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Cohort Profile

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Cohort Profile: The LoCARPoN—a population-based prospective cohort study in middle-aged and older adults in India

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Key Features

- LoCARPoN, funded by the Government of India, is the first prospective population-based Indian cohort to study incident stroke and dementia in an urban upper-middle class population in India, integrating sociodemographic, lifestyle, anthropometric, dental, biochemical and neuropsychological measurements with magnetic resonance imaging (MRI), neuroimaging and genomics.
- LoCARPoN was established to assess the associations of established as well as India-unique (e.g. yoga, vegetarianism, multilingualism, diet with herbs and spices, periodic fasting and unique sleep habits) factors with stroke and dementia and to develop risk prediction models for India's growing middle class.
- With door-to-door visits, 8858 participants aged 50 years and above from two areas in South Delhi were enrolled from 2016 to 2019, and 7505 persons attended hands-on assessments in the study centre (mean age, 64.6 years; 51% female; 92.4% Hindu; 91% multilingual; 80.8% college graduates; 54.2% vegetarian; 35% practising yoga regularly); the first 6-monthly telephone follow-up was completed in 93.4% of participants in January 2020.
- Neuropsychological assessments, carotid Doppler, 24-h diet recall, food frequency questionnaire, dental examination and MRI neuroimaging (2604 completed) were performed; the first 4-yearly in-person follow-up assessments have started.
- Data-sharing regulations are in place; interested investigators may contact the principal investigator for details of data sharing regulations [drkameshwarprasad@gmail.com].

Why was the cohort set up?

This cohort, nicknamed 'LoCARPoN' (Longitudinal Cognition and Aging Research on Population of the National capital region, in Hindi meaning 'dedication to the public') was set up because this is needed for India. The life expectancy at birth in India has increased from 54 years in 1980 to 68 years in 2015. This has led to a demographic transition in which the proportion of persons aged 60 years or above increased to an estimated 134 million in 2020.[1,2] Concurrent with the demographic transition there is an epidemiological transition, leading to the dominance of non-communicable diseases (NCDs) as cause of death and disability-adjusted life-years (DALYs). Globally neurological disorders are leading causes of DALYs, accounting for approximately 10% of the burden of disease; most of these DALYs arise from stroke(42%) and dementia(10%).[3] Moreover, these disorders pose a risk for each other: stroke doubles the risk of dementia, and the dementias very often have a vascular component, ranging from 61% in fronto-temporal dementia to 80% in Alzheimer's disease. Vascular and neurodegenerative pathologies interact synergistically, even in asymptomatic individuals.[4]

The incidence and prevalence of stroke and dementia are falling in the developed world and rising in the developing world.[5] This divergence cannot be explained only by differences in genetics and hence must be due to biological, environmental or social factors, which might lend themselves to prevention. Population-based cohort studies conducted in high-income countries, with a focus on neurological disorders like the Framingham Heart Study[6] or the Rotterdam Study,[7] have identified risk factors for stroke and dementia. These and other studies generated risk prediction models and scoring systems, which help target prevention efforts. However, external validation of existing models showed that prediction models developed in high-income countries cannot directly be extrapolated to low- and middle-income countries. 'It is essential to develop accurate and valid methods for successful prediction of dementia risk to ensure that right people are targeted for intervention' in low- and middle-income countries.[8] Moreover, there are unique putative protective factors in India (like yoga, vegetarianism, Indian diet, multi-lingualism, periodic fasting). Further, no population-based cohort integrated genomics or magnetic resonance imaging (MRI) neuroimaging in stroke and dementia research in India.

The study of a northern Indian population aged 50 years or above had the following objectives:

i. to determine the incidence of stroke and dementia in community-dwelling adults;
ii. to characterize diet, neuropsychological functioning, dental status, cardiovascular health, and anthropometry;
iii. to obtain improved and locally applicable quantitative estimates and thresholds of major risk factors for stroke and dementia;
iv. to develop risk prediction models for individuals at higher risk of developing stroke (ischaemic or haemorrhagic) or dementia, to allow targeted prevention strategies;
v. to discover and validate novel biomarkers using recent technological advances in genomics, proteomics and neuroimaging for early detection and prevention of mild cognitive disorders and dementia.

The study centre was located in All India Institute of Medical Sciences (AIIMS), New Delhi, India. The selected field sites, Vasant Kunj and Munirka, were 5 and 7 kilometres, respectively, away from the cohort study centre at AIIMS. The field sites were residential colonies developed by a public authority, Delhi Development Authority, and part of the South-West district of Delhi, with a total population of 2.3 million. According to the Census 2011, the population of Vasant Kunj consisted of 35 354 persons, mostly from the upper-middle class. The entire area was divided into five sectors and each sector was further subdivided into a variable number of pockets ranging from 3 to 11 pockets. Each pocket had a Residents' Welfare Association (RWA). Considering the local travel difficulties, all participants were provided free transport facility from their homes to the study centre and back. Initially, Vasant Kunj was the selected field site. However, in order to reach the intended sample size in a timely manner, the adjoining area of Munirka was subsequently included.

The study was approved by the Institutional Ethics Committee of All India Institute of Medical Sciences, New Delhi, India (reference number: IEC/NP-53/2014 RP-12/2014, dated 15 May 2014). Written informed consent was obtained from both the community leaders and the participants for assessment.

Who is in the cohort?

Inclusion criteria

The participants of this study had to meet all of the following inclusion criteria:

i. residing in the selected geographical area;
ii. being aged 50 years or above;
iii. consenting to participate.

Recruitment

The research workers, along with a permission letter from the presidents or secretaries of the RWAs, went to each home in the community to ascertain the presence of eligible individuals. Potential participants were provided an information leaflet (in English and Hindi), followed by personal interaction. Researchers sought written informed consent from eligible participants. Consenting participants were consecutively enrolled and administered a household interview schedule. Participants were given an appointment, as per their convenience, for fasting blood collection at home and transport to the study centre at AIIMS, New Delhi. A flow chart of participant recruitment is given in Figure 1. As per 7383 household visit records, 12 250 individuals were found eligible. Of these, 8858 (72.3%) individuals were enrolled in the study and 7505 (61.3%) participants visited the study centre for assessments completing baseline inclusion. Table 1 shows no meaningful differences between those who did and did not complete assessments. Non-consenting households refused to provide information. Information was not available from non-accessible households. We therefore provide a comparison between the respondents and an urban population of Census 2011(Supplementary Table S1, available as Supplementary data at *IJE* online). In our study sample, the proportions of adults aged 50–60 years and those with low levels of education were less than in the Census. However, all population characteristics are present in adequate numbers to permit analysis.

How often have they been followed up?

Participants will be followed up every 6 months by telephone. The first follow-up assessment was completed. The telephone interview by trained interviewers relies on the questionnaire to record the occurrence of self-reported events, including transient ischaemic attack, stroke, myocardial infarction, hospitalisation, any surgery, fall, fracture, cancer, incidents of hypertension, diabetes, memory problems and death. The events thus recorded are verified by relevant records, which are placed before the endpoint committee for adjudication. Further 6-monthly follow-up interviews by telephone are ongoing (Supplementary Table S2, available as Supplementary data at *IJE* online). The in-person 4-year follow-up is due to be started. Our social workers are planning to go door to door, as soon as the Covid-19 situation permits. Again, participants are provided free transport to the study centre to minimize the loss to follow-up.

What has been measured?

Questionnaires

Validated questionnaires were used to collect data on household and individual's demographic and clinical characteristics. This information was obtained during the home visit and included age, sex, education, family size, marital status, current and former employment, economic conditions and self-reported health conditions. Activities of daily living were assessed using the everyday abilities scale for India (EASI),[9] physical activity with the International Physical Activity Questionnaire (IPAQ)[10] and duration of yoga practice with a custom-built questionnaire. The assessment of handedness was conducted using the Edinburgh Handedness questionnaire,[11] followed by Mini-Mental Status Examination.[12]

Validated food frequency questionnaires (FFQ),[13] modified with local food habits, were used to collect the individual's dietary habits. In addition, we used two 24-h dietary recalls to gather information on the current diet. The nutrient analysis was performed with DietCal Software version 9 (Profound Tech Solutions).

A self-reported history of stroke, transient ischaemic attack (TIA), diabetes mellitus, high blood pressure and myocardial infarction with the age at occurrence, and data on past episodes of unconsciousness, limb weakness, head injury and any major acute illness were collected. The family history of cardiovascular events, diabetes mellitus and memory-related problems was obtained.

Current and former tobacco use (smoking/smokeless) including age at which tobacco use started, years of use, number of cigarettes or bidis smoked per day and any cessation attempts were recorded. Sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI),[14] Berlin's questionnaire,[15] and Morningness Eveningness questionnaire.[16] Questions were asked about the sleeping pattern, duration of sleep, snoring and overall quality of sleep. Below is an overview of the assessments at the study centre which took approximately 3 h including breaks.

Physical examination and anthropometric measurements

Weight was recorded in kilograms by a digital weighing machine, using standing scales supported on a steady surface. Height was measured without shoes, in centimetres, with a stadiometer with the head in the Frankfurt plane positioned at a 90° angle against a metallic metric tape measure mounted on a wall. Abdominal circumference was measured in centimetres with the help of a non-stretchable tape on a horizontal plane 1 cm above the belly button. All measurements were recorded to one decimal

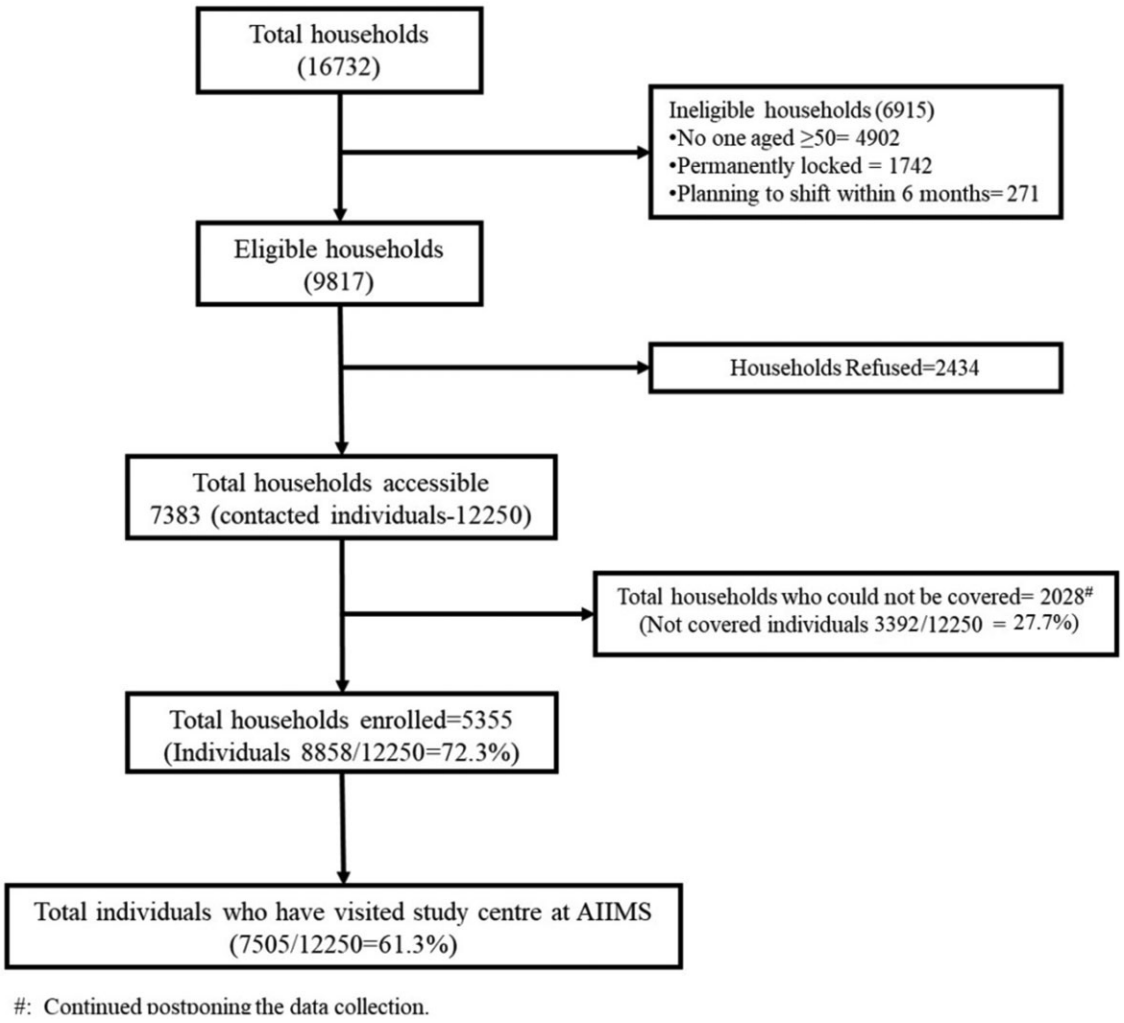

Figure 1 A flow chart of participant recruitment. #: Continued postponing the data collection.

Table 1 Distribution of participants by selected characteristics and visit to study centre

Characteristics	Did not attend the study centre (1353, 15.3%)		Attended the study centre (7505, 84.7%)		*P*-value
	n	%	*n*	%	
Age (mean ± SD) (years)	65.0 ± 9.9		64.6 ± 9.2		0.1057
Female	741	54.8	3825	51.0	0.0109
Marital status					0.0077
Currently married	1092	80.7	6327	84.3	
Widow or widower	226	16.7	988	13.2	
Separated or divorced	19	1.4	105	1.4	
Never married	16	1.2	85	1.1	
Religion					0.7217
Hindu	1253	92.6	6937	92.4	
Sikh	46	3.4	267	3.6	
Christian	18	1.3	116	1.5	
Muslim	19	1.4	78	1.0	
Other	17	1.3	107	1.4	
Mother tongue					0.1206
Hindi	914	67.6	5117	68.2	
Punjabi	245	18.1	1226	16.3	
Other	194	14.3	1162	15.5	
Number of languages (spoken) (mean ± SD)	2.3 ± 0.9		2.6 ± 0.9		0.6894
Number of languages (written) (mean ± SD)	2.2 ± 0.7		2.2 ± 0.7		0.9064
Years of education (mean ± SD)	15.6 ± 7.6		15.6 ± 5.8		0.8884
Highest level of education attained					0.0327
College	1063	78.6	6065	80.8	
Higher secondary	93	6.9	441	5.9	
Secondary	82	6.1	371	4.9	
Diploma/vocational training	45	3.3	289	3.9	
Primary or below primary	52	3.8	291	3.9	
No formal education	18	1.3	48	0.6	
Current/former occupation					<0.0001
Administrative	530	39.2	3394	45.2	
Housewife/homemaker	628	46.4	2207	29.4	
Clerical	21	1.6	96	1.3	
Agricultural/fisheries	3	0.2	8	0.1	
Others	171	12.6	1800	24.8	
Currently on medication	996	73.6	5527	73.6	0.2879
Dietary habit	1177		6565		0.0251
Vegetarian	502	42.6	2795	42.6	
Ovo-lacto vegetarian	167	14.2	759	11.6	
Non-vegetarian	508	43.2	3011	45.8	

place. Blood pressure was measured using an electronic blood pressure instrument (OMRON HEM-8712) three times on the participant's right arm after 5 min of seated rest. We calculated the mean value of the last two blood pressure readings for each participant.

Dental assessment

Participants were administered a standardized oral health questionnaire, and their periodontal examination was recorded using UNC 15 probe and standard methodology in terms of probe depth, clinical attachment loss, plaque index, number of missing/decayed/filled teeth and gingival recession.[17,18]

Blood measurements

Overnight fasting blood samples (10–20 ml) were drawn by venepuncture at the participant's home. Samples were transported within 30 min to the study centre for analysis and

storage. For all participants, fasting levels of blood glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), phosphate, calcium, serum creatinine, uric acid, total cholesterol, high-density lipoprotein (HDL), low-density lipoproteins (LDL), very-low-density lipoprotein (VLDL) and triglyceride levels were estimated in an Erba XL-640 Biochemistry Analyzer. Vitamin D, vitamin B12, folic acid, thyroid-stimulating hormone (TSH) and homocysteine levels were estimated in the Advia Centaur XP Immunoassay system. Haemoglobin A1c(HbA1c) levels were estimated by the HPLC method in a Biorad D10-HbAIC Analyser. High-sensitivity C-reactive protein (hs-CRP), antithrombin-III and cystatin C were analysed in a Nephelemetry analyser. Antithrombin III, protein C and protein S levels were analysed in the Instrumentation Laboratory, ACL Elite Pro coagulation analyser. Complete blood count measurements were carried out in Sysmex 1000i automated haematology analyser.

Echocardiography, electrocardiogram (ECG), and carotid Doppler

Transthoracic echocardiography (MyLab Five Esaote; The Netherlands) was performed by physicians trained in echocardiography. Standard echocardiographic views were acquired using a phased array transducer (1–4 MHz) and representative cine loops and still images were captured and stored for review. We assessed ventricular (systolic and diastolic) function and valve function using 2 D, colour flow and Doppler imaging.[19] Random samples were reviewed by a cardiologist to ensure quality. All abnormal and a fraction of normal echo-images were verified by a cardiologist. ECG was conducted with an SE-1200 Edan 12-lead electrocardiogram standardized at 25 mm/s and 1 mv of amplitude. ECGs flagged as abnormal by the study physician were reviewed by a cardiologist. Carotid Doppler was performed using Mindray L14-6P linear ultrasound transducer as described by Pozniak.[20]

Neurocognitive testing and psychosocial health questionnaires

All the assessments were done by qualified clinical psychologists/neuropsychologists. A detailed cognitive evaluation was done by using validated Indian tools using the following: Auditory Verbal Learning Test,[21] Colour Trail Test,[21] Animal Naming Test,[21] Purdue Pegboard Test,[22] Mini-mental Status Examination,[12,23] Digit Span Test (forward and backward),[24] Block Design test,[25] Geriatric Depression Scale,[26] Anxiety Scale,[27] Social Support Scale and Psychosocial Stress Assessment Questionnaire,[28] as listed in Table 2. The questionnaires were administered at the participant's residence and the neuropsychological assessment was performed at the study centre in Hindi or English.

Operational definition of risk factors

Hypertension was defined as a mean systolic blood pressure > 140 mmHg and/or diastolic blood pressure >90 mm Hg, and/or self-reported physician's diagnosis of hypertension or self-reported current use of antihypertensive medications. Obesity was defined as body mass index (BMI) >30 kg/m2 and overweight as BMI > 25kg/m^2, dyslipidaemia as total cholesterol >200 mg/dl, LDL cholesterol >130 mg/dl or HDL cholesterol <40 mg/dl, diabetes mellitus as fasting glucose >126 mg/dl or HbA1C >6.5% or self-reported use of anti-diabetic medications. Current smoking was defined as smoking at least one cigarette or bidi (local cigarette made of tobacco wrapped in leaves) per day at the time of the survey and quantified by number of cigarettes/bidis smoked daily and history of smoking. Former smokers were defined as those who had not smoked for at least 6 months. Passive smoking was defined as involuntarily breathing air contaminated by tobacco smoke. All the participants with Mini-mental State Examination (MMSE) and Hindi Mental State Examination (HMSE) scores below 26 were referred to a neurologist investigator who re-assessed their score for analysis and evaluation for dementia. Mild cognitive impairment (MCI) was diagnosed using modified International Consensus criteria.[29]

Brain imaging and genome-wide genotyping

The study included measures unique in India in a population-based study addressing stroke or dementia: (i) brain MRI; and (ii) genome-wide genotyping. As on 13 February 2020, 2604 participants had undergone brain MRI at AIIMS, New Delhi, in a 1.5 Tesla MR scanner (GE Discovery 450w, USA) using a 12-channel GEM head coil. The following MRI sequences were performed: (i) Scout localizer T2*GRE sequence; (ii) 3 D T1-weighted structural MRI; (iii) 3 D T2- weighted fluid-attenuated inversion recovery (FLAIR) sequence; (iv) 2 D DTI shell acquisition; (v) 3 D Axial SWAN- phase and mIP images; (vi) 2 D time of flight (TOF) MRA of Brain; (vii) 2 D TOF MRA of Neck; (viii) 2 D PC MRA of neck vessels; (ix) 3 D non-contrast ASL; (x) 2 D Axial T2 propeller. Finally, resting-state functional MRI (2 D rs-fMRI) was conducted. The total time of each subject's scanning session was approximately 55 min (for details, see Supplementary Table S3 and Figure S1, available as Supplementary data at *IJE* online).

Table 2 List of types of data collected and tools used at baseline, and follow-ups

Source	Type of data collected	Data variables and tools used	Participants (*n*)
Baseline (4 January 2016 to 23 July 2019)			
General questionnaire	Demographic	Demographic details including age, sex education, family size, marital status, current and former employment, economic conditions, and self- reported health conditions. Everyday abilities scale for India (EASI), International Physical Activity Questionnaire (IPAQ), duration of yoga practice, Edinburgh Handedness questionnaire, Sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI), Berlin's questionnaire, and Morningness Eveningness questionnaire.	8858
	Dietary	Validated food frequency questionnaires (FFQ), local food habits, two 24-hour dietary recalls	
	Medical history	Individual history: Stroke, transient ischemic attack (TIA), diabetes mellitus, high blood pressure, myocardial infarction each along with the age at occurrence; past episodes or events of unconsciousness, limb weakness, head injury, any major acute illness, and lifestyle behaviors (smoking and alcohol drinking); Family history: Cardiovascular events, diabetes mellitus and memory related problems	7505
	Physical examination and anthropometric measurements	Weight, height, waist and hip circumference, blood pressure, pulse, muscle power, ankle brachial index,	7495
	Dental assessment	Probe depth, clinical attachment loss, plaque index, number of missing/decayed/filled teeth, and gingival recession.	7090
	Blood investigations	Sugar (fasting), SGOT, SGPT, ALP, Creatine, Uric acid, Calcium, Phosphorous, Cholesterol, TG, HDL, LDL, VLDL, Vit.D, Vit.B12, Folic acid, TSH, Antithrombin-3, Homocystin, HSCRP, Cystatine C, HBA1C, Protein C&S, Haemogram, blood grouping;	7498
Medical assessment	Electrocardiogram (ECG) and echocardiography		7446
	Carotid Doppler	Velocity of blood flow in CCA, ICA and ECA; Peak systolic velocity (PSV) and end diastolic velocity (EDV) for CCA, ICA and ECA;. Intimal thickness (IMT) for common carotid artery (CCA); carotid arteries, thrombosis, plaque and/or stenosis	7429

(Continued)

Table 2 Continued

Source	Type of data collected	Data variables and tools used	Participants (*n*)
	Neuropsychological assessment	Auditory verbal learning test,[21] color trail test (A &B),[21] Animal naming test,[21] Purdue pegboard test,[22] Mini-mental status examination,[12,23] Digit span test (forward and backward),[29] Block design test,[25] Color figure maze,[26] Geriatric depression scale,[27] Anxiety scale,[28] Social supportscale,[28] Psychosocial stress assessmentquestionnaire,[29]	7413
Follow-ups	Brain MRI	Every six month telephone interview is done using pre-tested questionnaire to assess occurrence of self-reported events; includes transient ischaemic attack, stroke, myocardial infarction, hospitalization any surgery, fall, fracture, cancer, incidents of hypertension, diabetes and memory problem, and death. The events thus recorded are verified by relevant records, which are placed before the endpoint committee for adjudication	2604
Four-yearly physical follow-ups			
General questionnaire	Demographics	Demographic details: marital status, economic conditions and self-reported health conditions. Everyday abilities scale for India (EASI), International Physical Activity Questionnaire (IPAQ), duration of yoga practice; sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI), Berlin's questionnaire, and Morningness-Eveningness questionnaire	
	Dietary	Two 24-h dietary recalls	
	Medical history	Same as baseline	
	Physical and anthropometric measurements	Same as baseline	
Medical Assessment	Blood investigations	Same as baseline	
	Electrocardiogram (ECG) and echocardiography	Same as baseline	
	Carotid Doppler	Same as baseline	
	Neuropsychological assessment	Same as baseline	
	Brain MRI		
		Sit-to-stand time, timed-up-and-go test, 6-min timed walk test	
		Caregivers interview (to assess care burden)	

For each participant, two aliquots of DNA and one aliquot of plasma and serum were stored. We have secured funding for genome-wide genotyping of all the deeply phenotyped 7505 participants, with the aim of conducting genome-wide association studies for various participant characteristics as well as outcomes. The genotyping work has started and is completed for 412 participants using Illumina chip GSA version 2.0 (with AMD-Additional multi-disease content).

Table 3 Distribution of participants by selected baseline characteristics and sex

Characteristics	Total (7505)		Female (3825, 51.0%)		Male (3680, 49.0%)		*P*-value
	n	%	*n*	%	*n*	%	
Age (mean ± SD) (years)	64.6 ± 9.3		63.2 ± 8.7		65.9 ± 9.5		<0.0001
Age group							<0.0001
50-60	2745	36.6	1593	41.6	1339	31.3	
60-70	2813	37.5	1447	37.9	1576	37.1	
70-80	1562	21.8	661	17.3	1052	24.5	
80 and above	385	5.1	124	3.2	325	7.1	
Marital status							<0.0001
Currently married	6324	84.3	2992	78.2	3335	90.7	
Widow or widower	988	13.2	715	18.7	273	7.4	
Separated or divorced	105	1.4	67	1.8	38	1.0	
Never married	85	1.1	51	1.3	34	0.9	
Religion							0.3776
Hindu	6937	92.4	3539	92.5	3398	92.3	
Sikh	267	3.6	123	3.2	144	3.9	
Christian	116	1.6	65	1.7	51	1.4	
Muslim	78	1.0	40	1.1	38	1.0	
Other	107	1.4	58	1.5	49	1.4	
Mother tongue							0.8600
Hindi	5117	68.2	2626	68.6	2491	67.7	
Punjabi	1226	16.3	614	16.1	612	16.6	
Other	1162	15.5	585	15.3	577	15.7	
Number of languages (spoken) (mean ± SD)	2.6 ± 0.9		2.4 ± 0.9		2.8 ± 0.9		<0.0001
Number of languages (write) (mean ± SD)	2.2 ± 0.7		2.1 ± 0.7		2.3 ± 0.6		<0.0001
Years of education (mean ± SD)	15.6 ± 6.1		15.1 ± 7.5		16.0 ± 3.3		<0.0001
Highest level of education attained							<0.0001
College	6065	80.8	2879	75.2	3186	86.6	
Higher secondary	441	5.9	278	7.3	163	4.4	
Secondary	371	4.9	258	6.8	113	3.1	
Diploma/vocational training	289	3.9	122	3.2	167	4.5	
Primary or below primary	291	3.9	242	6.3	49	1.3	
No formal education	48	0.6	46	1.2	2	0.1	
Current/former occupation							<0.0001
Administrative	3394	45.2	1106	28.9	2288	62.2	
Housewife/homemaker	2207	29.4	2119	55.4	88	2.4	
Clerical	96	1.3	59	1.5	37	1.0	
Agricultural/fisheries	8	0.1	1	0.0	7	0.2	
Others	1800	24.8	540	14.1	1260	34.2	
Currently on medicine	5527	73.6	2789	72.9	2738	74.4	0.1126
Dietary habit	6565		3352		3213		<0.0001
Vegetarian	2795	42.6	1728	51.5	1067	33.2	
Ovo-lacto vegetarian	759	11.6	367	11.0	392	12.2	
Non-vegetarian	3011	45.8	1257	37.5	1745	54.6	
Sleep-related questionnaires, Pittsburgh Sleep Quality Index	3.9 ± 3.1		4.3 ± 3.3		3.5 ± 2.8		<0.0001
Berlin's questionnaires							
Category 1(±)	3530	47.1	1632	42.7	1898	51.6	<0.0001
Category 2(±)	1024	13.7	627	16.4	397	10.8	<0.0001
Yoga	3617		1816		1801		
Practising yoga	1265	35.0	663	36.5	602	33.4	0.0519
Duration (min)	31.3 ± 20.2		31.1 ± 19.7		31.5 ± 20.9		0.7203

(Continued)

Table 3 Continued

Characteristics	Total (7505)		Female (3825, 51.0%)		Male (3680, 49.0%)		*P*-value
	n	%	*n*	%	*n*	%	
Self-reported medical conditions							
Stroke	109	1.5	32	0.8	77	2.1	<0.0001
Transient ischaemic attack	73	1.0	18	0.5	55	1.5	<0.0001
Myocardial infarction or heart attack	323	4.3	75	2.0	248	6.7	<0.0001
Any heart disease	731	9.7	243	6.4	488	13.3	<0.0001
Head injury	1032	13.8	483	12.6	549	14.9	0.004
Migraine	439	5.8	351	9.2	88	2.4	<0.0001
Arthritis	2052	27.3	1384	36.2	668	18.2	<0.0001
Thyroid disorder	1250	16.7	936	24.5	314	8.5	<0.0001
Parkinson's disease	43	0.6	18	0.5	25	0.7	0.230
Seizure disorder	89	1.9	48	1.3	41	1.1	0.573
Breast cancer			63	1.7	NA		
Prostate cancer			NA		32	1.0	
Meningitis	22	0.3	9	0.2	13	0.4	0.340
Tuberculosis	412	5.5	214	5.6	198	5.4	0.680
Fracture during last 5 year	536	7.1	347	9.1	189	5.1	<0.0001
Chronic lung disease	53	0.7	27	0.7	26	0.7	0.990
Bronchial asthma	160	2.1	92	2.4	68	1.8	0.095
Gall bladder stone	215	2.9	136	3.6	79	2.1	<0.0001
Kidney disease	68	0.9	31	0.8	37	1.0	0.370

NA, not applicable.

Endpoints

The primary endpoints of the study were incident stroke and dementia. Secondary endpoints were transient ischaemic attacks, acute myocardial infarction, unstable angina, elective coronary revascularization, hospitalization for heart failure, and falls. The endpoints are captured in a telephone interview conducted every 6 months. Physical follow-ups are planned every 4 years. Their definitions are given in Supplementary Methods, available as Supplementary data at *IJE* online. All non-fatal endpoints were confirmed through records obtained from the participants and discussed in the Events Committee (Supplementary Table S4, available as Supplementary data at *IJE* online). For deaths with inadequate or no records, verbal autopsy was used to supplement or collect information to determine the cause of death.

Quality control

For quality control, besides scrutiny, automated logic and consistency checks, 5% of randomly selected participants were verified independently by the field supervisor to ensure completeness and accuracy of the data. In the initial stages of the study, one of the Rotterdam investigators observed the measurement process at each station and provided feedback. The laboratory participated in external quality control regularly. The LoCARPoN cohort had a biobank with standard operating procedures to ensure the quality of the biological specimens from collection to storage. The LoCARPoN data management system was maintained by two post-doctoral biostatisticians.

What has it found?

The number of cohort participants who completed the assessment at the study centre was 7505 (Table 1), of whom 3825(51%) were females. Mean age was 64.6 [standard deviation (SD) 9.3] years and females[mean 63.2 (SD 8.7) years] were slightly younger than males[mean 65.9 (SD 9.5) years]. The majority were married (84.3%), Hindu (92.4%) and college graduates (80.8%). Most participants had Hindi as their mother tongue, but 91% were multilingual (two languages 36.1%; three 43.1%, more than three 11.8%). More than half of the participants were vegetarian (54.2%: lacto 42.6% and ovo-lacto 11.6%) and 35% practiced yoga regularly (Table 3). Most participants belonged to the upper-middle class [household assets median 21; interquartile range (IQR) 2, range 2 to 29).

The key clinical characteristics, health conditions and prevalence or past history of self-reported morbidities are tabulated in Table 3; the table shows the prevalence of

stroke (1.5%), transient ischemic attacks (1a.0%), meningitis (0.3%), seizures (1.9%), arthritis (27.3%), fractures (7.1%), head injuries (13.8%) and gall bladder stone (2.9%). A history of myocardial infarction or heart disease was more common in males (6.7%) than females (2.0%), as was the self-reported heart disease; males 13.3% and females (6.4%).

The known vascular risk factors are shown in Table 4. Hypertension was the most prevalent risk factor (69%), followed by diabetes (39.5%), obesity (25.5%), smoking (ever 21.1%; current 6.6%) and chewing tobacco (ever 3.6%, current 2.9%). Among participants with hypertension, 74%, 69% and 33% were aware, treated and well controlled, respectively; for diabetes, we found 71% were aware, 66% were treated and 18% were well controlled. Alcohol use was more prevalent among males than females (65.6 % vs 12.6%). All the established vascular risk factors were more prevalent among males except obesity, which was more prevalent among females than males (35% vs 15.7%, respectively). Descriptive statistics of anthropometry and physical examinations by sex are presented in Table 5.

Among 6735 participants with complete data, age and education-adjusted prevalences of mild cognitive impairment (MCI) were (8.42%; 95% CI 7.78 to 9.08%; amnestic 5.55%; non-amnestic 2.87%) using data presented in Table 5.

The first 6-monthly telephone follow-up was completed for 7013 (93.4%) participants on 31 January 2020. Of the total, 164 (2.3%) participants had one or more events (154 single and 10 multiple; total events 176; 37 incident memory problems; 36 surgeries; 21 incident hypertension; 18 incident diabetes; 17 falls; 19 deaths; 12 incident strokes; and five incident myocardial infarctions (Supplementary Table S2, available as Supplementary data at *IJE* online). These results suggest that we will have sufficient power (accounting for an ageing population, high socioeconomic status and a healthy volunteer effect) to conduct

Table 4 Distribution of participants by selected risk factors and sex

Variables	Available cases *n* (F/M)	Total (*n* = 7505) (%)	Female (3825) (%)	Male (3680) (%)	*P*-value
Hypertension	7493 (3817/3676)	5168 (69.0)	2529 (66.3)	2639 (71.8)	<0.0001
Diabetes mellitus	7159 (3648/3511)	2831 (39.5)	1320 (36.2)	1511 (43.0)	<0.0001
Waist-hip ratio >= (0.85 for females and 0.90 for males)	7474 (3807/3667)	5899 (78.9)	2696 (70.8)	3203 (87.3)	<0.0001
Smoking (ever user)	7505 (3825/3680)	1583 (21.1)	78 (2.0)	1505 (40.9)	<0.0001
Smoking (current user)	7505 (3825/3680)	492 (6.6)	35 (0.9)	457 (12.4)	<0.0001
Chewing tobacco (ever user)	7505 (3825/3680)	272(3.6)	34(0.9)	238(6.5)	<0.0001
Chewing tobacco (current user)	7505 (3825/3680)	216(2.9)	29(0.8)	187(5.1)	<0.0001
Alcohol (ever user)	7505 (3825/3680)	2898(38.6)	483(12.6)	2415(65.6)	<0.0001
Alcohol (current user)	7505 (3825/3680)	2618(34.9)	449(11.7)	2169(58.9)	<0.0001
Passive smoker	7505 (3825/3680)	410 (5.5)	264 (6.9)	146 (4.0)	<0.0001
BMI	7486 (3811/3675)	27.5 ± 4.5	28.6 ± 4.8	26.4 ± 3.9	<0.0001
Underweight (<18.5)		69(0.9)	31(0.8)	38(1.0)	
Normal (18.5-25)		2155(28.8)	821(21.5)	1334(36.3)	
Pre-obese(25-30)		3351(44.8)	1626(42.7)	1725(47.0)	
Obese (>30)		1910(25.5)	1333(35.0)	577(15.7)	
Clinical attachment level	7090 (3614/3476)				<0.0001
Dentures		436 (6.2)	208 (5.8)	228 (6.6)	
Normal (<1)		7 (0.1)	2 (0.01)	5 (0.1)	
Mild(1-3)		4705 (66.4)	2561 (70.1)	2143 (61.7)	
Moderate(3-5)		1685 (23.8)	742 (20.5)	943 (27.1)	
Severe(≥5)		257 (3.6)	99 (2.7)	157 (4.5)	
Atrial fibrillation	7466 (3789/3657)	33 (0.4)	16 (0.4)	17 (0.5)	<0.0001
Left ventricular hypertrophy	7446 (3789/3657)	3688(49.5)	2079 (54.9)	1609 (44.0)	<0.0001
Left ventricular ejection fraction	7375(3755/3620)	59.7 ± 6.9	60.4 ± 6.8	59.0 ± 6.9	<0.0001
Right common carotid artery intima media thickness	7422 (3778, 3644)	0.8 ± 0.2	0.7 ± 0.1	0.8 ± 0.17	<0.0001
Left common carotid artery intima media thickness	7412 (3775,3637)	0.8 ± 0.17	0.77 ± 0.14	0.83 ± 0.19	<0.0001
Microbleeds (one or more)	2604 (1208/1396)	376 (14.4)	137 (11.3)	239 (17.4)	<0.0001
White matter hyperintensities [Median, IQR]	401 (186/215)	0.6, 1.4	0.4,1.0	0.7,1.7	0.0169

IQR, interquartile range.

Table 5 Descriptive statistics of anthropometry and physical examination variables by sex

Variables	Available cases *n* (F/M)	Total *n* (%) or mean±SD	Female *n* (%) or mean±SD	Male *n* (%) or mean±SD	*P*-value[a]
Anthropometry and physical examination					
Weight (kg)	7488 (3813/3675)	71.1 ± 13.0	67.9 ± 12.4	74.4 ± 12.7	<0.0001
Height (cm)	7486 (3811/3675)	160.8 ± 9.4	154.1 ± 6.2	167.7 ± 6.9	<0.0001
Waist circumference (cm)	7475 (3807/3668)	91.8 ± 10.4	89.5 ± 10.8	94.3 ± 9.4	<0.0001
Hip circumference (cm)	7474 (3807/3667)	99.7 ± 10.2	101.3 ± 11.1	98.1 ± 8.8	<0.0001
Participants use wheelchair, walker or stick	7488 (3817/3671)	267 (3.6)	140 (3.7)	127 (3.5)	0.4403
Gait abnormal	7479 (3813/3666)	228 (3.0)	112 (2.9)	116 (3.2)	0.4755
Pulse rate (per min)	7488 (3816/3672)	76.4 ± 12.1	77.6 ± 11.7	75.1 ± 12.3	<0.0001
Carotid bruits	7473 (3808/3665)	68 (0.9)	25 (0.7)	43 (1.2)	0.0627
Ankle oedema	7431 (3787/3644)	591 (8.0)	395 (10.4)	196 (5.4)	0.0002
Brachial BP (left) (mmHg)	7310 (3718/3592)	136.4 ± 19.6	135.4 ± 20.2	137.4 ± 18.9	<0.0001
Posterior tibial BP (left ankle) (mmHg)	7189, 3632/3557	137.3 ± 23.5	134.3 ± 23.2	140.3 ± 23.5	<0.0001
Posterior tibial BP (right ankle) (mmHg)	7223, 3662/3561	138.7 ± 23.9	135.9 ± 23.4	141.5 ± 23.8	<0.0001
Dorsalis pedis BP (left ankle) (mmHg)	7288, 3714/3574	137.0 ± 23.5	134.5 ± 23.2	139.6 ± 23.6	<0.0001
Dorsalis pedis BP (right ankle) (mmHg)	7287, 3714/3573	138.2 ± 24.9	135.6 ± 23.8	140.9 ± 25.8	<0.0001
Body fat (%)	7438 (3782/3656)	36.2 ± 7.7	40.6 ± 5.6	31.6 ± 6.7	<0.0001
Visceral fat (%)	7447 (3786/3661)	14.4 ± 7.7	13.0 ± 8.2	14.7 ± 7.0	<0.0001
Body age (years)	7447 (3732/3615)	67.6 ± 9.6	70.8 ± 8.7	64.2 ± 9.3	<0.0001
Resting metabolism (kcal)	7447(3786/3661)	1466.0 ± 234.3	1343.3 ± 187.2	1593.0 ± 209.2	<0.0001
Neuro-cognitive tests					
A: Mini Mental State Examination score	7380 (3758/3622)	28.4 ± 2.1	28.2 ± 2.3	28.6 ± 1.8	<0.0001
B: Auditory Verbal Learning Test (Number of hits)					
A1	7252 (3695/3557)	5.4 ± 1.8	5.8 ± 1.8	5.2 ± 1.7	<0.0001
A2	7240 (3690/3550)	7.7 ± 2.1	8.1 ± 2.1	7.3 ± 1.9	<0.0001
A3	7218 (3680/3538)	8.8 ± 2.2	9.3 ± 2.2	8.4 ± 2.1	<0.0001
A4	7182 (3664/3518)	9.5 ± 2.3	10.0 ± 2.3	9.0 ± 2.2	<0.0001
A5	7173 (3657/3516)	10.1 ± 2.5	10.6 ± 2.4	9.5 ± 2.4	<0.0001
B	7159 (3652/3507)	4.4 ± 1.9	4.6 ± 1.9	4.1 ± 1.8	<0.0001
Immediate recall-A	7151 (3648/3503)	8.6 ± 2.8	8.9 ± 2.7	7.6 ± 2.7	<0.0001
Delayed recall-A	7120 (3631/3489)	8.2 ± 2.9	8.9 ± 2.8	7.5 ± 2.9	<0.0001
Hits	7116 (3629/3487)	13.6 ± 2.0	13.8 ± 1.9	13.3 ± 2.3	<0.0001
C: Performance on Purdue Pegboard					
Overall average score	7197 (3665/3532)	14.6 ± 2.9	14.9 ± 2.9	14.2 ± 2.9	<0.0001
D: Colour Trail Test (time in s)					
Colour Trail Test 1	7009 (3561/3493)	82.8 ± 41.6	84.8 ± 43.8	80.7 ± 39.1	<0.0001
Colour Trail Test 2	6819 (3407/3412)	152.2 ± 73.9	156.0 ± 76.1	148.4 ± 71.4	<0.0001
E: Digit Span Forward					
(median, IQR)		(5.0, 1.0)	(5.0, 2.0)	(6.0, 1.0)	<0 .0001
Score <=3, *n* (%)	7281 (3704/3577)	130 (1.8)	98 (2.7)	32 (0.9)	<0.0001
F: Digit Span Backward					
(median, IQR)		(4.0, 1.0)	(4.0, 1.0)	(4.0, 2.0)	<0.0001
Score <=2, *n* (%)	7271 (3699/3572)	626 (8.6)	413 (11.2)	213 (6.0)	<0.0001
G: Block Design Test (average score)	7076 (3585/3491)	15.04 ± 6.2	14.37 ± 5.9	15.73 ± 6.3	<0.0001
H: Animal Naming Test score					
<7, *n* (%)	7310 (3720/3590)	265 (3.6)	139 (3.7)	126 (3.5)	0.604
Neuropsychological tests					
A: Geriatric Depression Scale	7321 (3698/3568)				
Normal (0-9), *n* (%)		6206 (84.7)	3063 (82.2)	3143 (87.4)	<0.0001
Mild (10-19) , *n* (%)		929(12.7)	550(14.8)	379(10.6)	
Severe (20-30) , *n* (%)		186(2.6)	114(3.0)	72(2.0)	
B: Anxiety score (median, IQR)	7309 (3721/3588)	(1.0,3.0)	(2.0,4.0)	(1.0,3.0)	<0.0001
Score >7, *n* (%)		245 (3.4)	142 (3.8)	103 (2.9)	0.0248

(Continued)

Table 5 Continued

Variables	Available cases *n* (F/M)	Total *n* (%) or mean±SD	Female *n* (%) or mean±SD	Male *n* (%) or mean±SD	*P*-value[a]
C: Social Support score (median, IQR)	7293 (3712/3581)	(6.0, 1.0)	(6.0, 1.0)	(6.0, 1.0)	0.2253
D: Psychosocial Stress Assessment score (number of adverse events in past 1 year)	7311 (3721/3590)				
No event , *n* (%)		3818 (52.2)	1915 (51.5)	1903 (53.0)	0.417
One event, *n* (%)		2246(30.7)	1162(31.2)	1084(30.2)	
More than one event, *n* (%)		1247(17.1)	644(17.3)	603(16.8)	

Available case number (*n*) is variable as some participants' data on some variables were not recorded; '*n*' refers to number of participants with available data for a given characteristic.

[a]*P*-value was calculated using the chi square test/Fisher's exact test statistic for categorical variables or using unpaired t test/Kruskal-Wallis Test statistic for continuous variables.

meaningful longitudinal analyses of incident memory problems and stroke within a few years.

What are the main strengths and weaknesses?

The LoCARPoN cohort derived its strength from a broad range of collaboration among neurologists, cardiologists, epidemiologists, dentists, biostatisticians, geneticists, neuroimaging and neuropsychologists from a top medical institution of the country. This was the first prospective population-based cohort of middle-aged and old adults from India, which integrates genomics (genome-wide genotyping), environment (air pollution data) and participants' lifestyle (anthropometric data, neuropsychology, diet and dental health) to investigate stroke and dementia. Besides established factors, it investigates the association of several unique Indian factors (like yoga, vegetarianism, Indian herbs and spices in diet, multilingualism, periodic fasting etc.) with stroke and dementia.

One of the strengths of this cohort study is the deep phenotyping, which included structure and function of the heart (electrocardiogram, echocardiography) as well as the brain (MRI including tractography, neuropsychological assessment) and its vessels (carotid Doppler and MRI measures). The LoCARPoN cohort had recruited participants who were generalizable to the lower-middle and higher class urban population of Delhi; findings are generalizable to many residents of large urban areas of North India (i.e. about 66 million people for the year 2020).[2]

The management structure of the study consisted of a team of Indian investigators, international investigators from the Rotterdam Study, an operations committee of investigators with a well-qualified and experienced research manager, an events committee and an International Advisory Committee.

The weaknesses of this cohort study are that urban poor were under-represented. To address this issue, a rural component of the study (sample size 7500) will be added which adequately represents the semi-urban and rural populations. Also, the study did not include age-related outcomes such as vision, hearing, skin and cancer. The study had measures of social support, occupation and socioeconomic status in detail but information on financial status, family relationship quality and religious practice was not obtained.

Can I get hold of the data? Where can I find out more?

LoCARPoN study data can be made available to interested researchers upon request. Requests can be directed to the principal investigator, Prof. Kameshwar Prasad [drkameshwarprasad@gmail.com] or visit the study website for more information [www.aiimscohortstudy.com], email: [aiimscohortstudy@gmail.com]. We were unable to place the data in a public repository due to legal and ethical restraints. Sharing of individual participant data was not included in the informed consent of the study.

Supplementary Data

Supplementary data are available at *IJE* online.

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Conflict of interest

Authors have no conflict of interest to declare.

References

1. Census of India. Search Details. 2011. http://censusindia.gov.in/pca/Searchdata.aspx (30 March 2020, date last accessed).
2. National Commission on Population, Ministry of Health & Family Welfare, Nirman Bhawan, New Delhi – 110011. Census of India 2011: Population Projections for India and States 2011 – 2036. Report of the Technical Group on Population Projections, November, 2019. https://nhm.gov.in/New_Updates_2018/Report_Population_Projection_2019.pdf (30 March 2020, date last accessed).
3. Kissimova-Skarbek K. Global, regional, and national burden of Alzheimer's disease and other dementias, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;**18**:88–106.
4. Rabin JS, Schultz AP, Hedden T *et al.* Interactive associations of vascular risk and β-amyloid burden with cognitive decline in clinically normal elderly individuals: Findings from the Harvard aging brain study. *JAMA Neurol* 2018;**75**:1124–31.
5. James SL, Abate D, Abate KH, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The Lancet* 2018;**392**:1789–858.
6. Tsao CW, Vasan RS. Cohort Profile: The Framingham Heart Study (FHS): overview of milestones in cardiovascular epidemiology. *Int J Epidemiol* 2015;**44**:1800–13.
7. Ikram MA, Brusselle GG, Murad SD *et al.* The Rotterdam Study: 2018 update on objectives, design and main results. *Eur J Epidemiol* 2017;**32**:807–50.
8. Stephan BC, Pakpahan E, Siervo M *et al.* Prediction of dementia risk in low-income and middle-income countries (the 10/66 Study): an independent external validation of existing models. *Lancet Glob Health* 2020;**8**:e524-3, e535.
9. Fillenbaum GG, Chandra V, Ganguli M *et al.* Development of activities of daily living scale to screen for dementia in an illiterate rural older population in India. *Age Ageing* 1999;**28**:161–68.
10. Craig CL, Marshall AL, Sjöström M *et al.* International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* 2003;**35**:1381–95.
11. Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 1971;**9**:97–113.
12. Folstein MF, Folstein SE, McHugh PR. Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;**12**:189–98.
13. Thimmayamma BVS. Diet survey methods. In: Thimmayamma BVS (ed). *A Handbook of Schedule and Guidelines in Socio-Economic and Diet Survey.* New Delhi: National Institute of Nutrition, Indian Council of Medical Research, 1987.
14. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989;**28**:193–213.
15. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med* 1999;**131**:485–91.
16. Adan A, Almirall H. Horne & Östberg. Morningness-eveningness questionnaire: a reduced scale. *Pers Individ Diff* 1991;**12**:241–53.
17. Zimmermann H, Hagenfeld D, Diercke K *et al.* Pocket depth and bleeding on probing and their associations with dental, lifestyle, socioeconomic and blood variables: a cross-sectional, multicenter feasibility study of the German National Cohort. *BMC Oral Health* 2015;**15**:7.
18. Machado V, Botelho J, Amaral A *et al.* Prevalence and extent of chronic periodontitis and its risk factors in a Portuguese subpopulation: a retrospective cross-sectional study and analysis of Clinical Attachment Loss. *Peer J* 2018;**6**:e5258.
19. Oh JK, Kane GC, Seward JB *et al. The Echo Manual,* 4th edn. Lippincott Williams & Wilkins, (LWW), Philadelphia, 2018
20. Pozniak MA, Allan PL. *Clinical Doppler Ultrasound E-Book: Expert Consult: Online.* Livingstone (Edinburgh, Scotland) and J & A Churchill (London, England): Elsevier Health Sciences, 2013.
21. Rao SL, Subbakrishna DK, Gopukumar K. *NIMHANS Neuropsychology Battery Manual.* Bangalore, India: National Institute of Mental Health and Neurosciences, 2004.
22. Reddon JR, Gill DM, Gauk SE, Maerz MD. Purdue Pegboard: test-retest estimates. *Percept Mot Skills* 1988;**66**:503–06.
23. Tiwari SC, Tripathi RK, Kumar A. Applicability of the Mini-mental State Examination (MMSE) and the Hindi Mental State Examination (HMSE) to the urban elderly in India: a pilot study. *Int Psychogeriatr* 2009;**21**:123–28.
24. Pershad D, Verma SK. *Handbook of PGI Battery of Brain Dysfunction (PGI–BBD).* Agra, India: National Psychological Corporation, 1999.
25. Hutt ML. The Kohs block-design tests, a revision for clinical practice. *J Appl Psychol* 1932;**16**:298–307.

26. Yesavage JA, Brink TL, Rose TL *et al*. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;**17**:37–49.
27. Yadav AK. Designing and validation of evidence-based questionnaire in English and Hindi for a population-based cohort study in North India. PhD thesis. Department of Neurology, New Delhi: All India Institute of Medical Sciences, 2020.
28. Rosengren A, Hawken S, Ounpuu S *et al*. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13 648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;**364**:953–62.
29. Frank AR, Petersen RC. Mild cognitive impairment. *Handb Clin Neurol* 2008;**89**:217–21.