Article

An assessment of intrinsic capacity among older Indian adults from the Longitudinal Ageing Study in India

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Intrinsic capacity (IC), which comprises all physical and mental capacities of individuals, is a key component in the World Health Organization's healthy aging framework. A validated IC measure is lacking in India, the most populous country in the world. The aim of this study is to develop an IC measure in older Indian adults using 60,591 participants aged ≥45 years from the Longitudinal Ageing Study in India. Confirmatory factor analysis incorporated 14 items of cognitive, locomotor, psychological, sensory and vitality capacities in a bifactor structure and estimated IC scores (range 0–100). The mean score was 69.7 (95% confidence interval of 69.6 to 69.8) and varied across the 36 states and union territories (range 63.4–77.8). A higher IC score had protective associations with poor self-rated health and functioning limitations after adjusting for demographic factors, socioeconomic status and chronic conditions. The score provides a comprehensive indicator that can be implemented in future aging research and practices in India.

Population aging is an important issue across the world, particularly in low- and middle-income countries. The World Health Organization (WHO) expects the number of people aged 60 years or older to increase from 1 billion in 2020 to 2.1 billion by 2050, with 80% of them living in low- and middle-income countries[1]. India, which has the largest population in the world, is estimated to have nearly 150 million older people (aged 60 years or older) in 2022, accounting for 10% of its total population[2]. This figure is projected to rise to 347 million (20%) by 2050[2]. The large and rapidly increasing numbers of older people in India will have profound implications for many dimension of society including health and social care systems, intergenerational dynamics and inclusive economic security[3]. Given financial and health system constraints, healthy aging research is vital to inform evidence-based policies and practices that cater to the needs of older adults and their families and communities.

In 2015, the WHO proposed a new framework for healthy aging, which is defined as a "process of developing and maintaining functional ability that enables well-being in older age"[4]. Functional ability, which includes "the capabilities that enable people to be and do what they have reason to value", is determined by two other components: intrinsic capacity (IC), which composites "all the mental and physical capacities that a person can draw on and includes their ability to walk, think, see, hear, and remember", and environments, which form the context of individuals' lives[4,5]. This framework moves away from the traditional disease-based approach in biomedicine and focuses on the positive aspects of aging and health, integrating diverse measurements of health and capacities into one component (IC)[6,7]. Over the past decade, a large body of health research has investigated this component, including the development of its conceptualization, operationalization and measurement[8,9].

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Table 1 | Descriptive information on the study population (*N*=60,591)

Category	*N* (%)	IC items	Mean (s.d.)
Age group (years)		Cognitive	
45–49	12,263 (20.2)	Memory (missing, 4,260)	9.3 (3.3)
50–54	10,115 (16.7)	Verbal fluency (missing, 190)	11.6 (4.4)
55–59	9,301 (15.4)	Arithmetic (missing, 4,219)	1.9 (0.8)
60–64	9,426 (15.6)	Orientation (missing, 1,289)	6.9 (1.4)
65–69	8,186 (13.5)	Psychology	
70–74	5,268 (8.7)	Affect (missing, 402)	9.6 (4.0)
75–79	3,110 (5.1)	Sleep (missing, 9)	3.5 (3.5)
80–84	1,715 (2.8)	Sensory	
85+	1,207 (2.0)	Hearing (self-rated) (missing, 7)	0.1 (0.3)
Sex		Eyesight–distal (self-rated) (missing, 24)	3.4 (0.8)
Women	32,482 (53.6)	Eyesight–near (self-rated) (missing, 75)	3.3 (0.8)
Men	28,109 (46.4)	Vision (examined) (missing, 124)	0.4 (0.5)
Place of residence		Locomotor	
Rural	39,770 (65.6)	Balance (missing, 2,538)	0.2 (0.5)
Urban	20,821 (34.4)	Walking speed (missing, 1,439)	5.4 (1.9)
Marital status		Vitality	
Currently married/cohabitation	45,271 (74.7)	Grip strength (missing, 2,675)	21.5 (8.0)
Widowed	13,347 (22.0)	Respiratory function (missing, 9,764)	1.9 (0.7)
Divorced/separated/deserted	892 (1.5)		
Never married	730 (1.2)		
Education (missing, 1)			
Less than primary	35,610 (58.8)		
Primary/middle school	13,850 (22.9)		
Secondary school	8,177 (13.5)		
Higher education	2,953 (4.9)		
MPCE quintile (missing, 274)			
Quintile 1 (poorest)	11,954 (19.8)		
Quintile 2	12,148 (20.1)		
Quintile 3	12,188 (20.2)		
Quintile 4	12,166 (20.2)		
Quintile 5 (richest)	11,861 (19.7)		
Multimorbidity (missing, 39)			
0	30,889 (51.0)		
1	17,046 (28.2)		
2 or more	12,617 (20.8)		
ADL (missing, 22)			
No limitation	52,055 (85.9)		
1+ limitations	8,514 (14.1)		
IADL (missing, 79)			
No limitation	40,682 (67.2)		
1+ limitations	19,830 (32.8)		
Self-rated health (missing, 30)			
Very good/good	25,191 (41.6)		
Fair	25,074 (41.4)		
Poor/very poor	10,296 (17.0)		

'Affect' refers to the total score of the ten-item CES-D scale[39]. 'Sleep' refers to the total score on the Jenkins Sleep Scale[40]. 'Memory' refers to the summary score of immediate and delayed word recall tests[35]. 'Verbal fluency' refers to the total number of unique animals and birds named in 1 min[36]. 'Arithmetic' refers to the total scores of three arithmetic tests[37]. 'Orientation' refers to a total score of time and place orientation tests[38]. 'Hearing' refers to self-reported hearing problems. 'Eyesight–distal' refers to self-reported distance eyesight. 'Eyesight–near' refers to self-reported near eyesight. 'Vision' refers to the results of vision tests (normal, low and blindness). 'Balance' refers to the results of semi and full tandem tests. 'Walking speed' refers to mean walking speed tests. 'Grip strength' refers to the average grip strength of both hands. 'Respiratory function' refers to the mean of forced vital capacity and forced expiratory volume per second.
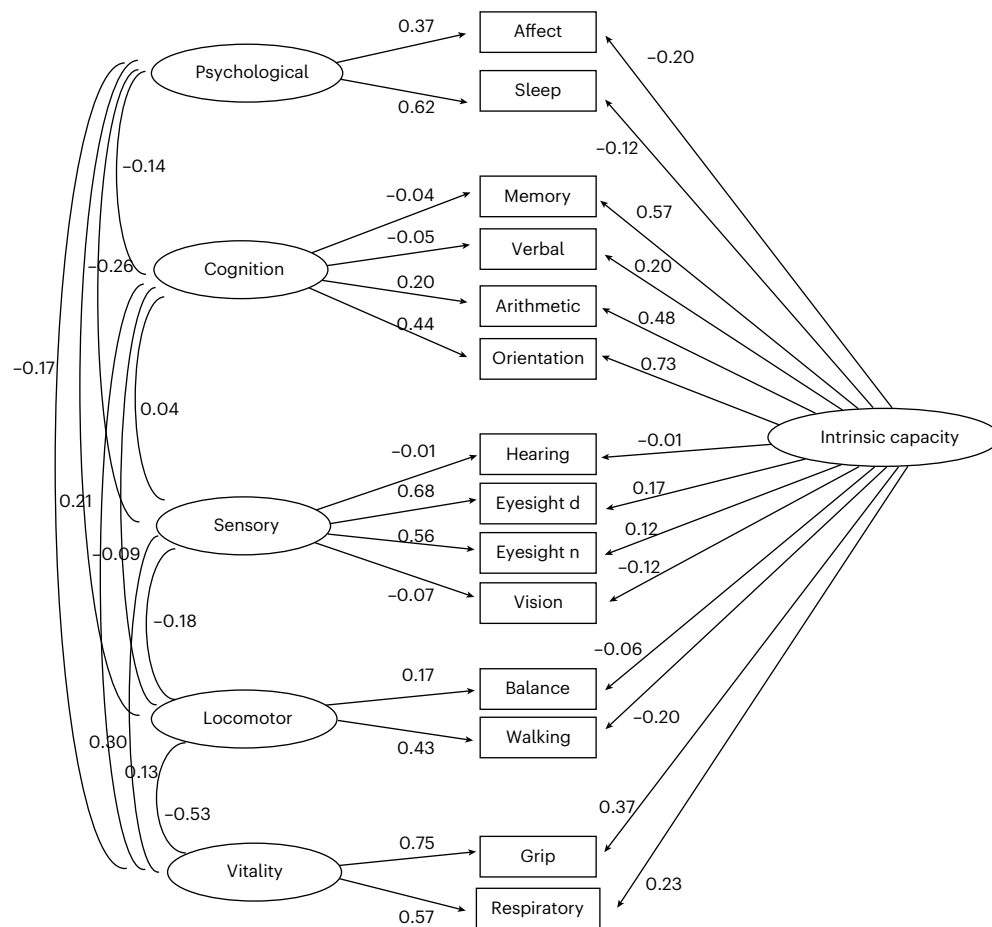
Fig. 1 | Bifactor model of IC. A total of 60,591 participants from the LASI wave 1 were used to estimate the factor structure of IC. Loadings were derived from the general factor of IC and from the five domains (psychological, cognition, sensory, locomotor and vitality). 'Affect' refers to the total score of the ten-item CES-D scale[39]. 'Sleep' refers to the total score on the Jenkins Sleep Scale[40]. 'Memory' refers to the summary score of immediate and delayed word recall tests[35]. 'Verbal' refers to the total number of unique animals and birds named in 1 min (ref. 36). 'Arithmetic' refers to the total scores of three arithmetic tests[37]. 'Orientation' refers to a total score of time and place orientation tests[38]. 'Hearing' refers to self-reported hearing problems. 'Eyesight d' refers to self-reported distance eyesight. 'Eyesight n' refers to self-reported near eyesight. 'Vision' refers to the results of vision tests (normal, low and blindness). 'Balance' refers to the results of semi and full tandem tests. 'Walking speed' refers to mean walking speed tests. 'Grip' refers to the average grip strength of both hands. 'Respiratory' refers to the mean of forced vital capacity and forced expiratory volume per second.

The theoretical framework of the IC construct has been developed to include five domains: cognitive, locomotor, psychological, sensory and vitality[10]. To generate a measure for this construct, several recent studies have utilized data from existing cohort studies of older people and assessed construct validity using measurements related to the five domains[11–16]. Both reflective (latent factor) and formative (composite indicator) approaches have been used to test the IC construct on the basis of different assumptions. Most existing studies employed a reflective approach, which considers IC as an underlying general factor causing changes in observed aspects of physical, cognitive and psychological health[9]. Research teams affiliated with the WHO[11] adopted this approach and applied it to cohort studies in the Gateway to Global Aging platform[11,12,17]. The bifactor structure, which was first developed in the English Longitudinal Study of Ageing (ELSA)[11], has been identified in other cohort studies of older populations in China and Brazil[12,14,18] with cross-cultural validation[19]. The IC measures developed in these studies were found to be associated with established scales of disability and dependence (that is, activities of daily living (ADL) and instrumental activities of daily living (IADL))[11–14,18,20] and are considered to be novel indicators that can provide comprehensive assessments of individual health in aging research and clinical practice[20].

Following the development and validation of IC measures in ELSA and its sister cohort studies, this study focuses on the older population in India, using data from the Longitudinal Ageing Study in India (LASI), one of the latest and largest studies in the Gateway to Global Aging platform[17,21]. On the basis of items related to cognitive, psychological and physical health aligned to the WHO healthy aging framework[5], the aim of this study is to develop an IC measure and establish its construct validity in older Indian adults. The study further examines variation in levels of IC across subgroups with different sociodemographic and health characteristics and investigates the associations between the IC measure and established scales of health and functional limitations.

Results

Table 1 reports descriptive information on the study population. Among the 60,591 participants, one-fifth was aged 45–49 years and only 2% were aged 85 years or older. More than half of the participants were women, and 75% were married or cohabitated. Most participants were from rural areas (66%) and had less than primary education (59%) but lived with no chronic condition (51%). The sample sizes of the 36 states and union territories (UTs) ranged from 788 in Chandigarh to 3,930 in Uttar Pradesh (Supplementary Table 3). About 17% reported poor
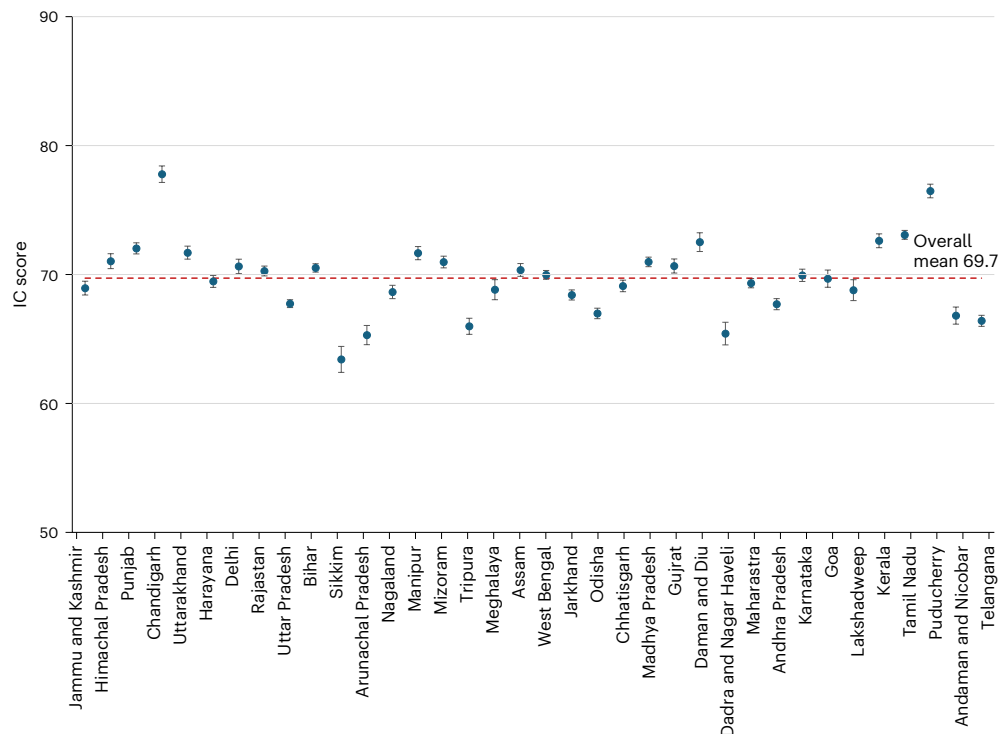
Fig. 2 | Estimated IC scores and 95% CIs by states and UTs in India (adjusted for age and sex). Using linear regression modeling, adjusting for age and sex, estimated IC scores (the center points) and 95% CIs (error bars) for the 36 states and UTs in India were generated on the basis of the LASI wave 1 data ($N = 60,591$).

self-rated health. The percentages of functional limitations were 14% for ADL and 33% for IADL.

The results of factor analysis based on the 30% subsample are provided in Supplementary Tables 1 and 2. On the basis of the cut-off of loading of >0.3, most items were loaded in one latent factor and generally corresponded to the five IC domains in literature (Supplementary Table 1). The hearing and vision items had weak loadings for all latent factors. Given the IC theoretical framework[11], these two items were still included in the sensory domain of the confirmatory factor analysis (CFA) model. On the basis of goodness-of-fit indicators, the bifactor model showed the best fit (a CFI of 0.982, a Tucker–Lewis index (TLI) of 0.969, a root mean square error of approximation (RMSEA) of 0.026 and a standardized root mean square residual (SRMR) of 0.018) and the lowest Bayesian information criterion (BIC) and Akaike information criterion (AIC) values among the four types of factor structure (Supplementary Table 2). When applying the bifactor model to the whole study population (Fig. 1), the model fit remained acceptable (a CFI of 0.982, a TLI of 0.969, an RMSEA of 0.026 and an SRMR of 0.018).

The bifactor model was used to estimate the IC scores. The mean score was 69.4 with a standard deviation of 11.2, while the median score was 70.7 with an interquartile range between 62.6 and 77.4. Figures 2 and 3 show estimated IC scores by the 36 states and UTs, with adjustment for age group and sex. The weighted mean score was 69.7 (95% confidence interval (CI) of 69.6 to 69.8) for the overall population. Higher mean scores were found in Puducherry (76.5 with a 95% CI of 76.0 to 77.0) and Chandigarh (77.8 with a 95% CI of 77.1 to 78.4), while lower mean scores were found in Sikkim (63.4 with a 95% CI of 62.4 to 64.4).

Box plots of the IC scores by subgroup are provided in Supplementary Fig. 1. Table 2 reports the IC scores across subgroups of demographic factors, socioeconomic positions and multimorbidity. Lower IC scores were found in older age groups, women, people with low education and monthly household per capita consumption expenditure (MPCE) levels, rural residences, those not married and those living with chronic conditions. When including all the variables in one model

(model 2), the effect sizes became smaller, but the direction of associations remained the same. Compared to the youngest age group, people aged 85 years or above had lower IC scores by 14 points (−14.43, 95% CI of −15.30 to −13.56). People with tertiary education had better IC scores, by 12 points (11.62, 95% CI of 11.27 to 11.97), than those with less than a primary education. The results of the five domain scores are provided in Supplementary Table 6.

Table 3 presents the associations between the IC scores, general health and functional limitations. A higher IC score had protective associations with poor self-rated health (odds ratio (OR) of 0.97 and 95% CI of 0.97 to 0.97), ADL limitations (0.96, 95% CI of 0.96 to 0.97) and IADL limitations (0.96, 95% CI of 0.96 to 0.96) after adjusting for the covariates. The associations were generally linear (Fig. 4). The ORs of poor health and functional limitations decreased from the second to fifth quintiles and the effect size was particularly strong for IADL limitations (OR of 0.31 and 95% CI of 0.28 to 0.34).

The distributions of demographic factors, socioeconomic positions, multimorbidity, general health and functional limitations, and the estimated latent scores differed across participants with complete ($N = 41,895$; 69%) and incomplete data ($N = 18,696$; 31%) on the 14 IC variables (Supplementary Table 4). Supplementary Table 5 reports the results of sensitivity analyses based on multiple imputation. The associations between IC scores, demographic factors, socioeconomic positions and multimorbidity remained similar when using the latent estimated scores and imputed scores.

Discussion

Using a population-based cohort study of more than 60,000 middle-aged and older adults in India, a measure for IC was developed to incorporate 14 variables related to cognitive, locomotor, psychological, sensory and vitality domains. The bifactor structure, which included five domain latent factors and one general latent factor, showed the best model fit. The estimated IC scores were rescaled to a range between 0 and 100. The mean score was estimated to be 69.7 in older Indian adults and varied across states. Higher scores were found in younger age
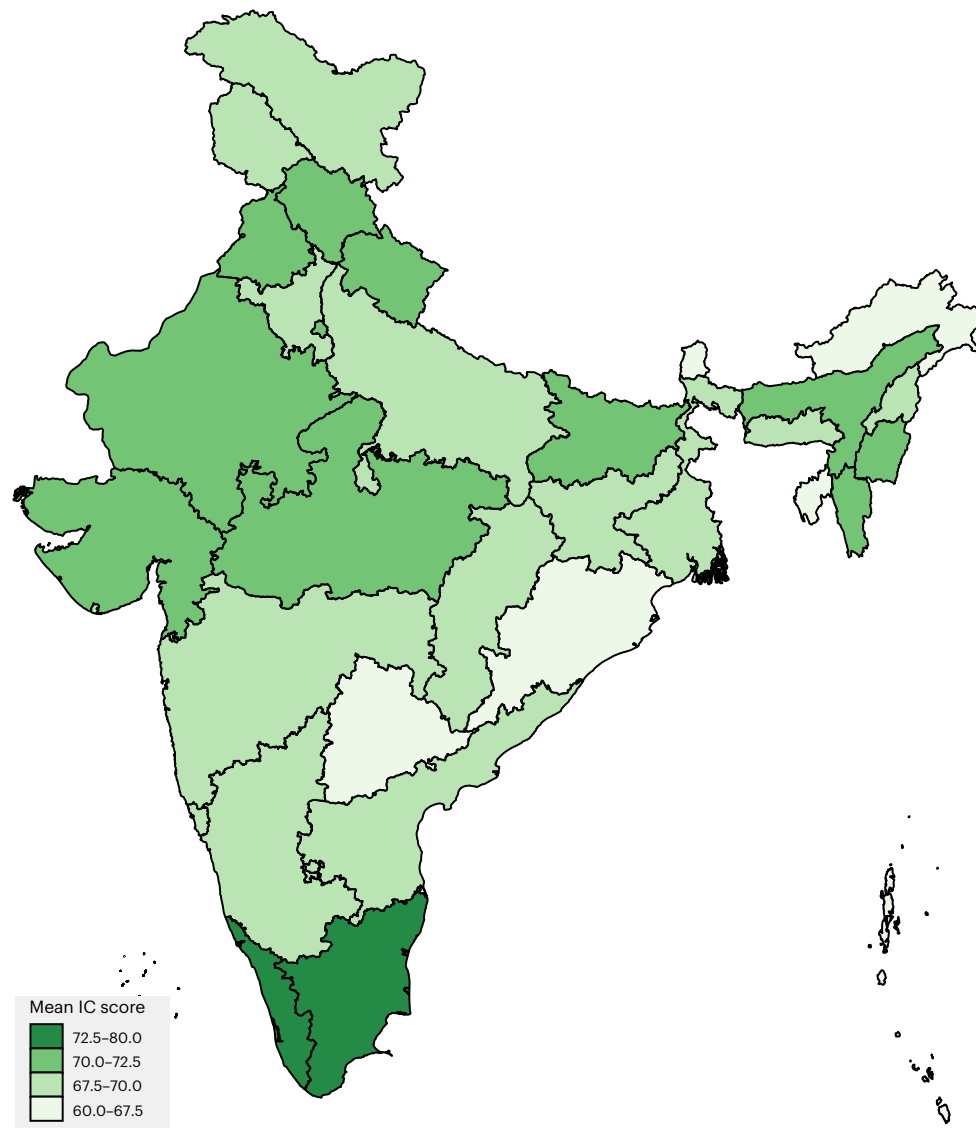
Fig. 3 | Estimated mean IC scores across the 36 Indian states and UTs (adjusted for age and sex). The map shows the estimated mean IC scores across the 36 states and territories adjusting for age and sex. Dark color indicates higher IC scores. Due to changes in administrative boundaries after the LASI data collection, the estimated scores of two UTs (Jammu and Kashmir, Ladakh) were based on the original Jammu and Kashmir UT. For the newly merged UT of Dadra and Nagar Haveli and Daman and Diu, the estimated score was based on the average of the original two UTs.

groups, men, people who were married, urban residents, participants with higher levels of education and economic quintiles, and those who lived with fewer chronic conditions. A higher IC score had protective associations with poor self-rated health, ADL and IADL limitations.

The bifactor structure, which allows multidimensionality at the item level, was the model with the best fit in the LASI study population. This corresponds to previous IC work in older populations across Brazil, China and the UK[11,12,14,18]. Compared with the earliest model of 16 items in ELSA[11], this study included similar measures in the cognitive, psychological and sensory domains but fewer items in the locomotor ($N = 2$) and vitality ($N = 2$) domains. While the latter two domains had fewer items, the five latent factors were identified in the exploratory factor analysis (EFA) results. Although several publications commonly report the bifactor model[11,12,14,18], other types of IC model are examined in aging cohort studies[22,23]. For example, a publication from ELSA used the item response theory model to fit a one-factor model (a unidimensional latent construct of IC) using 4,545 baseline participants aged 60 years or older[22]. On the basis of data from the Longitudinal Aging Study Amsterdam, a correlation model of five domains (no overall latent construct for IC) was validated in 2,333 people aged over 57 years

(ref. 23). These model structures also showed acceptable structural validity and predictivity of functional limitations and mortality.

The reflective approach, which was widely adopted in this and other studies, assumes that IC is a latent construct and that this underlying factor drives the variation in the observed items. A recent review discussed another approach, the formative model, which assumes that IC is a composite indicator of the observed items and that the variation in the observed items contributes to the IC scores[9]. This approach has also been applied to cohort studies of older adults in the Netherlands and several lower- and middle-income countries[13,15,16]. The validation studies of these composite IC scores showed clear associations with disability and mortality[13,15,16]. Given the definition of IC (the component that composites all the mental and physical capacities)[4,5], both approaches are justifiable when incorporating measures related to the five domains. This study used the reflective approach to consider IC as a universal construct of health and align with the previous work in the Gateway to Global Aging platform. Thus, exploring possible cross-country comparisons would be plausible in future studies[19]. If the analyses were based on the formative approach, the IC scores would be affected by the items selected in modeling.

Table 2 | Weighted differences in IC scores across subgroups of demographic factors, socioeconomic status and multimorbidity

	Model 1		Model 2	
	Regression coefficient (95% CI)	P value	Regression coefficient (95% CI)	P value
Age (years)				
45–49	Reference	<0.0001	Reference	<0.0001
50–54	−2.39 (−2.72 to −2.06)		−0.92 (−1.19 to −0.65)	
55–59	−3.84 (−4.18 to −3.50)		−1.75 (−2.02 to −1.48)	
60–64	−5.50 (−5.84 to −5.16)		−2.81 (−3.09 to −2.54)	
65–69	−7.11 (−7.48 to −6.75)		−4.18 (−4.49 to −3.88)	
70–74	−9.90 (−10.34 to −9.90)		−6.32 (−6.69 to −5.95)	
75–79	−12.08 (−12.65 to −11.51)		−8.06 (−8.54 to −7.58)	
80–84	−15.34 (−16.10 to −14.58)		−10.60 (−11.3 to −9.93)	
85+	−19.97 (−20.93 to −19.02)		−14.43 (−15.3 to −13.6)	
Sex				
Women	Reference	<0.0001	Reference	<0.0001
Men	7.91 (7.70 to 8.12)		4.50 (4.32 to 4.69)	
Education				
Less than primary	Reference	<0.0001	Reference	<0.0001
Primary/middle school	9.30 (9.08 to 9.52)		6.45 (6.23 to 6.66)	
Secondary school	13.73 (13.49 to 13.96)		9.56 (9.31 to 9.80)	
Higher education	16.51 (16.17 to 16.84)		11.62 (11.27 to 11.97)	
MPCE				
Quintile 1 (poorest)	Reference	<0.0001	Reference	<0.0001
Quintile 2	1.44 (1.09 to 1.79)		0.74 (0.47 to 1.01)	
Quintile 3	2.50 (2.15 to 2.85)		1.23 (0.96 to 1.50)	
Quintile 4	3.87 (3.52 to 4.22)		1.86 (1.59 to 2.13)	
Quintile 5 (richest)	5.39 (5.03 to 5.75)		2.31 (2.02 to 2.59)	
Place of residence				
Rural	Reference	<0.0001	Reference	<0.0001
Urban	5.33 (5.10 to 5.57)		2.49 (2.30 to 2.68)	
Marital status				
Married/cohabitation	Reference	<0.0001	Reference	<0.0001
Windowed	−8.62 (−8.89 to −8.34)		−1.95 (−2.19 to −1.70)	
Divorced/separated/deserted	−3.63 (−4.65 to −2.62)		−1.50 (−2.24 to −0.75)	
Never married	−0.88 (−2.16 to 0.40)		−2.76 (−3.69 to −1.83)	
Multimorbidity				
0	Reference	<0.0001	Reference	<0.0001
1	−0.74 (−1.00 to −0.48)		−0.18 (−0.38 to 0.02)	
2 or more	−1.07 (−1.36 to −0.77)		−0.54 (−0.78 to −0.31)	

Model 1 is the univariable model. Model 2 is the multivariable model including all the variables. P values were calculated using the Wald test, two sided, with no adjustment for multiple comparisons.

The IC scores in LASI showed the expected variation across subgroups with different demographic (age and sex) and socioeconomic characteristics (education and wealth). This aligns with existing evidence from other studies assessing the associations between socioeconomic status across the life course and healthy aging[24,25]. The scores were lower in older adults living with multimorbidity than in those who did not have any chronic conditions. However, the difference was minimal (a 0.5 point difference). Similar results were also identified in the analyses of ELSA and the China Health and Retirement Longitudinal Study[11,12]. In addition, the estimated IC scores had independent associations with general health and functional limitations when accounting for multimorbidity and other individual covariates. Similar results were found in recent studies in East Asia, suggesting that IC is a better indicator of predicting disability in later life than multimorbidity[26,27]. The evidence from empirical data indicates that IC, a capacity-centered construct, is relevant but different from multimorbidity, a traditional disease-based measure, and can be captured in older adults across different settings throughout the world.

The concept of IC and its operationalization and measurement have been investigated in health and aging research over the past decade[7,8]. Moving away from a disease-based method, the approach of capacity-centered, multidimensional assessment was introduced in the WHO 2015 World Report on Health and Ageing[4] and further

Table 3 | The weighted associations between IC scores, poor self-rated health, ADL and IADL limitations

	Poor health	ADL limitations	IADL limitations
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Model 1			
IC score	0.96 (0.96 to 0.96)	0.95 (0.95 to 0.95)	0.93 (0.93 to 0.93)
Model 2			
IC score	0.97 (0.97 to 0.97)	0.96 (0.96 to 0.97)	0.96 (0.96 to 0.96)
Age (years)			
45–49	Ref.	Ref.	Ref.
50–54	1.08 (0.96 to 1.20)	1.22 (1.07 to 1.40)	1.22 (1.12 to 1.33)
55–59	1.17 (1.05 to 1.31)	1.44 (1.26 to 1.65)	1.36 (1.24 to 1.48)
60–64	1.42 (1.27 to 1.58)	1.82 (1.60 to 2.06)	1.70 (1.56 to 1.85)
65–69	1.55 (1.39 to 1.73)	2.20 (1.93 to 2.50)	2.07 (1.89 to 2.26)
70–74	1.72 (1.52 to 1.94)	2.79 (2.43 to 3.20)	2.56 (2.32 to 2.83)
75–79	1.87 (1.63 to 2.15)	3.24 (2.79 to 3.78)	3.04 (2.69 to 3.43)
80–84	2.37 (2.01 to 2.80)	3.86 (3.24 to 4.60)	3.51 (3.02 to 4.09)
85+	2.41 (2.00 to 2.92)	5.10 (4.20 to 6.19)	4.65 (3.87 to 5.60)
Sex			
Women	Ref.	Ref.	Ref.
Men	1.09 (1.02 to 1.16)	0.90 (0.84 to 0.97)	0.63 (0.60 to 0.67)
Education			
Less than primary	Ref.	Ref.	Ref.
Primary/middle school	1.17 (1.09 to 1.27)	1.15 (1.05 to 1.25)	0.76 (0.71 to 0.81)
Secondary school	0.87 (0.78 to 0.97)	1.00 (0.88 to 1.13)	0.55 (0.50 to 0.60)
Higher education	0.57 (0.48 to 0.68)	0.91 (0.76 to 1.09)	0.50 (0.43 to 0.58)
MPCE			
Quintile 1 (poorest)	Ref.	Ref.	Ref.
Quintile 2	0.91 (0.84 to 1.00)	0.94 (0.85 to 1.03)	1.02 (0.95 to 1.10)
Quintile 3	0.88 (0.80 to 0.96)	1.02 (0.93 to 1.12)	0.94 (0.88 to 1.02)
Quintile 4	0.94 (0.86 to 1.03)	1.01 (0.92 to 1.12)	1.00 (0.92 to 1.07)
Quintile 5 (richest)	0.95 (0.86 to 1.04)	1.00 (0.90 to 1.11)	0.96 (0.89 to 1.04)
Place of residence			
Rural	Ref.	Ref.	Ref.
Urban	0.88 (0.82 to 0.94)	0.90 (0.84 to 0.97)	0.74 (0.70 to 0.78)
Marital status			
Married/cohabitation	Ref.	Ref.	Ref.
Windowed	1.05 (0.97 to 1.12)	1.05 (0.97 to 1.13)	1.11 (1.04 to 1.17)
Divorced/separated/deserted	1.40 (1.11 to 1.77)	1.02 (0.78 to 1.33)	1.05 (0.86 to 1.28)
Never married	1.34 (1.02 to 1.76)	1.43 (1.05 to 1.93)	1.11 (0.87 to 1.42)
Multimorbidity			
0	Ref.	Ref.	Ref.
1	2.22 (2.07 to 2.38)	1.70 (1.58 to 1.84)	1.43 (1.35 to 1.51)
2 or more	4.68 (4.35 to 5.03)	2.79 (2.59 to 3.02)	2.10 (1.97 to 2.23)

Model 1 is the unadjusted model. Model 2 is the adjusted model including all sociodemographic and health factors.

supported by the WHO guidelines for person-centered integrated care for older people in 2017[28], as well as the WHO Decade of Healthy Ageing: baseline report in collaboration with the United Nations (2021–30)[5,29]. Development of a valid IC measure may facilitate monitoring and evaluating healthy aging policies in India as well as assessing the integrated care programs for older people, such as Ayushman Bharat: the National Health Protection Scheme[30] and the National Programme for Health Care of the Elderly[31]. To support this, it is important to establish resources, procedures and infrastructure and enable data collection of measures related to the five domains. While a summarized IC score has been estimated in LASI and other cohort studies of older people, future research should consider how to implement the complex methods in clinical and healthcare data and allow meaningful comparisons across individuals and changes over time.
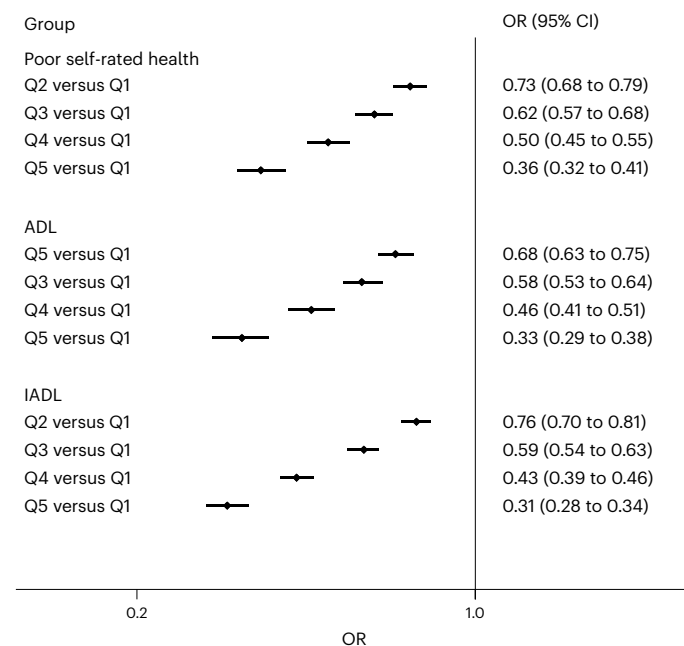
Fig. 4 | Estimated ORs and 95% CIs of poor self-rated health, ADL and IADL limitations across quintiles of IC score (Q1 lowest to Q5 highest). Logistic regression models were used to examine the associations between quintiles of IC scores and three established measures for self-rated health (N = 60,254), ADL (N = 60,258) and IADL (N = 60,201) limitations, adjusting for age group, sex, education, MPCE, place of residence, marital status and multimorbidity. ORs are shown as the center points with 95% CIs as error bars. Q, quintile.

This study included a large number of older adults across different regions, urban and rural settings in India. As part of the Gateway to Global Aging cohort studies, LASI used a similar study design, procedure and questionnaires to allow data harmonization. The IC variables were selected on the basis of the five domains in literature, and the established model structures were tested in this study population. The estimated IC scores were associated with demographic factors, socioeconomic status, multimorbidity and established scales for general health and functional limitations. This study has some limitations. While the LASI study population was nationally representative with a high response rate (87%), people with poor health may have been less likely to participate in the study and/or undertake physical examinations. Participants with missing data on the IC variables generally had worse health and lower estimated scores than those with complete data. Yet more than 99% of the participants had fewer than five missing variables and maximum likelihood estimation accounted for this issue. The results of the latent estimated and imputed scores were also similar in the sensitivity analysis. Some measures were based on self-reported information (for example, hearing impairment and multimorbidity) and might be affected by potential bias. Although standardized measurements (for example, the ten-item Center for Epidemiological Studies–Depression (CES-D) scale and self-rated health) were embedded in the interviews, some items showed unusual distributions. For example, most participants reported low negative and positive affects in the CES-D. Older Indian adults might perceive, understand and respond to these questions differently owing to cultural differences. This may affect the score distributions and their cutoff points. However, this study focused on relative differences across the population and the impact of this issue should be limited. This study did not investigate measurement invariance across subgroups and assumed that the IC structure applied to all participants. Because no gold standard measures exist for IC, the criterion validity could not be tested formally. Yet the IC scores showed linear associations with established scales of general health and functional limitations.

This study developed a comprehensive indicator of IC in older Indian adults, incorporating multiple domains of health and functioning. The IC scores appeared to vary across sociodemographic subgroups and geographical areas and had independent associations with general health and functional limitations in addition to multimorbidity. This capacity-centered measure can be applied in healthy aging research and future research should explore how to implement it in public health and clinical practices to support the growing older population in India.

Methods

Study population

This study was based on LASI[21], a nationwide survey of middle-aged and older adults aged 45 years and older and their spouses (irrespective of age), representing India and all its states and UTs. LASI is a comprehensive investigation of the health, social and economic well-being of older adults in India, harmonized with the Health and Retirement Study and its sister studies in more than 40 countries. LASI used a multistage stratified area probability cluster sampling design, adapted to rural and urban settings in each state, with household and individual response rates of 96% and 87%, respectively. Household and individual sample weights were calculated to generate national-level indicators and produce state-level indicators. Detailed information relating to the design, tools, process and sample characteristics of LASI is available elsewhere (www.iipsindia.ac.in/lasi)[21,32].

In addition to data collection through face-to-face interviews by trained survey investigators, trained health investigators conducted tests for physical functioning and performance-based markers, recorded anthropometric measurements, and collected dried blood spots to test for select health markers of chronic health conditions[21]. All collaborating institutions and the Indian Council of Medical Research granted ethical approval, with informed consent obtained for each survey component.

The LASI baseline wave (2017–18) included 73,408 people across 36 states and UTs (participants in Sikkim were interviewed in 2021 owing to administrative delays and the COVID-19 pandemic)[21]. After excluding 6,789 people aged less than 45 years and 6,028 participants who did not take part in physical examinations (that is, tests for locomotor, sensory and vitality capacities), this study focused on 60,591 older adults.

Measurements of IC

Previous studies on IC have included different measures for the five domains (cognitive, locomotor, psychological, sensory and vitality)[10,11]. On the basis of literature and expert consensus[10–12], 14 relevant measures were identified in the LASI dataset. The following criteria were applied to review these measures: (1) availability of prior evidence supporting an association with at least one domain of capacity, (2) applicability in various settings (population, community, clinical and laboratory), (3) ability to distinguish between high and low physical or mental capacity at older ages and (4) sensitivity to detect change within and among individuals over time. The following sections describe specific measures included in these five domains.

Cognitive. This domain included four measures on memory, verbal fluency, arithmetic and orientation. As part of the Gateway to Global Aging cohort, the LASI study followed the Health and Retirement Study methods to implement neuropsychological assessments and procedures for cognitive tests[33,34]. Two tests, immediate and delayed word recall tests[35], were used to measure episodic memory, which refers to the ability to recall specific past events and situations consciously. Participants received scores between zero and ten for each test. A summary score was calculated for these two tests (range between 0 and 20). The verbal fluency test was based on how many unique animals and birds a participant could name in 1 min (ref. 36). The score was based on the number of animals and birds that participants could

name. Three arithmetic tests included serial '7s' (ref. 37) and two simple computation problems. For the serial 7s test, participants were asked to subtract 7 from 100 and then again from 93 for five iterations. The two computational problems focused on calculation in daily life scenarios: (1) A shop is having a sale and selling all items at half price. Before the sale, a sari costs 300 Rs. How much will it cost in the sale? (2) If five people all have the winning numbers in the lottery and the prize is 1,000 Rs, how much will each of them get? Participants earned a score of one for each correct answer and a zero for incorrect answers. The total arithmetic score for the three tests was between zero and three. Orientation refers to an individual's cognitive capacity to know who they are, where they are, and what day and year it is[38]. Participants were asked to state the current date (day of week, day, month and year), place of interview and their own home address (street, village and district). Each correct answer received one point, and an incorrect answer received zero points. A total score summarized these eight questions between zero and eight.

Locomotor. This domain included two measures: walking speed and balance. For walking speed, participants who were able to walk were asked to walk 4 m at their usual walking pace twice (the use of walking aids was permitted). The time for both walks was recorded separately, and the mean speed (meters per second) of the two trials was calculated. Static balance was evaluated using semitandem and full tandem tests. All participants were required to complete the semitandem balance test. Those who were able to complete the task were then asked to take the full tandem test. The balance measure was based on these two tests and categorized into three levels: those who completed both semi- and full tandem tests, those who completed the semitandem test only and those who did not complete any one of the tandem balance tests.

Psychological. This domain included two measures, affect and sleep. Affect was measured using the ten-item CES-D scale[39]. Response options for each item range from 'rarely or none of the time' (score of zero) to 'all of the time' (score of three). Total scores ranged from 0 to 30. A higher score indicates greater severity of depressive symptoms. The Jenkins Sleep Scale[40] assessed sleep disturbance. Participants were asked about the frequency of delay in falling asleep, inability to stay asleep, waking up tired, disturbed sleep in the previous month and taking a nap during the day. Response categories were never (score of 0), rarely (one to two nights per week; score of 1), occasionally (three to four nights per week; score of 2) and frequently (five or more nights per week; score of 3). The total score was between 0 and 15. A higher score indicates more sleep disturbance.

Sensory. This domain included one measure for hearing and three measures for vision. Participants were asked "have you ever been diagnosed with any hearing or ear-related problem or condition?" with possible responses of yes or no. Self-reported eyesight included two questions. Participants, including those who wore glasses, contacts or corrective lenses, were asked to rate their distance eyesight (seeing things at a distance, such as recognizing a person across the street) and near eyesight (seeing things up close, such as reading ordinary newspaper print). Vision tests measured distance and near vision in both eyes using a computer-assisted personal interview with a Tumbling E LogMAR chart. Distance vision was measured at a 3-m distance in a sitting position after ensuring the participant's eye and the computer screen were on the same level. A near vision test was conducted at a 40-cm distance from the near vision Tumbling E LogMAR chart following the procedures used for distance vision. Participants were allowed to take a vision test if they perceived light and could count their fingers at 60 cm. Vision tests were performed with the visual aid that provided the best correction at the time of measurement. The results of vision tests were used to determine three groups: normal vision, low vision and blindness.

Vitality. This domain included two measures for grip strength and respiratory function. Hand grip strength, a test of upper body muscle strength, was assessed using a handheld dynamometer. Participants who were unable to stand could perform the test while seated with arm support. The grip strength of both hands was averaged to generate a single measure. Respiratory function was assessed using a THOR Spiro-Tube handheld spirometer. Participants were allowed a maximum of eight attempts. Of these, three technically acceptable and two repeatable attempts were considered for generating outcome measures. The respiratory function measure was based on the mean of forced vital capacity and forced expiratory volume in 1 s.

Demographic factors, socioeconomic status and chronic conditions

The LASI interviews collected information on demographic factors, including age, sex, marital status and place of residence (Table 1). Age was categorized in 5-year age groups (45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84 and 85+ years), and sex was categorized as women and men. The marital status measure included three categories: currently married, widowed and other (single and divorced/separated/deserted). The place of residence was categorized into rural and urban. The two measures used to indicate socioeconomic status were education and MPCE. Education was categorized into three levels: less than primary, intermediate and higher. MPCE, a proxy measure of economic status, was computed on the basis of self-reported consumption and divided into quintiles: poorest (Q1), poor (Q2), middle (Q3), richer (Q4) and richest (Q5).

The number of chronic conditions was based on self-reported diagnoses of hypertension, diabetes, cancer, lung disease (for example, asthma and chronic obstructive pulmonary disease), heart disease (for example, myocardial infarction and congestive heart failure), stroke, arthritis or osteoporosis, angina, neurological disease or psychiatric problems (for example, depression, Alzheimer's and dementia) and high cholesterol. The total number of these conditions was categorized into three groups: none, one, and two or more chronic conditions.

General health and functional limitations

For general health, the participants were asked to rate their overall health as very good, good, fair, poor or very poor. People who reported poor or very poor health were categorized as having poor self-rated health. Functional limitations were assessed using ADL and IADL scales[41,42]. The ADL scale included six items related to self-care (dressing, walking, bathing, eating, getting in/out of bed and toileting), reflecting the ability to meet basic needs, as done within the baseline analysis for the UN Decade of Healthy Ageing[5]. The IADL scale measured seven tasks for basic needs (preparing a hot meal, shopping for groceries, making telephone calls, taking medications, doing work around the house or garden, managing money and getting around or finding an address). The participants were asked to indicate whether they had any difficulties with these activities (yes or no). The scales were categorized into 'no limitations' (none) and 'ADL/IADL limitations' (one or more difficulties).

Statistics and reproducibility

Descriptive analyses investigated distributions of all the variables. To facilitate complex modeling of IC, continuous variables (more than ten categories) were standardized, including memory, affect, sleep, walking speed, grip strength and respiratory function. Owing to the skewed distribution of verbal fluency (scores ranged from 0 to 61), the score was converted to a logarithmic scale. Data distribution was assumed to be normal, but this was not formally tested.

To generate IC scores, factor analysis was employed to include the five domains and a general factor indicating overall levels of IC. A random sample was created on the basis of 30% of the total population ($N = 18,090$) and used to test the factor structure of IC. An EFA approach

identified latent factors among the 14 items. Oblique quartimin rotation was applied to the EFA model and a cutoff of loading >0.3 was used to determine the factor structure[43]. On the basis of the EFA results, a CFA model was built to further include a general latent factor for IC. Four types of models were tested, including a correlation model, with no general factor; a one-factor model, that had a unidimensional construct; a second-order model, that added another level incorporating all five domains; and a bifactor model that included a general latent factor at the item level and allowed covariance of the five domains. The variances of latent factors were set at one. Maximum likelihood estimation was used in all models. The model fitness was assessed using a set of goodness-of-fit indicators, including CFI (>0.95 for good fit), TLI (>0.95), RMSEA (<0.06), SRMR (<0.08), BIC and AIC[44,45].

The model with the best goodness-of-fit identified in the 30% subsample was applied to the whole study population and used to estimate latent scores of the five domains (domain scores) and the general factor (IC score) for all the participants. The estimated scores were computed using linear regression based on the mean vector and variance matrix from the fitted model. For the participants with missing data on the observed items, scores were estimated on the basis of the available items only. The estimated scores were rescaled to a range between 0 and 100 to provide a more straightforward interpretation of IC scores.

Since there is no gold standard of measuring IC, this study focused on examining the construct validity of the IC score, including structural (dimensionality of the IC construct), discriminative (differences between known groups) and convergent/discriminant (correlations between various measurements and constructs) validation[46]. Structural validity was established using the CFA model and the aforementioned goodness-of-fit indicators as above, including CFI, TLI, RMSEA and SRMR. Given that IC comprises "all the physical and mental capacities"[4,5], the score was expected to be negatively associated with age-related changes and presence of diseases (for example, older age and multimorbidity) but positively associated with socioeconomic status (for example, education and household consumption expenditure). To investigate discriminative validity, linear regression modeling examined differences in the IC total and domain scores across subgroups of demographic factors (age, sex, marital status and urban), socioeconomic status (education and MPCE) and the number of chronic conditions. A univariable model was built for each variable and a multivariable model including all the variables was employed to investigate their joint associations with the IC scores. Estimated IC scores across the 36 Indian states and UTs were calculated on the basis of the regression model adjusted for age and sex.

To test convergent and discriminant validity of the IC score, logistic regression modeling examined its associations with different but relevant measures of general health and functional limitations. A higher IC score was expected to be negatively associated with poor self-rated health, ADL and IADL limitations (that is, protective effects). The unadjusted models were first fit, and the adjusted models included all demographic factors, socioeconomic status and number of chronic conditions. To examine whether the associations were linear, the IC scores were further divided into quintiles and fitted into the adjusted models.

The individual-level LASI survey weights were applied to the regression models to account for study design, nonresponse and post-stratification[47]. Complete case analysis was carried out in EFA and CFA but the latent scores were estimated for all participants on the basis of available data. Although 31% of the participants (N = 18,696) had at least one missing IC variable, 99.5% had <5 missing items. Thus, the impact of missing data on latent score estimation was expected to be limited. Owing to small numbers of missing data on covariates (<1%), regression modeling was based on complete case analysis. Sensitivity analyses further addressed issues of missing data using multiple imputation by chained equations. The missing IC scores and covariates were imputed on the basis of all variables used in the analyses and 30 imputed datasets were generated to compare the results of estimated latent scores and

imputed scores. Rubin's rule was used to combine results from the imputed datasets[48]. All the analyses were conducted using Stata 18.5[49].

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The LASI data are available via the International Institute for Population Sciences website at www.iipsindia.ac.in/lasi, the data webpage of the Government of India at www.data.gov.in, the Harvard T.H. Chan School of Public Health website at lasi.hsph.harvard.edu, the University of Southern California website at lasi-india.org and the website of the Gateway to Global Aging Data at g2aging.org.

Code availability

Codes will be made available upon reasonable request by the corresponding author.

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Author contributions

A.P., Y.T.W., R.S. and M.P. contributed to the conceptual development and manuscript preparation. Y.T.W., A.P., Y.S. and M.P. participated in the data analysis and reporting of the results. R.S., D.E.B., J.L. and A.M.G. contributed to the interpretation of the study findings and revision of the manuscript. All authors reviewed and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

Additional information

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Reporting Summary

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Software and code

Policy information about availability of computer code

Data collection	We used cross-sectional data on 60,442 older adults aged 45 years and above from wave 1 of the Longitudinal Ageing Study in India, 2017–2018, a nationwide survey of older adults aged 45 and older and their spouses irrespective of age, representing India and all its states
Data analysis	All the analyses were conducted using Stata 18.5.39. Beginning with an exploratory factor analysis (EFA) followed by a confirmatory factor analysis (CFA), to ensure the most appropriate structure for intrinsic capacity in our population.Five IC domains were identified and four types of factor structure, including a correlation model, a unidimensional model, a second-order model and a bi-factor model, were investigated to select the best-fit structure for this population. The resulting structure was then tested through CFA on the whole LASI population to estimate the IC scores

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Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	LASI covered population representative sample of both men and women aged 45 years and above
Reporting on race, ethnicity, or other socially relevant groupings	LASI covered representative sample across socioeconomic spectrum
Population characteristics	The sample consisted of 50% of adults aged 45–59, including spouses younger than 45 years (around 10% of the total sample), 39% of older adults aged 60-74, and 11% older adults aged 75; 54% of participants were women; 70% were from rural areas; 74% were currently married; 62% had less than five years of primary schooling
Recruitment	Sampled households and individuals were interviewed between April 2017 and December 2018 by trained field investigators. Individual survey also included direct health measurements by trained health investigators. Household and individual survey of the LASI instrument was professionally translated into 16 regional languages to enhance response rates and data quality nrespondents were asked to provide a written informed consent. The English version health measurements by trained health investigators. Household
Ethics oversight	were informed of the purpose of the survey, ways of protecting their privacy, and the safety of the health assessments as part of the informed consent process. Consent forms used in LASI include : household informed consent, individual informed consent, and biomarker informed consent form.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	*Describe how sample size was determined, detailing any statistical methods used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.*
Data exclusions	*Describe any data exclusions. If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Replication	*Describe the measures taken to verify the reproducibility of the experimental findings. If all attempts at replication were successful, confirm this OR if there are any findings that were not replicated or cannot be reproduced, note this and describe why.*
Randomization	*Describe how samples/organisms/participants were allocated into experimental groups. If allocation was not random, describe how covariates were controlled OR if this is not relevant to your study, explain why.*
Blinding	*Describe whether the investigators were blinded to group allocation during data collection and/or analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.*

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	This is the first population-based study in India to apply the WHO healthy ageing framework, analyzing intrinsic capacity (IC) among older adults. The studyfive IC domains—cognition, locomotion, psychological, sensory, and vitality—using a national sample of 60,591 adults aged 45 and older, representing all 36 Indian states and union territories, based on the Longitudinal Ageing Study of India (LASI). examined five IC domains—cognition, locomotion, psychological, sensory, and vitality—using a national sample
Research sample	This study analysed cross-sectional data of 60,591 older adults aged 45 and older who completed both household and individual interviews as well the direct health examination of biomarkers from Wave 1 of the Longitudinal Ageing Study of India (LASI), 2017-18.
Sampling strategy	LASI used a multistage stratified area probability cluster sampling design, adapted to rural and urban setting in each state, with a household and individual response rates of 96% and 87% respectively. LASI used a multistage stratified area probability cluster sampling design, adapted to rural and urban setting in each state, with a household and individual response rates of 96% and 87% respectively
Data collection	Data collection through face-to-face interviews by trained survey investigators, trained health investigators conducted tests for physical functioning markers, performance-based markers, and anthropometric measurements, and collected dried blood spots to test for select health markers of chronic health conditions
Timing	Sampled households and individuals were interviewed and health examinations were conducted between April 2017 and December 2018 by trained field investigators.
Data exclusions	The target population for the Wave 1 of LASI included all Indian adult men and women aged 45 and older and their spouses regardless of age who reside in the same household (HH). Eligibility for the LASI survey has no upper limit. Population aged less tahn 45 were excluded according to the design of the study.
Non-participation	For India, the overall household response rate was 95.8%, and the overall individual response rate was 87.3%. Both household and individual response rates were higher in rural than in urban areas.
Randomization	None

Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	*Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.*
Research sample	*Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.*
Sampling strategy	*Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.*
Data collection	*Describe the data collection procedure, including who recorded the data and how.*
Timing and spatial scale	*Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken*
Data exclusions	*If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.*
Reproducibility	*Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.*
Randomization	*Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were*

Randomization	controlled. If this is not relevant to your study, explain why.
Blinding	Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.

Did the study involve field work? ☐ Yes ☐ No

Field work, collection and transport

Field conditions	LASI is nationwide survey of all states and union terrtorries of India. Pre-survey preparations inlcude approvals and permissions from authorities and stakeholder. Survey teams included fied supervisors and coordinators. Interviewers were trained how to approach the community leaders and households and seek permission for the survey. The overall cooperation for the survey was very good to excellent.
Location	LASI Wave 1 collected data from 36 of India's 36 states and union territories and its sample size included over 72 000individuals aged 45 and older and their spouses less than 45 years, including over 31,000 elderly aged 60 and above; follow-up waves are planned every 2–3 years for the next 25 years.
Access & import/export	Household, individual, and community data were collected using computer-assisted face-to-face personal interviews and direct health measurements. Data was directly exported from CAPI to dedicated LASI central server computer using a secured data tranfer protocol. Only the lead PI and authorized IT coordinator could access the data, All data were anonymised.
Disturbance	There was no recorded disturbance during field survey

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Not Applicable
Validation	Not Applicable

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	Not Applicable
Authentication	Not Applicable
Mycoplasma contamination	Not Applicable
Commonly misidentified lines (See ICLAC register)	Name any commonly misidentified cell lines used in the study and provide a rationale for their use.

Palaeontology and Archaeology

Specimen provenance	Not Applicable
Specimen deposition	Not Applicable
Dating methods	Not Applicable

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	Not Applicable

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Not Applicable
Wild animals	Not Applicable
Reporting on sex	Not Applicable
Field-collected samples	Not Applicable
Ethics oversight	Not Applicable

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies
All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Not Applicable
Study protocol	Not Applicable
Data collection	Not Applicable
Outcomes	Not Applicable

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☒	☐	Public health
☒	☐	National security
☒	☐	Crops and/or livestock
☒	☐	Ecosystems
☒	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
☒	☐	Demonstrate how to render a vaccine ineffective
☒	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
☒	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
☒	☐	Increase transmissibility of a pathogen
☒	☐	Alter the host range of a pathogen
☒	☐	Enable evasion of diagnostic/detection modalities
☒	☐	Enable the weaponization of a biological agent or toxin
☒	☐	Any other potentially harmful combination of experiments and agents

Plants

Seed stocks: NA

Novel plant genotypes: NA

Authentication: NA

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.: NA

Files in database submission: NA

Genome browser session
(e.g. UCSC): NA

Methodology

Replicates: NA

Sequencing depth: NA

Antibodies: NA

Peak calling parameters: NANA

Data quality: NA

Software: NA

Flow Cytometry

Plots

Confirm that:

☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☐ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☐ All plots are contour plots with outliers or pseudocolor plots.

☐ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	NA
Instrument	NA
Software	NA
Cell population abundance	NA
Gating strategy	NA

☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type	NA
Design specifications	NA
Behavioral performance measures	*State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).*

Acquisition

Imaging type(s)	NA
Field strength	NA
Sequence & imaging parameters	NA
Area of acquisition	NA

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software	NA
Normalization	NA
Normalization template	NA
Noise and artifact removal	NA
Volume censoring	NA

Statistical modeling & inference

Model type and settings	NA
Effect(s) tested	NA

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference

(See [Eklund et al. 2016](#))

| NA |

Correction

Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).

Models & analysis

n/a	Involved in the study
☒ ☐	Functional and/or effective connectivity
☒ ☐	Graph analysis
☐ ☒	Multivariate modeling or predictive analysis

Functional and/or effective connectivity

Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).

Graph analysis

Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).

Multivariate modeling and predictive analysis

| Multivariate models were used to predict IC scores across socioeconomic spectrum |