

## **Sarcopenia and mild cognitive impairment in older adults from six low- and middle-income countries**

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## **Abstract**

*Background:* Little is known about the relationship between sarcopenia and mild cognitive impairment (MCI) in low- and middle-income countries (LMICs).

*Objective:* This study aimed to investigate this association among community-dwelling adults aged  $\geq 65$  years from six LMICs.

*Methods:* Cross-sectional, nationally representative data from the Study on Global Ageing and Adult Health (SAGE) were analyzed. These data were obtained in China, Ghana, India, Mexico, Russia, and South Africa in 2007-2010. Participants were considered to have sarcopenia if they had low skeletal muscle mass (i.e., lower skeletal mass index) and a weak handgrip strength. MCI was defined using the National Institute on Aging-Alzheimer's Association criteria. Multivariable logistic regression analysis was conducted to assess associations.

*Results:* The final analytical sample consisted of 12912 individuals aged  $\geq 65$  years with preservation in functional abilities without stroke (mean [standard deviation] age 72.2 [10.8] years; 45.2% males). The overall prevalence of sarcopenia and MCI were 11.3% and 18.1%, respectively. After adjusting for potential confounders, there was a positive association between sarcopenia and MCI in all countries (i.e., odds ratio [OR] $>1$ ) with the exception of South Africa, and the overall estimate was OR=1.60 (95% confidence interval [CI]=1.32-1.93) with a low level of between-country heterogeneity ( $I^2=0.0\%$ ).

*Conclusion:* There was a positive association between sarcopenia and MCI in this sample of older adults living in LMICs. Causality should be assessed in future longitudinal research, while the utility of sarcopenia as a marker of MCI should also be investigated.

**Keywords:** sarcopenia; mild cognitive impairment; community-dwelling adults; low- and middle-income countries; multicountry study



## Introduction

The world is presently facing an unprecedented ageing of the population. Indeed, the proportion of adults aged >60 years will increase from 12% in 2015 to 22% in 2050 [1]. The burden related to this global ageing is particularly high in low- and middle-income countries (LMICs), with four out of five older adults projected to be living in LMICs by 2050. In this context, the number of people with dementia is rising [2], with the majority of these individuals residing in LMICs [3]. Unfortunately, there are currently no effective treatments for dementia, and thus, it is of vital importance to identify the correlates or risk factors of its preclinical stage such as mild cognitive impairment (MCI) to prevent dementia or delay its onset. MCI has a high conversion rate to dementia (annual conversion rate between 5% and 10%) [4] and is increasingly being recognized as an important stage to intervene.

Well-known risk factors for MCI are age, the *APOE*  $\epsilon$ 4 allele, low educational level, hypertension, and depressive symptoms [5,6]. In the past years, there has also been a growing body of literature showing that sarcopenia may be an additional risk factor or marker of cognitive decline. Sarcopenia is one of the most prominent physiological changes related with aging, and is characterized by a gradual loss of muscle mass and function [7]. Sarcopenia may increase the risk for cognitive decline [8], and this relationship may be explained by shared pathophysiological mechanisms (e.g., inflammation [9,10], hormonal dysregulations [11,12] and malnutrition [13,14]), brain atrophy [15] and several mediating factors (e.g., depression [16,17], metabolic syndrome [18,19] and hypertension [20,21]). A systematic review and meta-analysis of 15 studies showed that sarcopenia was significantly and positively associated with cognitive impairment (odds ratio [OR]=2.25, 95% confidence interval [CI]=1.70-2.97) [22]. Furthermore, although not specifically on sarcopenia, previous studies have shown that

individual components of sarcopenia (e.g., slow gait speed or decreased physical performance) increase the risk for future cognitive decline and dementia [23,24].

However, to the best of our knowledge, apart from two small studies conducted in Japan and South Korea [25,26], all previous studies on sarcopenia and cognition were on cognitive function in general (which may not necessary carry a high risk for conversion to dementia) and not MCI. Furthermore, there is very little information on sarcopenia and/or MCI from LMICs, despite the projected sharp increase in these conditions in the coming years due to rapid population ageing in this setting. Therefore, the goal of this study was to investigate the association between sarcopenia and MCI in community-dwelling adults aged  $\geq 65$  years from six LMICs (China, Ghana, India, Mexico, Russia, and South Africa), which broadly represent different geographical locations and levels of socio-economic and demographic transition.

## **Materials and Methods**

### *The survey*

Data from the Study on Global Ageing and Adult Health (SAGE) were used for the present study. All data can be found at <http://www.who.int/healthinfo/sage/en/>. Initially, the SAGE survey aimed to collect data on health and well-being in LMICs [27]. There were six countries (China, Ghana, India, Mexico, Russia, and South Africa) included in the SAGE survey between 2007 and 2010. All countries were LMICs at the time of the acquisition of the data (low-income country: Ghana; lower middle-income countries: China and India; and upper middle-income countries: Mexico, Russia and South Africa). The methodology of the SAGE survey has been described in detail elsewhere [28]. Briefly, the samples were obtained with a multistage clustered sampling method, and were nationally representative. In each participating country,

the SAGE survey targeted 6000 households, and all household members had a nonzero probability of being selected [29]. Participants of the survey were aged  $\geq 18$  years, and those aged  $\geq 50$  years were oversampled. Data were obtained during face-to-face interviews conducted by trained staff using a standard questionnaire. This questionnaire was translated using standard procedures, and this allowed comparability between countries. China (93%) and Mexico (53%) had the highest and the lowest response rate, respectively. The structure of the populations was further taken into account and, based on statistics provided by the United Nations Statistical Division, sampling weights were constructed. Finally, formal ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards, while written informed consent was obtained for each individual participant.

### *Study sample*

The flow chart of participants is provided in **Figure 1**. The final analytical sample consisted of 12912 individuals aged  $\geq 65$  years with preservation in functional abilities and without stroke.

### *Sarcopenia (exposure)*

Following the criteria of the revised European consensus on the definition and diagnosis of sarcopenia [30], participants were considered to have sarcopenia if they had low skeletal muscle mass (SMM) (i.e., lower skeletal mass index [SMI]) and weak handgrip strength, while participants were considered to have severe sarcopenia if they had low SMM, weak handgrip strength, and low gait speed. SMM was calculated based on the equation proposed by Lee and colleagues:  $SMM = 0.244 * \text{weight} + 7.8 * \text{height} + 6.6 * \text{sex} - 0.098 * \text{age} + \text{race} - 3.3$  (where female=0 and male=1; race=0 [White and Hispanic], race=1.9 [Black] and race=-1.6 [Asian]) [31]. SMM was further divided by BMI based on measured weight and height to create a SMI [32]. Low SMM corresponded to the lowest quintile of sex-stratified values of SMI. Gait speed

was based on a 4m timed walk and was measured by asking the participant to walk at a normal pace. The time to completion of the 4m walk was recorded by the interviewer. Slow gait speed corresponded to the lowest quintile of height, age, and sex-stratified values of walking speed [33]. Weak handgrip strength was defined as <27kg for men and <16kg for women using the average value of the two handgrip measurements of the dominant hand [30].

*Mild cognitive impairment (outcome)*

MCI was defined following the recommendations of the National Institute on Aging-Alzheimer's Association [34]. Algorithms already used in previous SAGE studies were applied to identify people with MCI [35]. Participants were considered to have MCI if at least one of the four following criteria was fulfilled:

(a) Concern about a change in cognition: individuals were considered to have concern about a change in cognition if they answered "bad" or "very bad" to the question "How would you best describe your memory at present?" or "worse" to the question "Compared to 12 months ago, would you say your memory is now better, the same or worse than it was then?"

(b) Objective evidence of impairment in one or more cognitive domains: several aspects of cognition were assessed. Learning and episodic memory was tested using the word list immediate and delayed verbal recall from the Consortium to Establish a Registry for Alzheimer's disease [36]; attention and working memory were tested using the digit span forward and backwards from the Weschler Adult Intelligence Scale [37]; and verbal fluency was tested using the animal naming task [36].

(c) Preservation of independence in functional abilities: questions on self-reported difficulties in activities of daily living (ADL) in the past month were used to assess preservation of independence in functional abilities [38]. These questions were: "How much difficulty did you have in getting dressed?" and "How much difficulty did you have with eating (including cutting

up your food)?” (answer options: “none”, “mild”, “moderate”, “severe”, and “extreme (cannot do)”). Preservation of independence in functional activities corresponded to answering “none”, “mild” or “moderate” to both questions. Participants without preservation of independence in functional activities were excluded from the analyses (i.e., 962 individuals aged  $\geq 65$  years).

(d) No dementia: if adults were unable to undertake the survey because of cognitive impairments, these individuals were not included in the study.

### *Control variables*

Past literature was used to select the control variables to include in the statistical analyses [39]. These variables were years of education, wealth quintiles based on income, physical activity, smoking (never, past, current), alcohol use in the past 30 days (yes or no), diabetes, and hypertension. Diabetes was based solely on lifetime self-reported diagnosis. Hypertension was defined using one of the following three criteria: systolic blood pressure  $\geq 140$  mmHg; diastolic blood pressure  $\geq 90$  mmHg; or self-reported diagnosis. Physical activity was assessed with the Global Physical Activity Questionnaire and, using conventional cut-offs [40], physical activity was included in the analyses as a three-category variable (low, moderate and high).

### *Statistical analysis*

The statistical analysis was performed with Stata 14.1 (Stata Corp LP, College station, Texas). Given that sarcopenia and MCI are age-related conditions, only participants aged  $\geq 65$  years were included in the analyses. Individuals with stroke were also excluded as this condition can lead to both cognitive decline and sarcopenia [41,42]. A country-wise multivariable logistic regression analysis was conducted to assess the association between sarcopenia or severe sarcopenia (exposures) and MCI (outcome). The regression analysis was adjusted for years of education, wealth, physical activity, smoking, alcohol use, diabetes, and hypertension.

Furthermore, in order to assess the between-country heterogeneity that may exist in the association between sarcopenia and MCI, the Higgins's  $I^2$  was calculated based on estimates from each country. The Higgins's  $I^2$  corresponds to the degree of heterogeneity that is not explained by sampling error with a value of <40% often considered as negligible and 40-60% as moderate heterogeneity [43]. A pooled estimate was obtained by fixed-effect meta-analysis. Sex-stratified analyses were also conducted. All variables were included in the models as categorical variables with the exception of years of education (continuous variable). Complete case analysis was done. The sample weighting and the complex study design were taken into account in the analyses. Results from the regression analyses are presented as ORs with 95% CIs. The level of statistical significance was set at  $P < 0.05$ .

## Results

The mean (standard deviation) age of the sample was 72.2 (10.8) years and 45.2% were males (**Table 1**). Percent of missing values for the variables used in the study are displayed in **Table S1**, while differences in sample characteristics between those missing and not missing values on either sarcopenia or mild cognitive impairment are shown in **Table S2**. The overall prevalence of MCI was 18.1%, while that of sarcopenia and severe sarcopenia were 11.3% and 2.5%, respectively. In the overall sample, compared to those without sarcopenia, the prevalence of MCI was much higher in people with sarcopenia (27.6% vs. 16.8%) (**Figure 2**) and severe sarcopenia (25.5% vs. 17.6%) (**Appendix Figure S1**). **Figure 3** illustrates the country-wise association between sarcopenia and MCI based on multivariable logistic regression, and the overall estimate based on meta-analysis in the sample including both males and females. There was a positive association between sarcopenia and MCI in all countries (i.e.,  $OR > 1$ ) with the exception of South Africa, and the overall estimate was  $OR = 1.60$  (95% $CI = 1.32-1.93$ ) with a

low level of between-country heterogeneity ( $I^2=0.0\%$ ). Overall, significant positive associations were also observed in samples restricted to males (OR=1.74; 95%CI=1.35-2.23) and females (OR=1.63; 95%CI=1.25-2.13) (**Figure 4**). In terms of severe sarcopenia, the pooled OR (95%CI) was 1.78 (1.21-2.63) in the overall sample (Appendix **Figure S2**), while that for males and females was 1.79 (1.05-3.07) and 1.74 (1.06-2.85), respectively (Appendix **Figure S3**).

## **Discussion**

### *Main findings*

In this multinational study including nearly 13000 older adults living in LMICs, sarcopenia and severe sarcopenia were associated with a significant 1.60- and 1.78-fold increase in the risk of MCI, respectively. These results were corroborated in the sex-stratified analyses. To the best of our knowledge, this is the first multinational study to investigate the relationship between sarcopenia and MCI, and the first from LMICs, while it is also the largest study on this topic to date.

### *Interpretation of findings*

The findings of our study are in line with the only two studies on this topic (i.e., sarcopenia and MCI) from Japan and South Korea. In the Japanese study which included 250 older individuals, of which approximately 20% had sarcopenia and 40% MCI, there was a positive and significant association between sarcopenia and MCI (OR=2.96) after adjustment for several factors such as smoking status and cardiovascular diseases [25]. These findings were corroborated in the other study conducted among 201 community-dwelling women living in South Korea, where sarcopenia was associated with a 4.50-fold increase in the odds of MCI [26]. In addition, several

studies have also found that sarcopenia is a risk factor for an overall poor cognitive performance. For example, a systematic review and meta-analysis including 5994 individuals reported a significant and positive association between sarcopenia and cognitive impairment (OR=2.25) [44]. The higher OR in the Japanese and Korean studies than ours may be explained by the fact that these previous studies did not control for several potentially important confounders (e.g., wealth and physical activity), while it can also be attributable to methodological differences. In our study which used standardized methods across countries, there was no significant between-country heterogeneity in the association between sarcopenia and MCI in the overall sample, suggesting that this relationship may not be context-specific at least in LMICs.

Although the mechanisms linking sarcopenia and MCI are unclear, two hypotheses may explain this relationship. First, chronic physical and psychiatric conditions may be involved as mediating factors in the sarcopenia-MCI relationship. One chronic condition likely playing a major role in this association is metabolic syndrome. A systematic review and meta-analysis of 12 studies including middle-aged and older adults without obesity showed a positive association between sarcopenia and metabolic syndrome, and this may involve insulin resistance and decreased secretion of myokines protecting against the deleterious effects of the adipose tissue [19]. As a matter of fact, the muscle plays a key role in the metabolism of glucose and in the prevention of insulin resistance [45]. Meanwhile, a study including 2102 community elders from China found that those with metabolic syndrome were at an increased risk for MCI compared with their counterparts without metabolic syndrome [18], and potential underlying mechanisms are cerebrovascular disease and an alteration in the  $\beta$ -amyloid deposition [46]. Interestingly, depression could also be a major mediating factor in the association between sarcopenia and MCI. Indeed, a longitudinal study of 691 older adults living in China revealed

that sarcopenia was associated with a 3.57-fold increase in the 12-month incidence of depressive symptoms [17]. Another prospective study using data of 8855 patients from the United States indicated that late-life depression was a risk factor for progression from normal cognition to MCI, and it was hypothesized that sleep disruption and changes in the activity of frontal and limbic circuits might contribute to the depression-MCI relationship [16]. Besides chronic physical and psychiatric conditions, the association between sarcopenia and MCI may be explained by brain atrophy. It was observed in a study of 70 patients with early Alzheimer's disease and 70 patients without dementia that lean mass was reduced in the dementia group compared with the no dementia group, while lean mass was associated with whole-brain volume, white matter volume and global cognitive performance [15].

Second, it is also possible that sarcopenia and MCI are not causally linked but that they share common risk factors such as physiopathological mechanisms including inflammation, hormonal dysregulations and malnutrition. In terms of inflammation, a five-year prospective cohort study including 115 older adults found that interleukin 6 (IL-6) and C-reactive protein (CRP) were risk factors for increased loss of total appendicular skeletal muscle [9]. In addition, a longitudinal study, using data from 2574 individuals residing in the United States, indicated that systemic inflammation predicted a significant decrease in cognitive performance [10], and these deleterious effects may be related to the occurrence of cerebral small vessel disease [47]. Next, as for hormonal dysregulation, a study including 337 volunteers aged 64 years and over showed that bioavailable testosterone was positively associated with appendicular skeletal muscle mass, highlighting the key role played by this anabolic hormone in skeletal muscle metabolism [11]. On the other hand, higher levels of serum free testosterone were identified as a protective factor against longitudinal decline in visual memory in a US longitudinal study of 407 elderly men [12]. Finally, malnutrition is a risk factor for both sarcopenia [14] and cognitive

impairment [13]. The malnutrition-sarcopenia relationship may be explained by the fact that several nutritional factors (e.g., proteins, calcium and vitamin D) are necessary to maintain muscle mass [14], while a wide range of different nutrients such as omega-3 fatty acids and vitamin E may have a beneficial impact on cognition [48].

#### *Clinical implications and directions for future research*

Based on these findings, sarcopenia may be a risk factor for the development of MCI, or it may serve as a marker of those who are at heightened risk for dementia. If confirmed to be a risk factor based on future longitudinal research, it may be important to improve the diagnosis and the management of sarcopenia in older adults for the prevention of MCI and ultimately dementia. There is presently no pharmaceutical treatment for sarcopenia, making physical therapy a key component of the management of this condition. Given that access to physiotherapy may be limited in LMICs [49], general practitioners and other health professionals should promote an increase in levels of physical activity (resistance and strength exercises) in patients diagnosed with or at risk for sarcopenia. As increasing physical activity in older adults may also directly reduce the risk of dementia [50], promotion of physical activity may have a dual positive effect of addressing or preventing both sarcopenia and dementia in LMICs. Although there is also some evidence suggesting that dietary interventions may improve muscle outcomes in the elderly population [51], such interventions may be difficult to implement in LMICs, where undernutrition and malnutrition are highly common, because the cost of these interventions is substantial [52]. In terms of future research, longitudinal data is necessary to elucidate direction of associations and causality. Furthermore, more data are needed to better comprehend the mechanisms underlying the association between sarcopenia and MCI. Finally, a wide range of different criteria are used to define sarcopenia [53], and further studies are warranted to harmonize the definition of sarcopenia across the world.

### *Strengths and limitations*

The use of large nationally representative datasets from six LMICs which collectively comprise a substantial proportion of the worldwide population [28] is a clear strength of this study. Nonetheless, the study results must be interpreted in light of several limitations. First, SMM was estimated using an equation and was not directly assessed due to lack of data on objective measures. However, previous research has reported good concordance rates between this formula and gold standard methods (e.g., dual-energy X-ray absorptiometry and magnetic resonance imaging) [39]. Second, the equation used to estimate SMM was validated in a US population [31], and the estimation of SMM with this equation may not be accurate in other populations. Third, as the study design did not allow for formal dementia diagnoses, it is possible that some people with mild dementia were included in the analyses. That being said, the prevalence of MCI in our sample was similar to figures previously reported in the literature [54]. Fourth, diet was not included as a control variable in the analyses, although it may be associated with both sarcopenia and MCI [55,56]. Thus, residual confounding due to this factor is possible. Fifth, there is currently no consensus regarding the definition of MCI [57] and the acceptable level of functional impairment that individuals with MCI could present. We used a definition based on disabilities in eating and getting dressed so as not to exclude individuals with MCI but with disability not related with their cognitive ability. However, it is possible for the results to have differed if a different definition for preservation on functional abilities was used. Finally, since this was a cross-sectional study, causality and temporality of the sarcopenia-MCI relation could not be assessed.

### *Conclusions*

Overall, sarcopenia was associated with higher odds for MCI in this sample of approximately 13000 adults aged  $\geq 65$  years from LMICs. Future studies should investigate the mechanisms underlying the sarcopenia-MCI association, while the utility of sarcopenia as a marker of MCI should also be assessed. In addition, longitudinal studies are necessary to elucidate whether addressing sarcopenia may lead to reduction in MCI and ultimately dementia. Finally, addressing modifiable risk factors (e.g., nutrition and physical activity) for both conditions may help reduce this comorbidity.

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### **Conflict of Interest**

We have no conflict of interest to declare.

### **Author contributions**

Louis Jacob contributed to the design of the study, managed the literature searches, wrote the first draft of the manuscript, and corrected the manuscript. Karel Kostev, Lee Smith, Hans Oh, Guillermo F López-Sánchez, Jae Il Shin, Adel S. Abduljabbar, and Josep Maria Haro contributed to the design of the study and corrected the manuscript. Ai Koyanagi contributed to the design of the study, performed the statistical analyses, wrote the first draft of the manuscript, and corrected the manuscript. All authors contributed to and have approved the final manuscript.

### **Ethical standards**

Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards, in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all participants.

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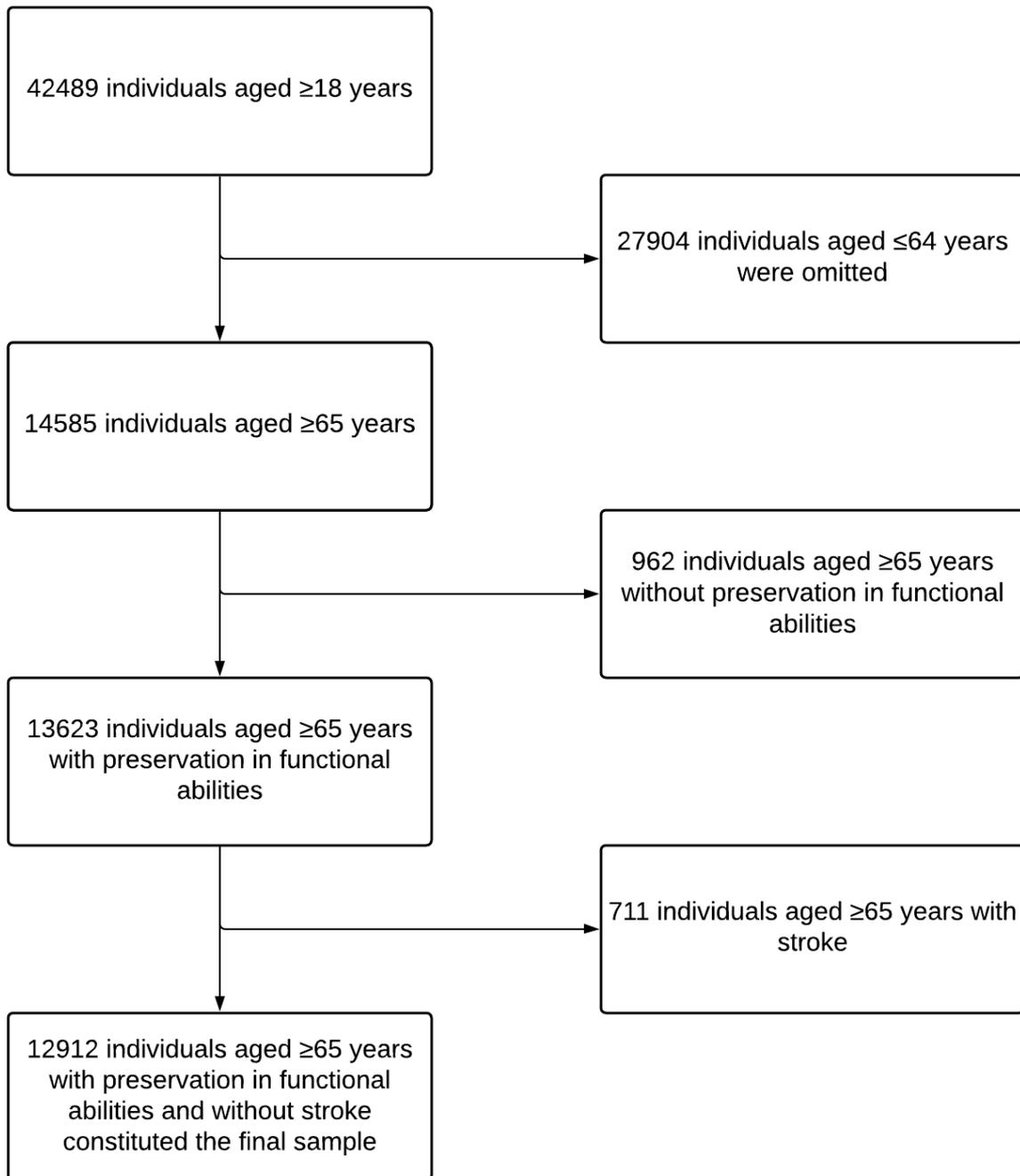
## **Tables and Figures**

**Table 1** Sample characteristics

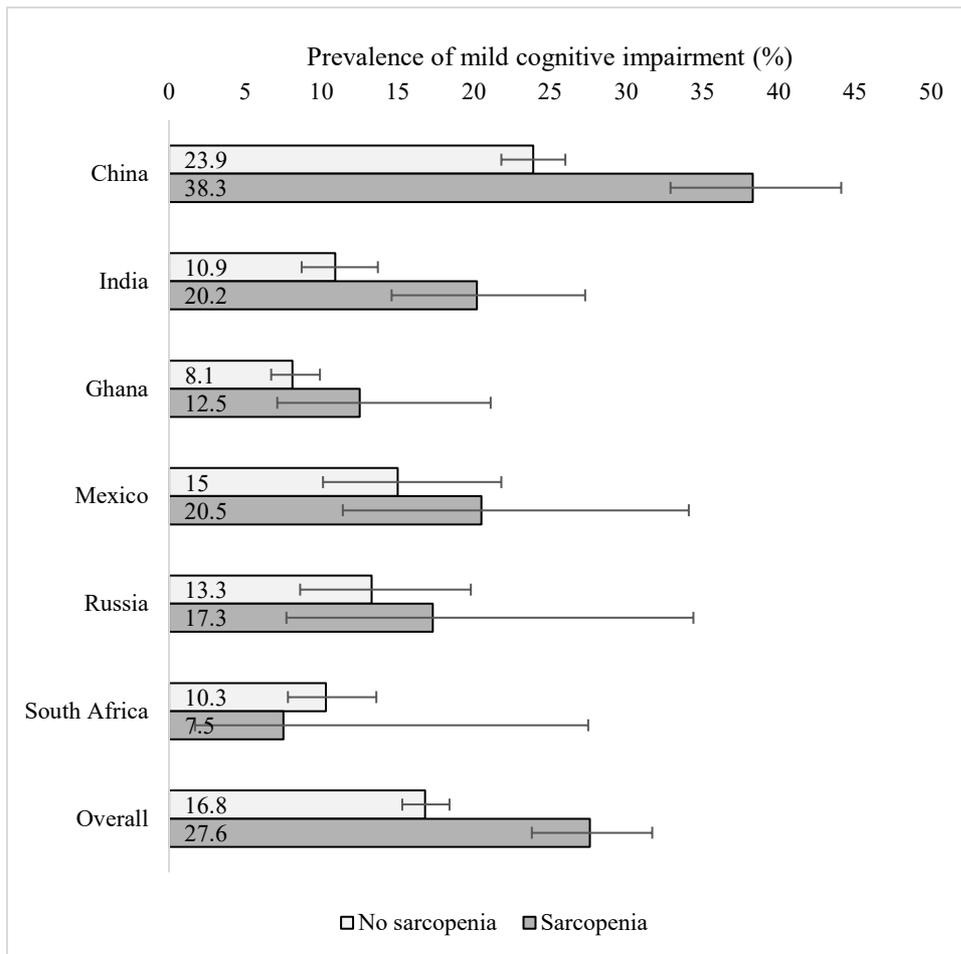
Characteristic	Category	Overall (N=12912)	China (N=4823)	Ghana (N=1841)	India (N=2149)	Mexico (N=1124)	Russia (N=1663)	South Africa (N=1312)
Mild cognitive impairment	Yes	18.1	25.9	9.3	12.3	17.1	14.5	11.0
Sarcopenia	Yes	11.3	11.7	8.6	13.0	9.8	8.1	6.2
Severe sarcopenia	Yes	2.5	1.6	4.0	2.5	2.9	4.9	3.3
Sex	Male	45.2	46.3	52.3	52.8	45.6	31.7	37.6
Age	Mean (SD)	72.2 (10.8)	72.1 (10.5)	73.9 (13.8)	71.2 (9.3)	73.9 (14.2)	73.7 (9.7)	72.8 (14.8)
Years of education	Mean (SD)	5.2 (9.3)	4.6 (9.1)	2.7 (8.7)	3.2 (7.1)	4.1 (9.1)	9.8 (6.1)	5.4 (10.7)
Physical activity	High	37.0	32.8	55.1	38.0	27.2	44.2	19.7
	Moderate	26.0	30.8	12.6	26.8	25.9	18.6	14.9
	Low	37.0	36.5	32.3	35.2	46.9	37.2	65.5
Smoking	Never	62.3	67.9	73.7	42.5	58.9	80.6	67.8
	Quit	29.8	23.6	11.8	51.8	17.4	9.9	20.1
	Current	8.0	8.5	14.4	5.6	23.7	9.4	12.1
Alcohol use	Yes	14.5	17.7	27.2	5.6	12.3	21.8	11.0
Diabetes	Yes	8.2	9.1	3.2	6.8	16.4	8.5	11.1
Hypertension	Yes	62.2	68.6	58.9	40.8	73.6	80.8	82.3

Abbreviation: SD Standard deviation.

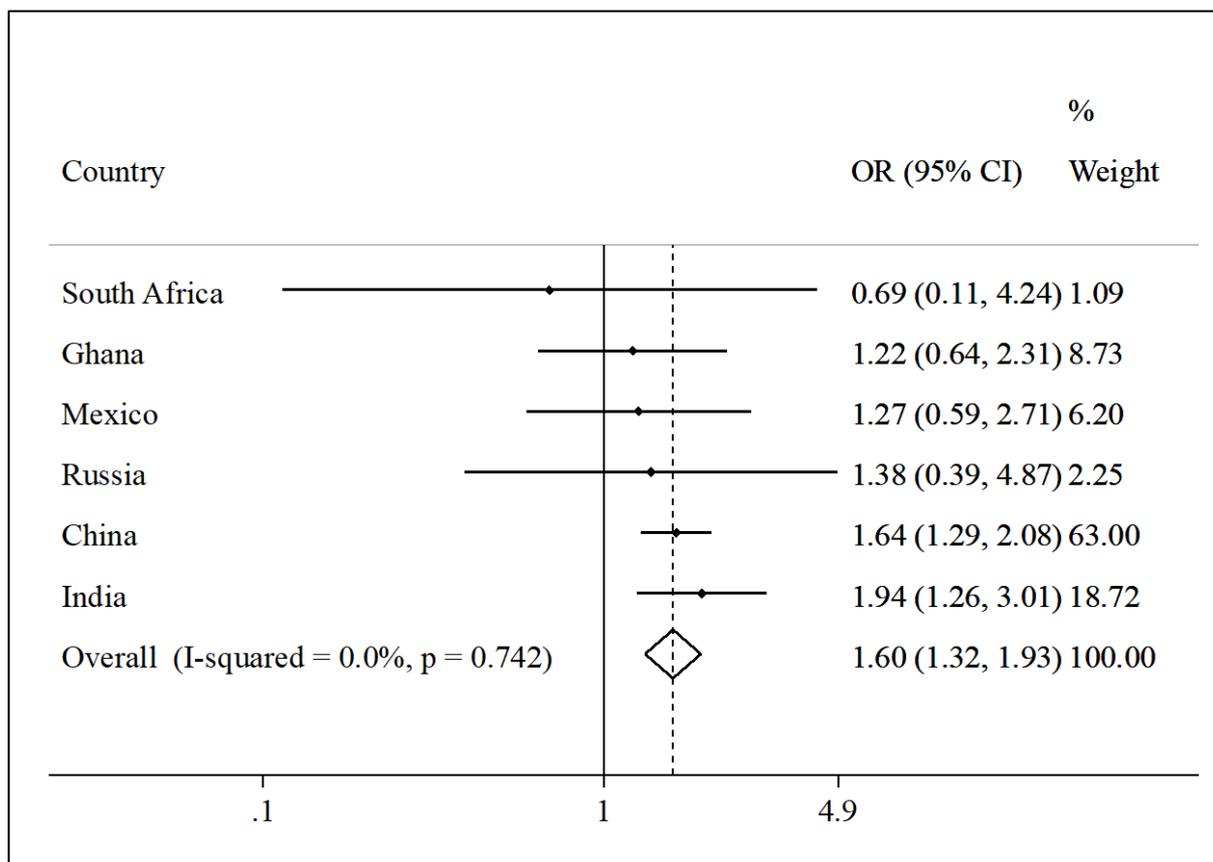
Data are % unless otherwise stated.



**Figure 1** Flow chart of participants



**Figure 2** Prevalence of mild cognitive impairment by presence or absence of sarcopenia  
 Bars denote 95% confidence interval.



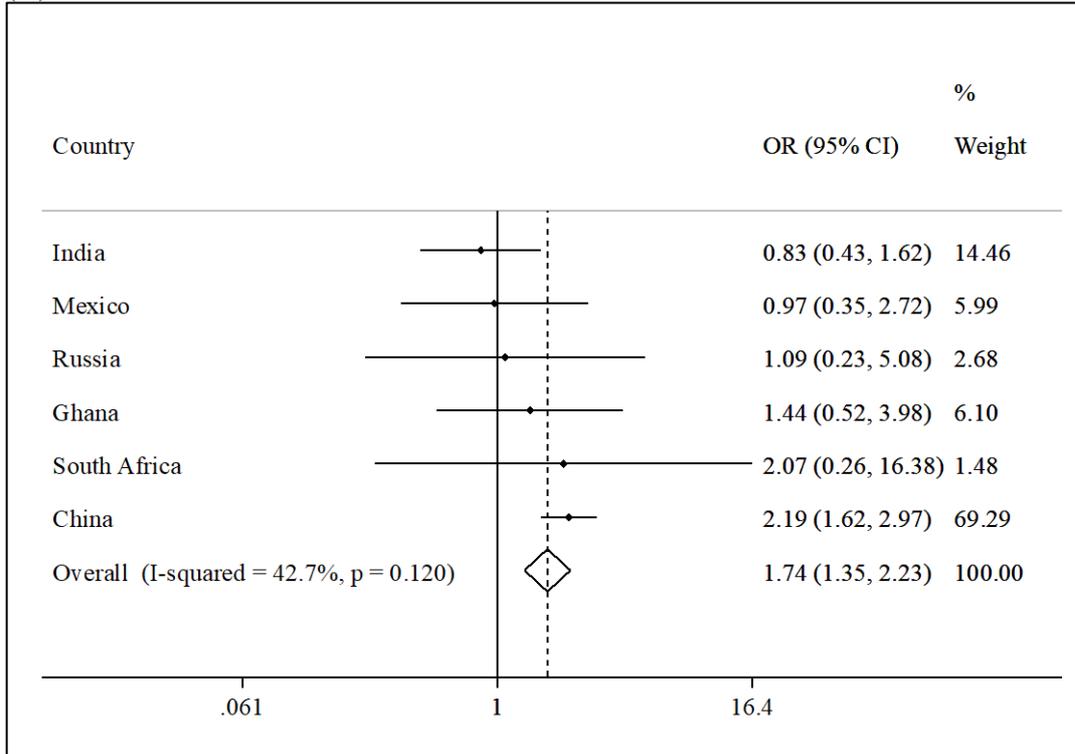
**Figure 3** Association between sarcopenia (exposure) and mild cognitive impairment (outcome) estimated by multivariable logistic regression

Abbreviation: OR Odds ratio; CI Confidence interval.

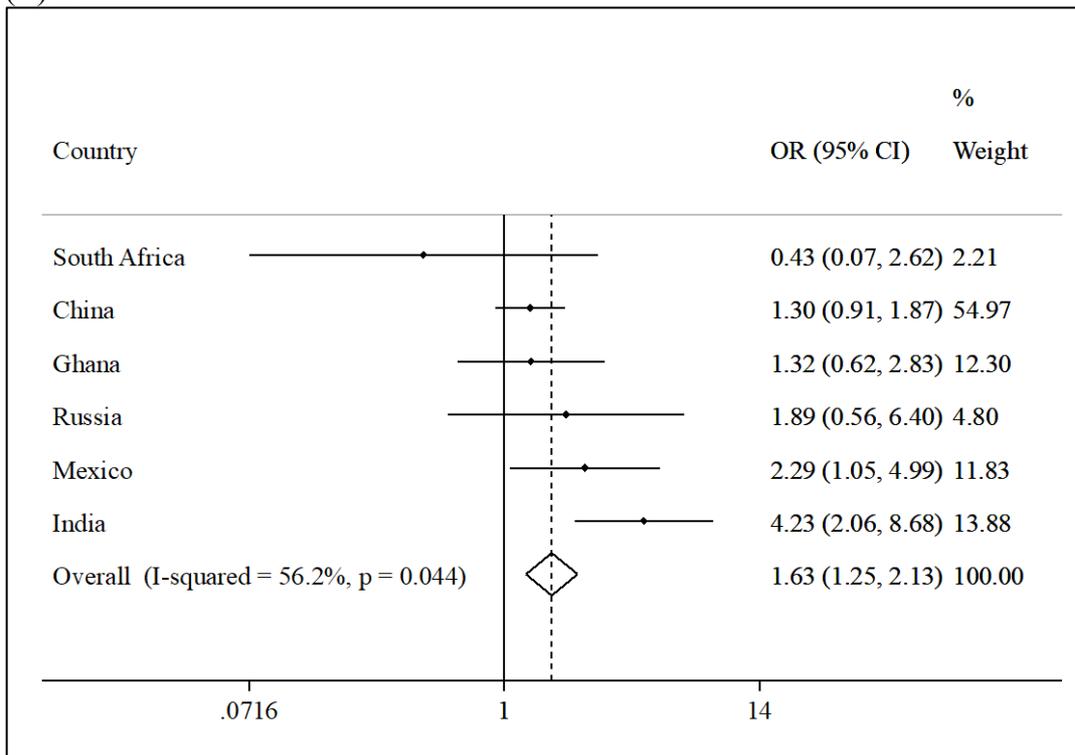
Models are adjusted for years of education, wealth, physical activity, smoking, alcohol use, diabetes, and hypertension.

Overall estimate was obtained by meta-analysis with fixed effects.

(A) Males



(B) Females



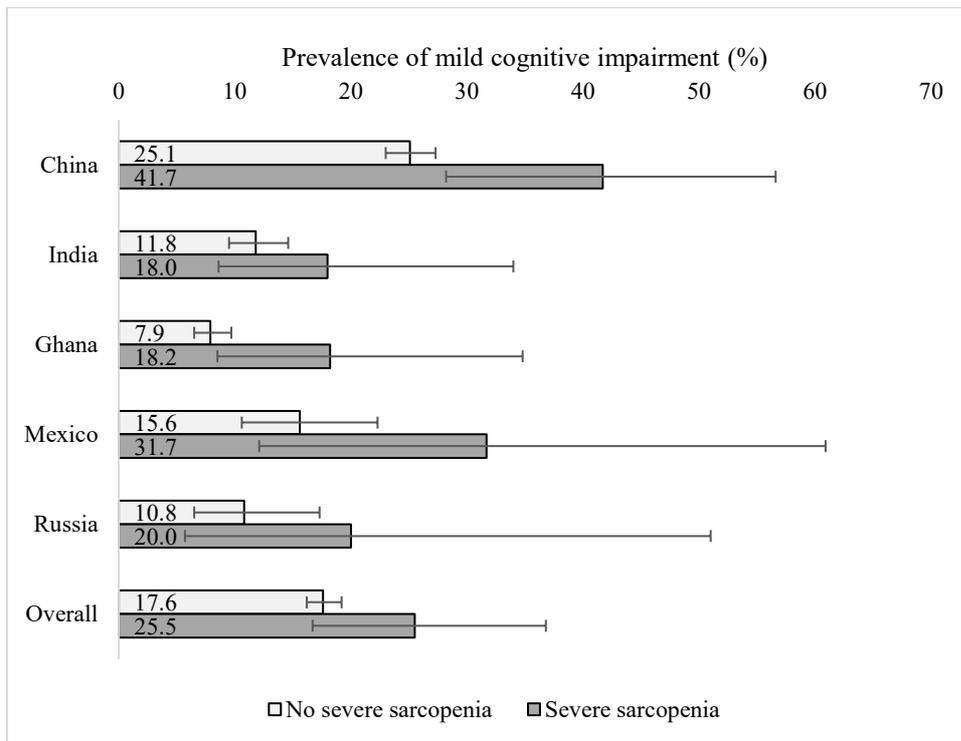
**Figure 4** Association between sarcopenia (exposure) and mild cognitive impairment (outcome) among (A) males and (B) females estimated by multivariable logistic regression

Abbreviation: OR Odds ratio; CI Confidence interval.

Models are adjusted for years of education, wealth, physical activity, smoking, alcohol use, diabetes, and hypertension.

Overall estimate was obtained by meta-analysis with fixed effects.

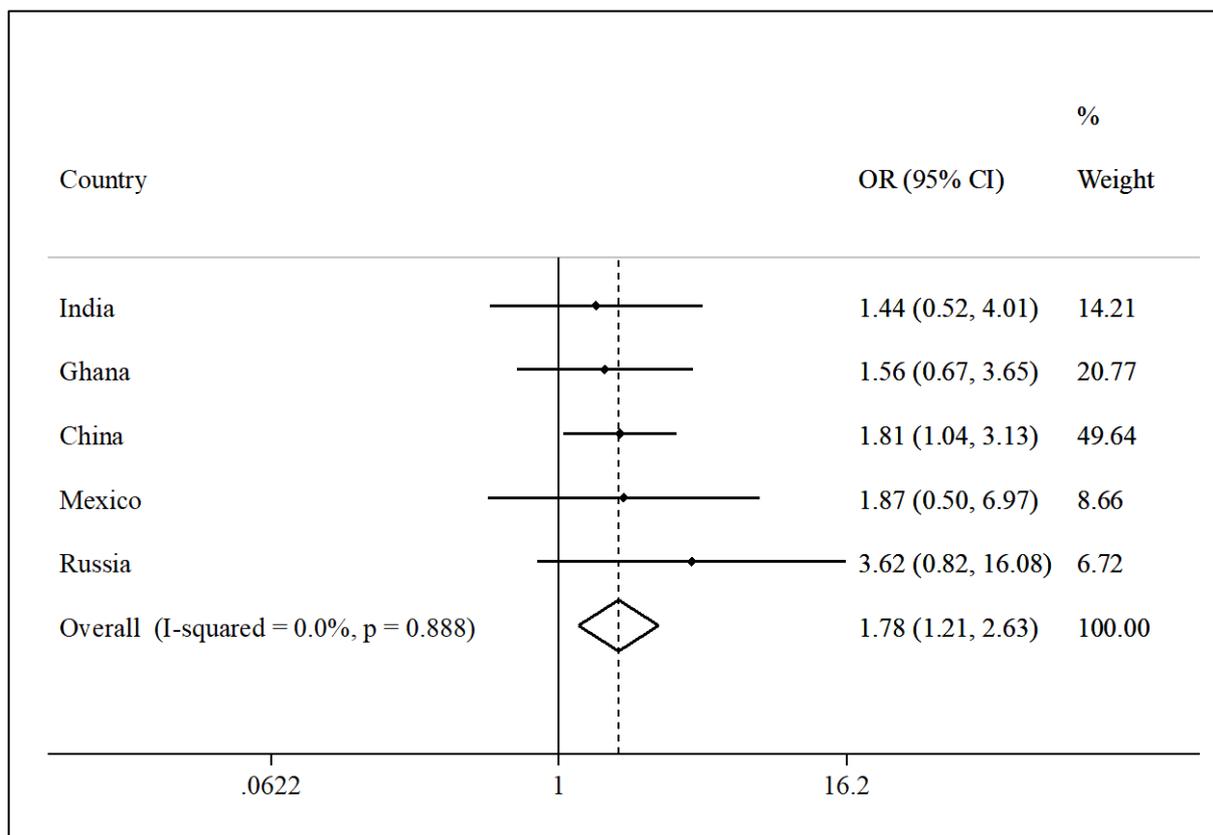
## APPENDIX



**Figure S1** Prevalence of mild cognitive impairment by presence or absence of severe sarcopenia

Bars denote 95% confidence interval.

Estimates for South Africa could not be obtained due to the very small number of people with severe sarcopenia.



**Figure S2** Association between severe sarcopenia (exposure) and mild cognitive impairment (outcome) estimated by multivariable logistic regression

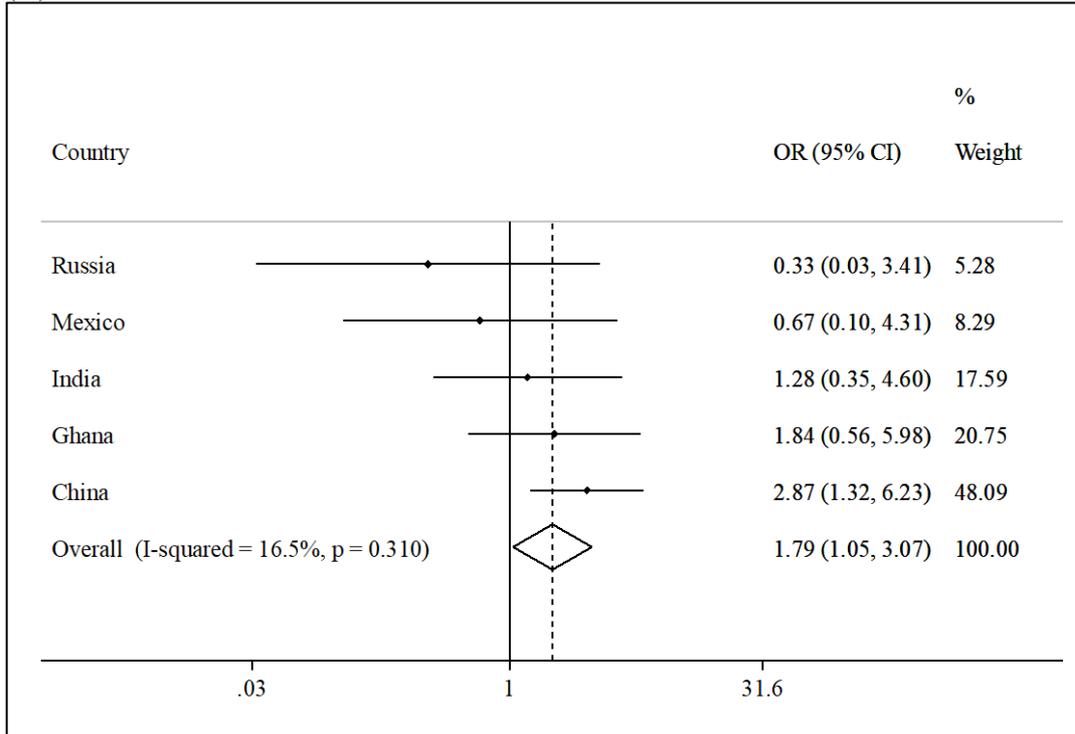
Abbreviation: OR Odds ratio; CI Confidence interval.

Models are adjusted for years of education, wealth, physical activity, smoking, alcohol use, diabetes, and hypertension.

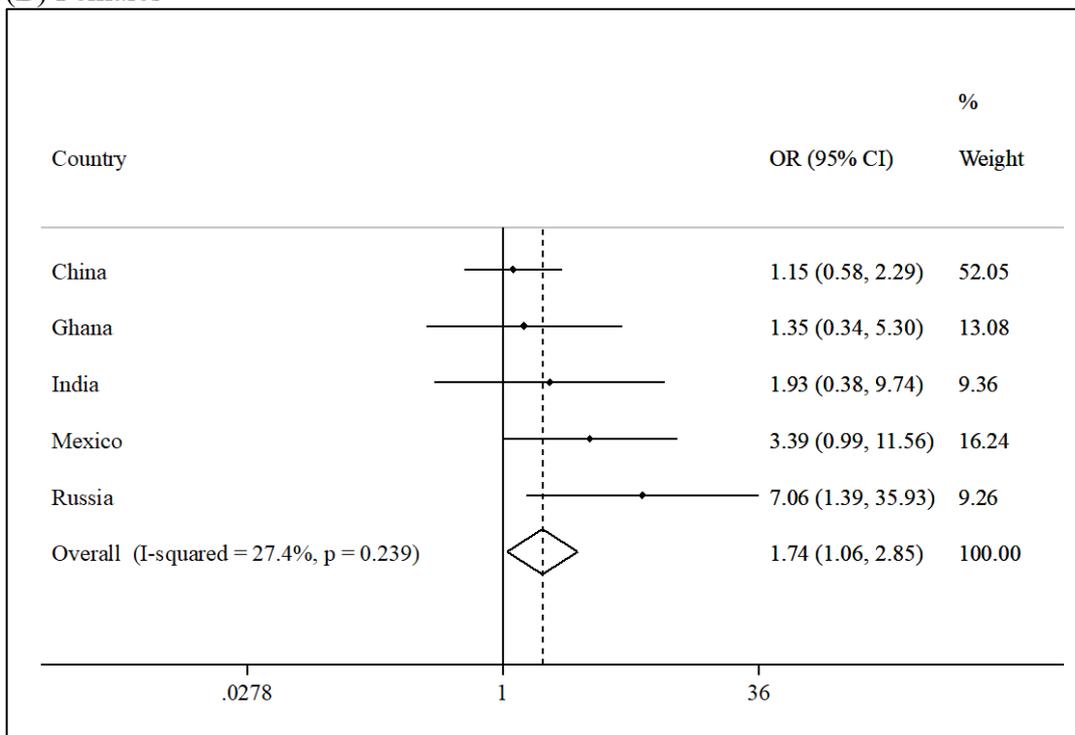
Overall estimate was obtained by meta-analysis with fixed effects.

Estimates for South Africa could not be obtained due to the very small number of people with severe sarcopenia.

(A) Males



(B) Females



**Figure S3** Association between severe sarcopenia (exposure) and mild cognitive impairment (outcome) among (A) males and (B) females estimated by multivariable logistic regression

Abbreviation: OR Odds ratio; CI Confidence interval.

Models are adjusted for years of education, wealth, physical activity, smoking, alcohol use, diabetes, and hypertension.

Overall estimate was obtained by meta-analysis with fixed effects.

Estimates for South Africa could not be obtained due to the very small number of people with severe sarcopenia.

**Table S1** Percent of missing values for the variables used in the study

Variable	% missing
Mild cognitive impairment	2.84
Sarcopenia	14.68
Sex	0.03
Age	0.00
Years of education	1.29
Wealth	0.38
Physical activity	0.01
Smoking	0.28
Alcohol use	0.05
Diabetes	0.10
Hypertension	0.06

**Table S2** Difference in sample characteristics between those missing and not missing values on either sarcopenia or mild cognitive impairment

Characteristic	Category	Missing values on sarcopenia or mild cognitive impairment		P-value <sup>a</sup>
		No	Yes	
Sex	Male	46.3	38.4	0.005
Age	Mean (SD)	71.9 (10.5)	74.0 (12.0)	<0.001
Years of education	Mean (SD)	4.9 (9.2)	7.1 (9.4)	<0.001
Wealth	Poorest	21.8	19.2	0.241
	Poorer	20.3	25.5	
	Middle	20.1	22.7	
	Richer	18.2	12.9	
	Richest	19.7	19.7	
Physical activity	High	38.5	28.1	<0.001
	Moderate	26.9	20.9	
	Low	34.7	51.0	
Smoking	Never	60.5	72.7	<0.001
	Quit	31.8	17.9	
	Current	7.7	9.4	
Alcohol use	Yes	14.6	13.6	0.563
Diabetes	Yes	7.9	9.7	0.238
Hypertension	Yes	61.5	66.6	0.143

<sup>a</sup>P-value was calculated based on Chi-squared tests and Student's t-tests for categorical and continuous variables, respectively.