativeness could be a discrepancy in the frequency of occurring events, namely cerebrovascular disease and dementia could be lower than expected in the general population.

In 2013, to explore the cardiovascular disease and age-related brain disorder determinants, both environmental and hereditary, our research group in Beijing established the Shunyi study as a prospective cohort (Han *et al.*, 2020). The BANC-PUMC study used a similar study design for the collection of clinical information to that of the Shunyi study. Physicians, neurologists, and ultrasound technicians had centralized training. The MRI sequences and parameters were the same, and the images were transferred to the same center for centralized measurements. The Shunyi research concentrated on a population anchored in the rural area of Beijing, a region undergoing economic transformation, constituted of a significant number of individuals with limited educational attainment and exhibiting relatively elevated incidences but inadequate management of vascular risks. By contraries, the BANC-PUMC study was composed of participants who volunteered to donate body for medical research. Most of the donors live in urban areas of Beijing, predominantly equipped with high educational backgrounds and good awareness of health. A comparison of baseline data between the two groups revealed that the average age in BANC-PUMC (71.3) was higher than the Shunyi cohort (56.7). While over 40% of the participants in BANC-PUMC had a college degree or higher education, only 2% of the Shunyi population held such qualifications. Education has been linked to both cognitive performance and circulatory health, as well as its associated hazards. For example, the BANC-PUMC study showed that almost half of the male participants and all female participants had never smoked, whereas in the Shunyi study, only about 25% of the men and less than 94% of the women were non-smokers. These age and socio-economic disparities lead to a lower frequency of cognitive issues, cerebrovascular diseases, and health problems in the BANC-PUMC cohort compared to the Shunyi study. By combining these two studies, our future research aims can be achieved and reinforced.

In the future, with increasing numbers of donors and the continuous construction of human brain banks in China, this initiative shall persist and facilitate subsequent monitoring and augmentation of present inquiries. Our prospective objectives for the imminent decade encompass utilizing neuropathology to examine connections with pre-death imaging and utilizing cerebral tissue for genomic and gene expression explorations. Furthermore, we will investigate how the genetic and environmental risk factors relate to the observed neuropathology and identify the pathophysiologic pathways between risk factors and age-related brain diseases.

## CONCLUSION

To summarize, the BANC-PUMC examination holds the possibility of advancing the understanding of the origins and impacts of vascular brain injury and age-related neurodegenerative diseases in the elderly by investigating the clinicopathological correlations and radiological-pathological correlations. It constitutes a suitable milieu for investigating numerous hazards and safeguarding elements in correlation to specific maladies among subjects possessing diverse cognitive and operational competencies.

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	No. of subjects (n=885)	%
Sex, men	383	43.3
Age, mean (SD), years	71.3 (8.2)	
Age range, years		
<60	31	3.5
60-69	388	43.8
70-79	290	32.8
80-89	164	18.5
≥90	11	1.2
Education level		
Less than primary school	7	0.8
Primary school	35	4.0
Middle school	183	20.7
High school	300	33.9
College and above	357	40.3
Education, mean (SD), years	12.0 (3.6)	
Marital status		
Never married	29	3.3
Married	665	75.1
Divorced	63	7.6
Widowed	121	13.7
Unknown	3	0.3
Currently living alone	217	24.6
Family income per year		
<10,000 Chinese Yuan	60	6.8
10,000-50,000 Chinese Yuan	310	35
50,000-100,000 Chinese Yuan	390	44.1
>100,000 Chinese Yuan	91	10.3
Lifestyle habits		
Current cigarette smoking*	85	9.6
Current alcohol drinking*	141	15.9

Abbreviations: SD, standard deviation

\* Current cigarette smoking was defined as smoking at least within the prior month; current alcohol drinking was defined as drinking at least within the prior month

**Table 1.** General characteristics of the participants.

	No. of subjects (n=885)	%
Self-reported history of		
Hypertension*	543	61.4
Diabetes mellitus*	192	21.7
Hyperlipidemia	346	39.1
Stroke	96	10.8
Myocardial infarction	52	5.9
Coronary surgery	49	5.5
Atrial fibrillation	37	4.2
Parkinson's disease	2	0.2
Severe head trauma	27	3.1
Osteoporosis	243	27.5
Fracture after 50 years old	110	12.4
Thyroid disease	77	8.7
Prostate disease	152	17.2
Cancer	72	8.1
Medication Use		
Antihypertensive agent	356	40.2
Antidiabetic agent or insulin	138	15.6
Lipid-lowering agent	293	33.1
Antiplatelet agent	184	20.8
Anticoagulant	16	1.8
Anthropometric measurement, mean (SD)		
Body mass index, kg/m <sup>2</sup>	23.9 (3.5)	
Waist to hip ratio	0.87 (0.07)	
Systolic blood pressure, mmHg	135.4 (17.1)	
Diastolic blood pressure, mmHg	70.9 (9.9)	
Blood sample collected	857	96.8
Total cholesterol, mean (SD), mmol/L	4.93 (1.08)	
Low-density lipoprotein cholesterol, mean (SD), mmol/L	2.90 (0.93)	
High-density lipoprotein cholesterol, mean (SD), mmol/L	1.38 (0.35)	
Triglyceride, mean (SD), mmol/L	1.45 (0.97)	
Fasting blood glucose, mean (SD), mmol/L	5.8 (1.4)	
hemoglobin A1c, mean (SD), %	5.9 (0.9)	
Homocysteine, mean (SD), mmol/L	15.6 (7.8)	
Cognitive function		
MMSE, mean (SD)	27.8 (2.7)	
MMSE score below 24	36	4.3
MOCA, mean (SD)	23.5 (4.0)	

Abbreviations: MMSE, Mini-Mental State Examination; MOCA, Montreal Cognitive Assessment; SD, standard deviation

\* Hypertension was defined as self-reported hypertension, treatment with antihypertensive medication, systolic blood pressure  $\geq 140$  mm Hg, or diastolic blood pressure  $\geq 90$  mmHg. Diabetes mellitus was defined as self-reported diabetes, use of oral antidiabetic drugs or insulin, fasting serum glucose  $\geq 7.0$  mmol/L, or hemoglobin A1c  $\geq 6.5\%$

**Table 2.** Baseline medical characteristics (self-reported) and measures.

Study	Country	Number of subjects	Number of brains collected	Start date
<b>Community-based cohort</b>				
Hisayama study (Zaccai <i>et al.</i> , 2006)	Japan	3167	817 (as of 2007), 64% of deaths	1985
The Cambridge City over - 75s Cohort Study (Brayne <i>et al.</i> , 2009)	UK	2166	230 (as of 2007)	1985-1987
Cognitive Function and Ageing Study (Foltynie <i>et al.</i> , 2006)	UK	More than 18000	More than 500, 20-55% of deaths	1989-1993
Honolulu-Asia Aging Study(Stephan <i>et al.</i> , 2022; White & Launer, 2006; White <i>et al.</i> , 2002)	USA	3734	852 (as of 2013), 20% of deaths	1991-1993
Cache County Study on Memory and Aging (Tschanz <i>et al.</i> , 2005)	USA	5092	65 (as of 2002)	1995-1997
Adult changes in thought study(Sonnen <i>et al.</i> , 2007; Sonnen <i>et al.</i> , 2009)	USA	3700	323 (as of 2011), 20% of deaths	1994-1996
Vantaa 85+ Study (Polvikoski <i>et al.</i> , 2006)	Finland	601	180 (as of 2006), 45% of deaths	1991
<b>Brain donation volunteer cohort</b>				
The Nun study (Mortimer, 2012; Riley <i>et al.</i> , 2002; SantaCruz <i>et al.</i> , 2011)	USA	678	548 (as of 2012), 98% of deaths	1986
The Religious Orders Study (Bennett, Schneider, Arvanitakis, <i>et al.</i> , 2012)	USA	More than 1150	550 (as of 2014), >80% of deaths	1994
The Rush Memory and Aging Project (Bennett, Schneider, Buchman, <i>et al.</i> , 2012)	USA	More than 1550	425 (as of 2014), >80% of deaths	1997
The Framingham Brain Donation Program(Au <i>et al.</i> , 2012)	USA	433 (as of 2009)	139 (as of 2009), 75% of deaths	1997
<b>Clinic cohort</b>				
The Alzheimer's Disease Neuroimaging Initiative Neuropathology Core (Franklin <i>et al.</i> , 2015)	USA / Canada	404 (as of 2015)	45 (as of 2015), 58% of deaths	2007

**Table 3.** Key information from the population-based neuropathological studies of old age.



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