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SPECIAL ARTICLE

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Design and methodology of the harmonized diagnostic assessment of dementia for the longitudinal aging study in India: Wave 2

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Abstract

The rising burden of dementia calls for high-quality data on cognitive decline and dementia onset. The second wave of the Harmonized Diagnostic Assessment for the Longitudinal Aging Study in India (LASI-DAD) was designed to provide longitudinal assessments of cognition and dementia in India. All Wave 1 participants were recruited for a follow-up interview, and a refresher sample was drawn from the Longitudinal Aging Study in India, a nationally representative cohort of Indians aged 45 and older. Respondents underwent a battery of cognitive tests, geriatric assessments, and venous blood collection. Their health and cognitive status were also assessed through an interview with a close family member or friend. Clinical consensus diagnosis was made based on the Clinical Dementia Rating®, and comprehensive data on risk factors of dementia were collected, including neurodegenerative biomarkers, sensory function, and environmental exposures. A total of 4635 participants were recruited between 2022 and 2024 from 22 states and union territories of India, accounting for 97.9% of the population in India. The response rate was 84.0%, and 71.5% of the participants provided venous blood specimen. LASI-DAD provides rich new data to study cognition, dementia, and their risk factors longitudinally in a nationally representative sample of older adults in India. Longitudinal cognitive data, together with longitudinally assessed biomarker data and novel data on sensory function and environmental exposures, provide a unique opportunity to establish associations between risk factors and biologically defined cognitive aging phenotypes.

KEYWORDS

AD biomarkers, aging, Alzheimer's disease, cognitive decline, dementia

Pranali Y. Khobragade and Sarah Petrosyan are co-first authors.
Members of the LASI-DAD Authorship Team and their affiliations are given at the end of Acknowledgments.

INTRODUCTION

The Harmonized Diagnostic Assessment of Dementia for the Longitudinal Aging Study in India (LASI-DAD) is the first nationally representative study of dementia in India, developed to provide a better understanding of the determinants of late-life cognition, cognitive aging, and dementia.[1,2] The sample was drawn from the parent study, the Longitudinal Aging Study in India (LASI), a nationally representative, multidisciplinary study on aging in India[3] that collects comprehensive data on health, as well as social and economic well-being, from over 73,000 adults aged 45 and older. The LASI-DAD adopted the Health and Retirement Study's (HRS) Harmonized Cognitive Assessment Protocol (HCAP) to enable cross-country comparisons but modified the project protocol to make it suitable for the Indian population. The second wave of LASI-DAD data collection is complete, enabling longitudinal assessment of cognition in India. In this article, we describe the design and methodology of the second wave, starting with the study aims and followed by an overview of the study protocol. We highlight the innovations introduced in Wave 2, the sampling strategy for the refresher sample, fieldwork procedures, and sample characteristics, including response rates.

Key points

- The second wave of LASI-DAD provides longitudinal data on late-life cognition and dementia for a nationally representative sample of older adults in India for the first time.
- LASI-DAD's innovative protocol covers not only a rich set of longitudinal cognitive phenotype data but also longitudinally assessed biomarker data, including neurodegenerative biomarkers, and novel data on sensory function and environmental exposures, providing a unique opportunity to study risk factors of dementia.

Why does this paper matter?

The second wave of LASI-DAD collected a longitudinal assessment of cognitive function, dementia status, and their risk factors for a nationally representative sample of older adults in India. As with its first wave, this unique data resource is publicly available for the larger research community. This paper provides essential information on the data collection methods, enabling all interested researchers to use these rich new data for their own scientific investigation.

Purpose of the study

India is the most populous country in the world with over 1.4 billion people.[4] With population aging, the proportion of people aged 60 and above is projected to double in the next 30 years from 10% in 2020 to 19% in 2050.[5] This rise in the older adult population is expected to lead to an increased burden of dementia. From Wave 1 LASI-DAD, we estimated dementia prevalence for adults aged 60 and older at 7.4%,[6] suggesting that over 8.8 million Indians aged 60 and older live with dementia. There are variations in the prevalence of dementia by demographic characteristics such as age, sex, education, urban/rural residence, and state of residence. This heterogeneity underscores the need for targeted approaches aimed at prevention and detection of cognitive impairment and dementia.

Longitudinal assessments of cognitive function and dementia status provide a new scientific resource, allowing researchers to study cognitive decline, dementia incidence, and establish temporality between hypothesized risk factors and cognitive outcomes. Existing insights from longitudinal data are mainly based on research from high-income countries, whereas longitudinal data from India is limited to studies in specific geographic localities or clinical samples. The second wave of the LASI-DAD study provides an opportunity to study key risk factors for dementia and late-life cognitive decline. In developing the Wave 2 protocol, we aimed to collect high-quality data on late-life cognition and dementia (1) to study cognitive changes and dementia onset at the population level and across demographic groups; (2) to investigate risk and protective factors comprehensively; and (3) to estimate the caregiving burden of dementia.

METHODS

Study design

The Wave 2 protocol consists of cognitive tests; informant report; clinical consensus diagnosis; geriatric assessments, including a newly introduced audiometry test; venous blood collection and assays; language assessment; food frequency questionnaire; and environmental assessment. For deceased respondents, an end-of-life interview was administered to an informant who knew the respondent well. All questionnaires and study materials were

TABLE 1 LASI-DAD Wave 2 protocol.

Cognitive tests	Geriatric assessment
Literacy test[a] ($N = 1613$)	Anthropometry measurements
Hindi mental state examination[7] ($N = 4358$)	Blood pressure and pulse ($N = 4431$)
HRS orientation[8] ($N = 4532$)	Height and weight ($N = 4433$)
Word recall[9] ($N = 4507$)	Mid-arm circumference ($N = 4464$)
Delayed recall[9] ($N = 4516$)	Calf circumference ($N = 4456$)
Word list recognition[9] ($N = 4551$)	Head circumference ($N = 4463$)
Digit span forward and backward[10] ($N = 4517$)	Waist circumference ($N = 4396$)
Symbol cancellation[b,11] ($N = 3924$)	Functional status
Logical memory[10] ($N = 4423$)	Activities of daily living ($N = 4358$)
Logical memory delayed[10] ($N = 4422$)	Instrumental activities of daily living ($N = 4475$)
Retrieval fluency ($N = 4497$)[12]	Mobility[a] ($N = 3287$)
Constructional praxis[b,13] ($N = 4023$)	Fall risk[a] ($N = 4467$)
Constructional praxis recall[b,13] ($N = 3482$)	Chair stand test[a] ($N = 2937$)
Raven's standard progressive matrices[b,14] ($N = 4386$)	Mental health
Community Screening Interview for Dementia (CSI-D) ($N = 4469$)[15]	Center for Epidemiological Studies Depression Scale[22] ($N = 4471$)
Go/No-Go test ($N = 3593$)[16]	Beck's anxiety inventory[23] ($N = 4460$)
Judgment and problem solving[a,c,17] ($N = 4421$)	Physical health status
Serial 7's[18] ($N = 3071$)	Health history[c,d] ($N = 4449$)
Trail-making test[a],[19] ($N = 4091$)	Mini Nutritional Assessment[24] ($N = 4430$)
Hand movement sequence test[b,20] ($N = 4348$)	Social activities ($N = 4478$)
Token test[b] ($N = 4361$)[21]	Audiometry test[a] ($N = 4492$)
Language assessment[a] ($N = 496$)	Venous blood specimen ($N = 3202$)
Informant report	**Food frequency questionnaire[a]**
Informant demographics ($N = 4488$)	Food consumption habits ($N = 4459$)
JORM-IQCODE test[25] ($N = 4489$)	Food frequency ($N = 4454$)
CSI—Community Screening Interview[15] ($N = 4637$)	Ayurvedic herbal supplements ($N = 4443$)
Activities questionnaire ($N = 4486$)	Spice intake ($N = 4447$)
10–66 dementia research group informant questionnaire[26] ($N = 4481$)	**End-of-life interview[a]**
Blessed test—part 1[27] ($N = 4481$)	Information about informant (relationship, gender, years known to the respondent) ($N = 890$)
Blessed test—part 2[27] ($N = 4487$)	Information about Respondent Death (month and year of death, age at death) ($N = 875$)
Judgment and problem solving ($N = 4477$)	JORM—IQ Code Test[25] ($N = 890$)
Caregiver stress and burden[a] ($N = 4479$)	Blessed Test—Parts 1 and 2[27] ($N = 890$)

Abbreviation: HRS, Health and Retirement Study.
[a]New in Wave 2.
[b]Mode of administration modified in Wave 2.
[c]Questions added Wave 2—Judgment and Problem solving: Two questions on similarities and differences, three questions on calculations, one question on judgment.
[d]Health history included brain injury and the following doctor diagnosed conditions: hypertension or blood pressure, diabetes mellitus, type II or high blood sugar, heart diseases, stroke, and neuropsychological or psychiatric problems, such as depression, Alzheimer's/dementia, bipolar disorders convulsions, or Parkinson's.

translated into 12 languages—Hindi, Kannada, Malayalam, Gujarati, Tamil, Punjabi, Urdu, Bengali, Assamese, Odiya, Marathi, and Telugu. Forward and backward translations were conducted to minimize differences due to language. During Wave 2, we used Samsung S6 tablets instead of the mini laptops previously used in Wave 1. The tablets had longer battery life and enabled us to capture images and scan barcodes using one device. A summary of the protocol is presented in Table 1 and the Wave 2 protocol innovations are described below.

Cognitive assessment protocol

The cognitive test battery was kept consistent with the Wave 1 protocol (see Table 1 for the cognitive tests administered in both waves), with a few modifications. First, it was expanded to better capture executive function. Specifically, a trail-making test using shapes and sizes was added.[19] We also modified hand movement sequencing tests (palm-up palm-down movement and

clenched-extended hand movements) to have the respondent use both hands for an added challenge, whereas only one hand was used in Wave 1. Second, we included additional questions on differences (stone and potato) and similarities (table and chair), three additional calculations, and a question to assess problem-solving capacity (what to do if it started raining heavily while out). Third, to better measure literacy, respondents were asked to read a story aloud and answer a series of questions to assess comprehension. Fourth, additional modifications were made to improve cultural relevance. In Wave 1, many respondents were not familiar with a "coconut," used for the object naming task. Therefore, for Wave 2, "coconut" was replaced with "tree." Finally, we administered the symbol cancellation test on a tablet instead of using paper and pencil. Because the tablet screen is smaller than the paper we used, we reduced the number of symbols shown to the respondents on the screen while keeping the size of the symbols the same.

Informant report

We expanded the Wave 1 informant questionnaire to ask questions about the respondent's social behavior and disinhibition (e.g., whether they speak rudely, or laugh or cry for no reason) and their ability to manage emergencies. Additionally, as we aim to assess caregiving burden, we asked whether the informant provides care on an ongoing basis and whether they are primarily responsible for helping the respondent with their daily activities. Caregivers' stress was then assessed through four items from the Perceived Stress Scale,[28] five items from the Center for Epidemiological Studies Depression Scale (CESD),[22] and two questions on psychological overload.[29] Finally, questions measuring positive effects of caregiving,[30] as well as spirituality and religiosity, were included.

Clinical consensus diagnosis of dementia

In Wave 2, we followed the online consensus clinical dementia rating (CDR®) procedure developed in Wave 1,[31] with a few modifications. First, we collected additional information on the respondent's judgment and problem-solving abilities. For refresher samples, clinicians were provided with cross-sectional information as in Wave 1. For follow-up respondents who participated in both waves of data collection, clinicians were provided with longitudinal data. Second, while in Wave 1 each case was rated by three clinicians, in Wave 2 each case was rated by two human clinicians and an artificial intelligence rater trained using the Wave 1 clinical consensus rating.[32] Any inconsistencies between these three ratings were discussed at a virtual clinical consensus conference. When further clarification was needed, such as missing data required for diagnosis, in-person or telemedicine interviews were arranged with clinical experts. After reviewing the online consensus data, clinicians prepared notes and asked clarifying questions to the respondents and informants during the in-person visits or phone calls.

Geriatric assessment

Anthropometry and physical measures were assessed in both waves (Table 1), with a few modifications made in Wave 2. First, questions on grooming and washing clothes were added to bolster the measurement of limitations on instrumental activities of daily living. Second, questions on mobility, fall risk, a health history, including brain injury and doctor-diagnosed health conditions, were added. Third, the 6-min timed walk test from Wave 1 was dropped, as space was often limited for administration. Instead, a repeated chair stand test was included. Finally, a pure-tone audiometry test was administered, using the hearTest from the hearX group on a tablet.[33] The respondent listened through headphones to tones and beeps that varied in pitch, getting softer and louder over time, raising their hand when they heard a tone.

Language assessment

A language assessment was developed in Wave 2 to investigate potential protective effects of multilingualism in cognition. Respondents first reported all the languages they knew. Among respondents who reported knowing two or more languages, the following information was collected for up to three languages: age of acquisition, place of learning, frequency of use, self-report proficiency in understanding, speaking, reading, and writing, and extent of exposure to each language in different settings. To measure objective language proficiency, the respondent narrated a familiar story in all their spoken languages and their responses were recorded. Audio recordings of this narrative are currently being evaluated by language experts.

Food frequency questionnaire

A semi-quantitative food frequency questionnaire (FFQ) was developed in Wave 2 to capture the respondent's eating and drinking habits over the past 12 months. The

FFQ was administered to an informant knowledgeable about food purchased and/or cooked in the household. Information about food consumption habits, as well as the types, amounts, and frequency of foods and beverages consumed by the respondent over the past 12 months, was collected. Spice intake and use of health and ayurvedic health supplements were also assessed.

End-of-life interview

An end-of-life interview was administered to an informant if a respondent who participated in Wave 1 had passed away. Informant information was collected, including their relationship to the deceased respondent, how long they knew the respondent, and how often they were in contact with them over the last year of their life. Month and year of the respondent's death and age at death was also collected. The cognitive status of the respondent before their death was assessed by asking many of the same questions used in the main informant interview: JORM-IQCODE,[25] questions on judgment and problem solving, and Blessed Tests (Part 1 and 2).[27]

Venous blood specimen collection

The Wave 1 venous blood specimen (VBS) collection protocol was followed in Wave 2. Certified and trained phlebotomists drew 17 mL of VBS from respondents. Fasting blood was preferred, and fasting status was noted. We collected five tubes: A and B (each 3.5 mL serum separation tubes with a gel separator), C (2 mL EDTA tube), D (3 mL EDTA tube), and E (5 mL plasma preparation tube). Upon reaching the local laboratory, tubes A, B, and E were centrifuged at 3500 revolutions per minute (rpm) for 10 min. The samples were then shipped to the central Metropolis Laboratory for running blood-based assays. The same whole blood and serum-based assays conducted in Wave 1[34] were implemented in Wave 2. Three additional serum-based assays were added in Wave 2, namely, ferritin, iron, and total iron-binding capacity. The residual serum, plasma, and whole blood samples were separated into aliquots and assigned a unique cryogenic barcode. Later, these samples were shipped to the Department of Biophysics at the All India Institute of Medical Sciences (AIIMS), New Delhi for running neurodegenerative biomarker assays (beta-amyloid 42, beta-amyloid 40, total-tau, phosphorylated tau^{181}, glial fibrillary acidic protein, and neurofilament light). The plasma and serum samples remaining after running the assays were stored in a −80°C deep freezer.

Environmental measurements

Particulate matter air pollution samples from the respondent's homes were collected using Ultrasonic Personal Aerosol Samplers (UPAS) v2.0 with a 2.5-micrometer size selective inlet developed by Access Sensor Technologies.[35] A UPAS monitor was stationed in the kitchen, approximately one meter away from the stove, for 24 h. This instrument uses a battery-powered pump to collect particles on a filter at 1 L/min while recording the real-time air flow rates. From Phase 2 of fieldwork onwards, we stationed an Aranet4 device[36] in the respondent's home for 24 h to record levels of CO_2 (as an indicator of the air exchange in the home), temperature, relative humidity, and barometric pressure. This instrument was placed indoors, near the respondent's sleeping area.

Neuroimaging

For a subsample, we aimed to collect MRI-based neuroimaging data, building on our experience in the Wave 1 neuroimaging pilot study ($N = 137$). As in Wave 1, our Wave 2 protocol measures gray matter volume and cortical thickness (T1-weighted), white matter lesions (FLAIR), resting-state functional connectivity (rs-fMRI), and cerebral microbleeds (T2* SWI). However, there are a few differences in Wave 2: we acquired a single T1-weighted image instead of two; rather than acquiring single-shell DTI, we acquired a multi-shell DWI sequence, allowing for the measurement of both white matter connectivity and microstructure using more advanced biologically informed modeling approaches; and rather than using an axial T2-weighted sequence focused on the hippocampus to aid segmentation of hippocampal subfields, we used a whole-brain isotropic T2-weighted sequence for measuring perivascular spaces (PVS). The acquisition time in Wave 2 was targeted at 40–45 min, rather than 55 min, to reduce the burden on participants.

The number of scanning sites was increased from three sites in Wave 1 to eight sites in Wave 2. These sites were: the National Institute on Mental Health and Neurosciences (NIMHANS) in Bengaluru, Karnataka; NM Medical Center in Mumbai, Maharashtra; Medical College in Kolkata, West Bengal; All India Institute of Medical Sciences in Mangalagiri, Andhra Pradesh; Sanjivini Scanning Solutions in Chandigarh, Punjab; Graphic Era Institute of Medical Sciences in Dehradun, Uttarakhand; Narula Diagnostics, Gurugram, Haryana; and NIMS University Medical College in Jaipur, Rajasthan. Site participation is based on harmonized scanning equipment (3.0 Tesla MRI scanners with 32 head-coils) and successful

implementation of the multi-modal protocol that is based on the Alzheimer's Disease Neuroimaging Initiative (ADNI) MRI protocol.

Sampling strategy

For Wave 2, we aimed to conduct follow-up interviews with all Wave 1 respondents and recruit refresher samples. For follow-up interviews, we collected contact information for both respondents and informants and traced them to their new residences, if they moved. For the recruitment of newly age-eligible respondents, we followed the same sampling strategy as in Wave 1. Specifically, we first stratified the age-eligible LASI samples across state of residence and cognitive impairment risk as assessed within the LASI core interview. We then set the sample size for each state to be proportional to that of the core LASI sample, which is in turn proportional to population size, and randomly drew 50% of individuals at high and low risk of cognitive impairment for each state. We determined whether respondents were at high risk of cognitive impairment based on cognitive test performance and proxy interviews. We also aimed to recruit additional new respondents 64 and older, as we expected higher mortality due to COVID-19. The sample was also expanded from 18 to 22 states and union territories, improving the representativeness of the population (see Figure 1).

Fieldwork procedure

We conducted two pre-tests. The first pre-test, conducted from August 25, 2021 to September 3, 2021, on a sample of 53 respondents from AIIMS, New Delhi, tested the feasibility of new study components, including retinal photography, an audiometry test, a caregiver stress and burden questionnaire, and a food frequency questionnaire. Due to administration difficulties with the retinal photography protocol, we did not proceed with this initiative. The audiometry test protocol was successful;

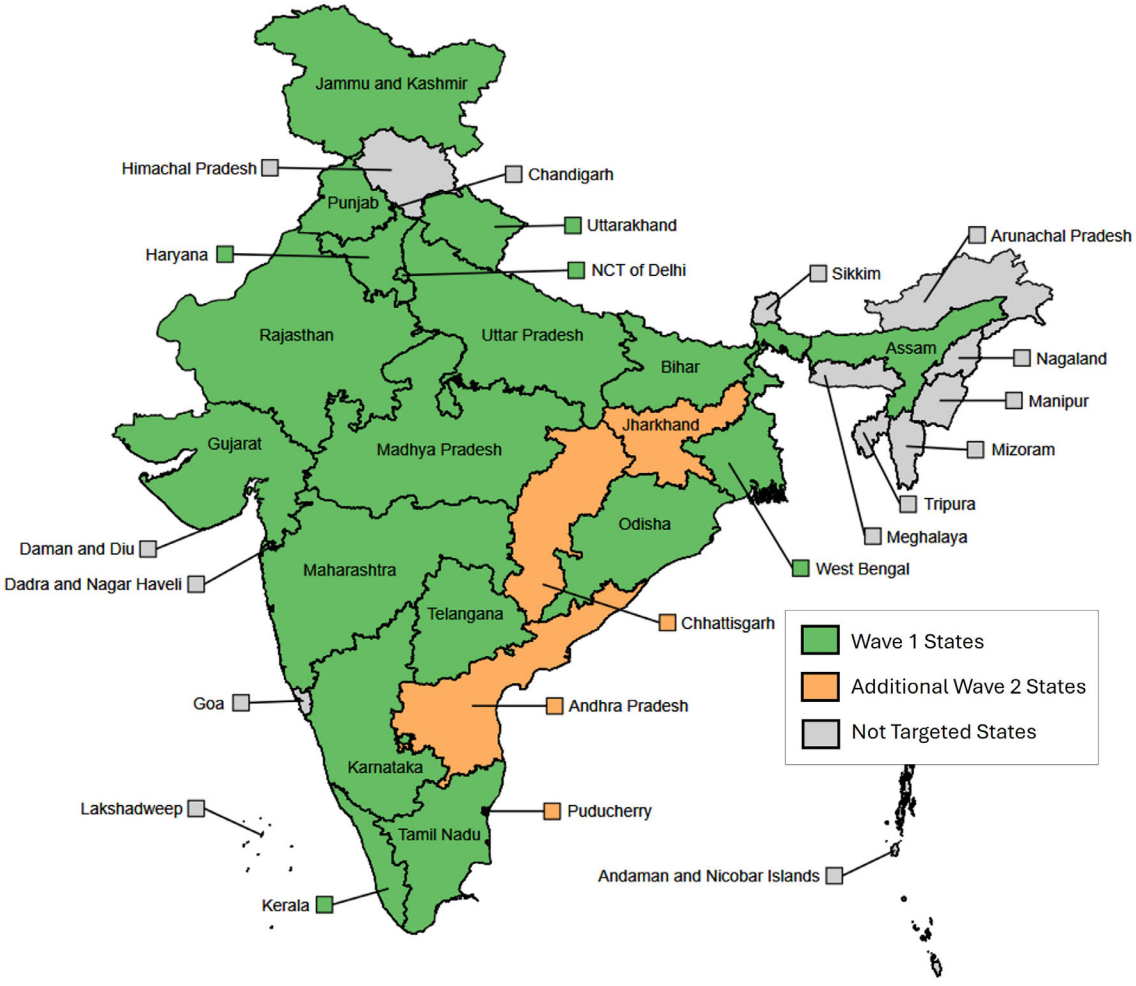

FIGURE 1 LASI-DAD Wave 2 study sample.

however, the administration time was too long. Therefore, the protocol was streamlined to reduce the test time. After reviewing the data, both the caregiver stress and burden questionnaire and the food frequency questionnaire were streamlined to reduce their length.

In the second pre-test, conducted from March 7 to 21, 2022, we administered the entire Wave 2 study protocol to 163 respondents and 147 informants from Delhi, Rajasthan, and Puducherry. Here, we aimed to assess the feasibility of the entire study and test the administration of the protocol on a tablet, as opposed to mini laptops that were used in Wave 1. A total of 131 respondents consented to blood collection, and 57 environmental monitoring devices were placed inside respondent's homes. After this second pre-test, the protocol was further refined. We changed the air pollution sampling design from collecting personal and household samples to only household samples to reduce participant burden. Respondents also found the trail-making test to be too long and complicated, so we reduced the number of images on the screen allowing respondents to better distinguish between the different shapes and sizes. Further, some response options had similar meanings after translation, such as "seldom" and "sometimes." Answer scales were updated to combine these options into one. Once these changes were incorporated, the protocol was finalized for the main data collection.

Wave 2 fieldwork was conducted in three phases from December 2, 2022 to May 27, 2024. Extensive two-week trainings were held before the start of each phase of fieldwork. Field teams consisted of one supervisor and three interviewers for each state. The interviewers were postgraduates with diverse backgrounds, including medical social work, clinical psychology, biotechnology, physiotherapy, and nursing.

Interviewers visited respondents and scheduled appointments for the interviews. Cognitive interviews were completed first on the day of the appointment. Geriatric assessments were scheduled on a separate day to prevent respondent fatigue. Informant interviews were mostly conducted face-to-face, with 2% administered via telephone calls. Once all interviews in a village or ward were completed, we arranged blood draws and advised respondents to fast, if possible. For neuroimaging, once the protocol was established at each center, MRI appointments with the respondents were scheduled. Transportation was organized for the respondents and their accompanying family members on the day of the scan. Data management and review were completed by the study team on a biweekly basis to ensure high-quality data.

On average it took 56 min (SD = 15.59) for cognitive tests, 21 min (SD = 9.17) for informant reports, 35 min (SD = 14.89) for the geriatric assessments, 31 min (SD = 15.99) for the food frequency questionnaire, 10 min (SD = 9.05) for the language assessment, and 10 min (SD = 4.87) for the end-of-life interviews.

TABLE 2 Response rates by follow-up interview and refresher sample.

%	Follow-up interview	Refresher sample
Overall	83.8	83.5
Age (years)		
60–64	83.2	84.7
65–69	82.6	82.8
70–74	86.2	84.1
75–79	84.1	83.2
75+	81.0	82.5
Sex		
Male	84.0	83.2
Female	83.6	83.8
Education		
No school	84.9	87.5
Less than secondary	85.1	82.2
Secondary or more	78.4	67.5
Urbanicity		
Urban	77.3	72.0
Rural	87.7	88.3
Cognitive impairment risk		
Low	83.9	80.4
High	80.3	86.8

Consent

We obtained consent to participate directly from the respondents for the following: cognitive assessment, language assessment, geriatric assessment, environmental monitors; VBS draw, assays, and genomic work; the neuroimaging study; and the in-person/telemedicine CDR® diagnosis. For cognitively impaired respondents, consent was obtained from a close family member, such as a spouse or adult child, who could legally represent the respondent. We obtained the informant's consent to participate in the informant interview, the food frequency assessment, and the end-of-life interview. If the respondent was unable to read the consent forms, the interviewer reads them to the respondent. Respondents unable to provide a digital signature made a cross mark on the tablet screen and had a legally authorized person

TABLE 3 LASI-DAD Wave 2 demographic characteristics of the study participants.

	Full sample		Follow-up sample		Refresher sample	
	N	%	*N*	%	*N*	%
Overall	4635	100	2565	100	2070	100
Age (years)						
60–64	633	20.0	62	3.7	571	38.8
65–69	1261	41.7	829	51.9	432	30.0
70–74	1185	16.8	817	21.8	368	11.0
75+	1556	21.5	857	22.6	699	20.2
Gender						
Male	1945	49.2	1116	50.4	829	47.8
Female	2690	50.8	1449	49.6	1241	52.2
Education						
No education	2598	49.3	1234	41.3	1364	58.5
Less than secondary	1361	32.7	871	36.7	490	28.1
Secondary or more	676	18.0	460	21.9	216	13.4
Rurality						
Urban	1399	29.4	880	33.4	519	24.9
Rural	3236	70.6	1685	66.6	1551	75.1
Cognitive impairment risk						
Low	3445	78.4	2424	95.9	1021	58.3
High	1190	21.6	141	4.1	1049	41.7

Note: Unweighted sample size, weighted percentages. Sample includes respondents who answered both cognitive assessments and informant reports, cognitive assessments only, and informant reports only.

sign on their behalf. The consent materials were translated into 12 languages. Consent and interviews were collected and conducted in the respondent's language.

Sample characteristics and response rate

Of 4096 Wave 1 LASI-DAD respondents, 2565 completed the Wave 2 interview.

Among the Wave 1 follow-up respondents, 324 refused to respond, 225 were unable to be located, and 982 had passed away, resulting in a response rate of 84%. Of 2479 selected refresher respondents, 2070 completed the LASI-DAD interview, with a response rate of 84%. Table 2 presents response rates for the follow-up and refresher samples and Table 3 presents the sample characteristics. For 148 cases, only a cognitive assessment was conducted, as no informant was available. There are 76 cases where only an informant interview was conducted. Respondents were unable to complete the interview if they were bedridden, unable to speak, or experienced psychiatric disorders that hindered them from participating. Altogether, 95% of respondents completed both the cognitive assessment and the informant interview. We observed a mortality rate of 24% among the follow-up LASI-DAD respondents. Among the refresher sample, 409 (16%) refused to participate (see Figure 2).

We created sample weights to account for differential selection probabilities produced by the adopted sampling strategy and adjust for differential non-response. The starting point is the LASI base weight, which accounts for differential probabilities of selection into LASI, adjusted by individual-level non-response. LASI participants have a differential probability of being selected for LASI-DAD, depending on their state of residence, age, and cognitive test performance. We compute this inclusion probability and multiply its inverse by the LASI base weight to obtain a LASI-DAD base weight. We then apply a raking algorithm to produce poststratification weights. The resulting sample weights align sample distributions of key demographic variables to their population benchmarks. Specifically, the following variables are used as raking factors: gender (male/female) × age (60–69/70+); gender × literacy (literate/illiterate); and urbanicity (rural/urban). Benchmark distributions for these variables are taken from the Indian Census 2011 and refer to the population of individuals aged 60 and above in India.

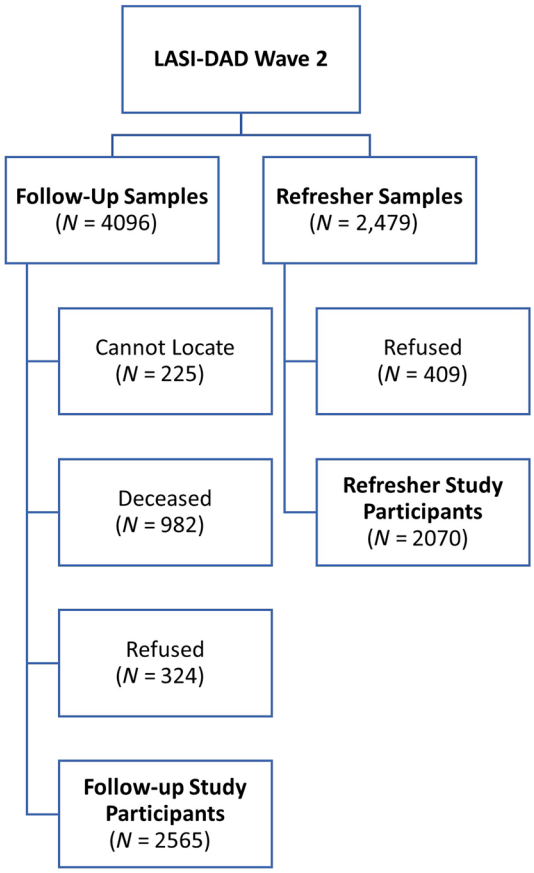

FIGURE 2 LASI-DAD Wave 2 study participant flowchart.

CONCLUSIONS

Wave 2 LASI-DAD provides rich new data to study late-life cognition and dementia, and their risk factors longitudinally in a nationally representative sample of older adults in India. Based on the evaluation of Wave 1 data, further improvements were made to the protocol for measuring executive functioning, judgment, and problem solving. In addition to longitudinal cognitive phenotype data, longitudinally assessed biomarker data provide a unique opportunity to establish associations between risk factors and biologically defined phenotypes related to cognition and dementia. Several innovations were incorporated in the Wave 2 LASI-DAD protocol, including adding an audiometry test, providing objective data on hearing impairment; assessment of caregiving burden; measures of indoor air pollution, temperature, and humidity; using mobile devices; and measurement of neurodegenerative blood-based biomarkers. Wave 2 LASI-DAD will be a public resource for interested scientists around the world at no cost. LASI-DAD data will be publicly available on the LASI-DAD website (g2aging.org/dad) in February 2025. Genotyped data from Wave 1 are available through the National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site, NIAGADS (niagads.org), and neuroimaging data from Wave 1 are available through Alzheimer's Disease Neuroimaging Initiative, ADNI (adni.loni.usc.edu).

AUTHOR CONTRIBUTIONS

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REFERENCES

1. Lee J, Banerjee J, Khobragade PY, Angrisani M, Dey AB. LASI-DAD study: a protocol for a prospective cohort study of late-life cognition and dementia in India. *BMJ Open*. 2019;9(7):e030300. doi:10.1136/bmjopen-2019-030300
2. Lee J, Khobragade PY, Banerjee J, et al. Design and methodology of the longitudinal aging study in India-diagnostic assessment of dementia (LASI-DAD). *J Am Geriatr Soc*. 2020;68(suppl 3):S5-S10. doi:10.1111/jgs.16737
3. Perianayagam A, Bloom D, Lee J, et al. Cohort profile: the longitudinal ageing study in India (LASI). *Int J Epidemiol*. 2022;51(4):e167-e176. doi:10.1093/ije/dyab266
4. UN DESA Policy Brief No. 153: India overtakes China as the world's most populous country. Department of Economic and Social Affairs. United Nations. Accessed June 5, 2024. www.un.org/development/desa/dpad/publication/un-desa-policy-brief-no-153-india-overtakes-china-as-the-worlds-most-populous-country/
5. United Nations, Department of Economic and Social Affairs, population division (2019). *World Population Prospects 2019: Highlights*. United Nations; 2019.
6. Lee J, Meijer E, Langa KM, et al. Prevalence of dementia in India: national and state estimates from a nationwide study. *Alzheimers Dement*. 2023;19(7):2898-2912. doi:10.1002/alz.12928
7. Ganguli M, Ratcliff G, Chandra V, et al. A Hindi version of the MMSE: the development of a cognitive screening instrument for a largely illiterate rural elderly population in India. *Int J Geriatr Psychiatry*. 1995;10(5):367-377. doi:10.1002/gps.930100505
8. Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. *Neuropsychiatry Neuropsychol Behav Neurol*. 1988;1(2):111-117.
9. CERAD. Consortium to establish a registry for Alzheimer's disease: clinical assessment packet for clinical/neuropsychological assessment for Alzheimer's disease. 1987. Accessed June 5, 2024. https://sites.duke.edu/centerforaging/cerad/
10. Wechsler D. *Wechsler Memory Scales—Fourth Edition (WMS-IV): Technical and Interpretive Manual*. Pearson Clinical Assessment; 2009.
11. Lowery N, Ragland JD, Gur RC, Gur RE, Moberg PJ. Normative data for the symbol cancellation test in young healthy adults. *Appl Neuropsychol*. 2004;11(4):218-221. doi:10.1207/s15324826an1104_8
12. Woodcock RW, McGrew KS, Mather N. *The Woodcock–Johnson III (WJIII), Tests of Achievement*. Riverside Publishing Co; 2001.
13. Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry*. 1984;141(11):1356-1364. doi:10.1176/ajp.141.11.1356
14. Raven J. The Raven's progressive matrices: change and stability over culture and time. *Cogn Psychol*. 2000;41(1):1-48. doi:10.1006/cogp.1999.0735
15. Hall KS, Hendrie HC, Brittain HM. The development of a dementia screening interview in 2 distinct languages. *Int J Methods Psychiatr Res*. 1993;3(1):1-28.
16. Gomez P, Ratcliff R, Perea M. A model of the go/no-go task. *J Exp Psychol Gen*. 2007;136(3):389-413. doi:10.1037/0096-3445.136.3.389
17. Morris JC. The clinical dementia rating (CDR): current version and scoring rules. *Neurology*. 1993;43(11):2412-2414.
18. 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(3):189-198. doi:10.1016/0022-3956(75)90026-6
19. Bucks RS. Trail-making test. In: Gellman MD, Turner JR, eds. *Encyclopedia of Behavioral Medicine*. Springer; 2013, pp. 1986-1987. doi:10.1007/978-1-4419-1005-9_1538
20. Mattis S. *Dementia Rating Scale. Professional Manual*. Psychological Assessment Resources; 1988.
21. De Renzi E, Vignolo LA. The token test: a sensitive test to detect receptive disturbances in aphasics. *Brain*. 1962;85:665-678. doi:10.1093/brain/85.4.665
22. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Measur*. 1977;1:385-401.
23. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol*. 1988;56(6):893-897. doi:10.1037//0022-006x.56.6.893

24. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition*. 1999;15(2):116-122. doi:10.1016/s0899-9007(98)00171-3
25. Jorm AF, Jacomb PA. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. *Psychol Med*. 1989;19(4):1015-1022. doi:10.1017/s0033291700005742
26. Prince M, Ferri CP, Acosta D, et al. The protocols for the 10/66 dementia research group population-based research programme. *BMC Public Health*. 2007;7:165. doi:10.1186/1471-2458-7-165
27. Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiatry*. 1968;114(512):797-811. doi:10.1192/bjp.114.512.797
28. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24(4):385-396.
29. Bédard M, Molloy DW, Squire L, Dubois S, Lever JA, O'Donnell M. The Zarit Burden Interview: a new short version and screening version. *Gerontologist*. 2001;41(5):652-657. doi:10.1093/geront/41.5.652
30. Given CW, Given B, Stommel M, Collins C, King S, Franklin S. The caregiver reaction assessment (CRA) for caregivers to persons with chronic physical and mental impairments. *Res Nurs Health*. 1992;15(4):271-283. doi:10.1002/nur.4770150406
31. Lee J, Ganguli M, Weerman A, et al. Online clinical consensus diagnosis of dementia: development and validation. *J Am Geriatr Soc*. 2020;68(suppl 3):S54-S59. doi:10.1111/jgs.16736
32. Weerman A, Jain D. Leveraging machine learning to assist clinicians with clinical dementia rating (CDR) scores in online dementia diagnosis. Center for Economic and Social Research Working Paper No. 2023-010. Accessed August 5, 2024. https://cesr.usc.edu/documents/WP_2023_010.pdf
33. hearTest by hearX Group. Pure tone clinical audiometer. Accessed August 5, 2024. https://www.hearxgroup.com/heartest
34. Lee J, Petrosyan S, Khobragade P, et al. Deep phenotyping and genomic data from a nationally representative study on dementia in India. *Sci Data*. 2023;10(1):45. doi:10.1038/s41597-023-01941-6
35. Volckens J, Quinn C, Leith D, Mehaffy J, Henry CS, Miller-Lionberg D. Development and evaluation of an ultrasonic personal aerosol sampler. *Indoor Air*. 2017;27(2):409-416. doi:10.1111/ina.12318
36. Allen JG, MacNaughton P, Satish U, Santanam S, Vallarino J, Spengler JD. Associations of cognitive function scores with carbon dioxide, ventilation, and volatile organic compound exposures in office workers: a controlled exposure study of green and conventional office environments. *Environ Health Perspect*. 2016;124(6):805-812. doi:10.1289/ehp.1510037

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