SARCOPENIA AND FALL-RELATED INJURY AMONG OLDER ADULTS IN FIVE LOW- AND MIDDLE-INCOME COUNTRIES

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ABSTRACT

Sarcopenia is a common condition in older people and increasing evidence suggests that it can be considered as a potential risk factor for falls and fractures. However, no studies on this topic from low- and middle-income countries (LMICs) are available. Thus, we assessed this association among older adults from five LMICs (China, India, Ghana, Mexico, and Russia). Community-based, nationally representative, cross-sectional data of the Study on Global Aging and Adult Health were analyzed. Sarcopenia was defined as the presence of low skeletal muscle mass based on indirect population formula, and either slow gait or low handgrip strength. The presence of fall-related injury was ascertained through self-reported information. Multivariable logistic regression analysis and meta-analysis were conducted. The sample consisted of 13,101 individuals aged ≥65 years (mean (SD) age 72.6 (11.3) years; 45% males). The prevalence of fall-related injury was higher among those with sarcopenia than in those without this condition (e.g., Mexico 9.8% vs. 2.7%). Adjusted analyses showed that sarcopenia was associated with a 1.85 (95%CI=1.24-2.77) times higher odds for fall-related injury, with a low level of between-country heterogeneity. Future studies of longitudinal design may shed light on whether sarcopenia in LMICs may be considered as a risk factor for falls.

Key words: sarcopenia; falls; older people; low- and middle-income countries.

HIGHLIGHTS

- This study is the first study on sarcopenia and falls from LMICs
- Sarcopenia was associated with increased odds for fall-related injury
- There was a low level of between-country heterogeneity.

INTRODUCTION

Falls are among the most important, but still underrepresented problems in geriatric medicine (Rubenstein 2006). It is estimated that about one-third of older adults fall at least once a year, making falls a real emergency among geriatricians (Bergen and others 2016; James and others 2020). A number of factors seems to be important as predisposing factors of falls among older adults, e.g., increasing age, fear of falling, dementia, low mobility, and gait problems (Gale and others 2018; Yeung and others 2019). Among them, sarcopenia is attracting more and more interest since this condition might influence the incidence of falls and fall-related injuries (Yeung and others 2019). Sarcopenia, i.e., the pathological loss of muscle mass typical of older age, has an elevated prevalence in older people (from 2 to 37%) (Shafiee and others 2017), being associated with several negative outcomes (Veronese and others 2019a). The loss of muscle mass and strength, that ultimately affects balance, gait, lower-limb proprioception (Zou and others 2019) and overall ability to perform tasks of daily living, may be considered as relevant risk factors for falls (Landi and others 2012).

However, research evidence on sarcopenia as a potential risk factor for falls or fall-related injury still remains largely unexplored. In one systematic review and meta-analysis, the authors identified 32 studies and found that there is a significant and strong association between sarcopenia and falls (Yeung and others 2019). However, some limitations of this work were recognized by the same authors. First, the sample size of the studies was generally small. Second, no study was specifically conducted in low- and middle-income countries (LMICs) where both sarcopenia (Brennan-Olsen and others 2019) and falls (Tan and others 2014) are exponentially increasing as problems. Finally, no study was conducted in a multi-country setting that could be of importance in order to better understand if any significant difference across countries exists.

Given this background, the aim of the study was to examine the potential association of sarcopenia with falls, using large nationally representative data comprising more than 13,000 older adults aged ≥65 years from five LMICs (China, Ghana, India, Mexico, and Russia), which broadly represent different geographical locations and levels of socio-economic and demographic transition.

METHODS

Data from the SAGE were analyzed. These data are publically available through http://www.who.int/healthinfo/sage/en/. This survey was undertaken in China, Ghana, India, Mexico, Russia, and South Africa between 2007 and 2010. All countries were LMICs based on the World Bank classification at the time of the survey. Details of the survey methodology have been published elsewhere (Kowal and others 2012). In brief, in order to obtain nationally representative samples, a multistage clustered sampling design method was used. The sample consisted of adults aged ≥18 years with oversampling of those aged ≥50 years. Trained interviewers conducted face-to-face interviews using a standard questionnaire. Standard translation procedures were undertaken to ensure comparability between countries. If a respondent was unable to undertake the interview because of limited cognitive function, then a separate questionnaire was administered to a proxy respondent. These individuals were not included in the current study. The survey response rates were: China 93%; Ghana 81%; India 68%; Mexico 53%; Russia 83%; and South Africa 75%. Sampling weights were constructed to adjust for the population structure as reported by the United Nations Statistical Division. Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards. Written informed consent was obtained from all participants.

Fall-related injury

The variable on fall-related injury of the SAGE was derived from questions of the WHO guidelines on injuries (Stewart Williams and others 2015). First, the participant was asked "In the past 12 months, have you had any other event (other than a road traffic accident) where you suffered from bodily injury?" Those who answered affirmatively were prompted to the next question "What was the cause of the injury?" If there were multiple injuries, the respondent was instructed to refer to the most recent injury. If the respondent answered "Fall", then he or she was considered to have had a fall-related injury in the past year.

Sarcopenia

Following the criteria used in previous publications using the same dataset (Koyanagi and others 2020; Smith and others 2020; Tyrovolas and others 2016), sarcopenia was defined as having low skeletal muscle mass (SMM) as reflected by lower skeletal mass index (SMI) and either a slow gait speed or a weak handgrip strength (Dam and others 2014). Skeletal muscle mass (SMM) was calculated as the appendicular skeletal muscle mass (ASM) based on the equation proposed by Lee and colleagues: ASM= 0.244*weight + 7.8*height + 6.6*sex–0.098*age + race–3.3 [where female=0 and male=1; race=0 (White and Hispanic), race=1.9 (Black) and race=-1.6 (Asian)] (Lee and others 2000b). ASM was further divided by BMI based on measured weight and height to create a skeletal muscle mass index (SMI) (Studenski and others 2014). Low SMM was defined as the lowest quintile of the SMI based on sex-stratified values. Country-specific cut-offs were only used to determine low SMI, as this indicator is likely to be affected by racial differences in body composition.(Ortiz and others 1992) Gait speed was based on a 4m timed walk and was measured by asking the participant to walk at a rapid pace, as fast as he/she safely can. The interviewer recorded the time to completion of the 4m walk. Slow gait speed referred to the lowest quintile of walking speed based on height, age, and sex-stratified values (Capistrant and others 2014; Tyrovolas and others 2015). 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. (Cruz-Jentoft and others 2019)

Covariates

The selection of covariates was based on past literature (Tanimoto and others 2014) and included sex, age, wealth quintiles based on income, years of education received, living arrangement (alone or not), alcohol consumption in the past 30 days (yes or no), smoking (never, current, former), physical activity, body mass index (BMI) based on measured weight and height [<18.5 (underweight), 18.5–24.9 (normal), 25.0–29.9 (overweight), ≥30 (obese) kg/m^2], number of chronic conditions, and disability. Levels of physical activity were assessed with the Global Physical Activity Questionnaire and were classified as low, moderate, and high based on conventional cut-offs (Bull and others 2009). The total number of 11 chronic physical conditions (angina, arthritis, asthma, stroke, diabetes, edentulism, visual impairment, chronic lung disease, hypertension, chronic back pain, and hearing problems) was calculated for each participant. The diagnosis was based on the presence of either one of the following: self-reported diagnosis; or symptom-based diagnosis based on algorithms etc. Details on the diagnosis are provided in Appendix Table S1. Activities of daily living (ADL) disability was assessed by standard basic ADL questions (Al Snih and others 2010; Backholer and others 2012) which included six questions with the introductory phrase "overall in the last 30 days, how much difficulty did you have" followed by: in washing your whole body?; in getting dressed?; with moving around inside your home?; with eating (including cutting up your food)?; with getting up from lying down?; with getting to and using the toilet? Answer options were none, mild, moderate, severe, extreme/cannot do. Those who answered severe or extreme/cannot do to any of the six questions were considered to have limitations in ADL.

Statistical analysis

The statistical analysis was performed with Stata 14.1 (Stata Corp LP, College station, Texas). We excluded those aged <65 years as sarcopenia is an age-related condition. We conducted country-wise multivariable logistic regression analysis to assess the association between sarcopenia (exposure) and fall-related injury (outcome). Although data for South Africa was available, due to the very low prevalence of fall-related injuries in this country, stable estimates could not be obtained. Thus, South Africa was omitted from the analysis. The regression analysis was adjusted for sex, age, wealth, education, living arrangement, alcohol consumption, smoking, physical activity, BMI, number of chronic conditions, and disability. Furthermore, in order to assess the between-country heterogeneity that may exist in the association between sarcopenia and fall-related injury, we calculated the Higgins's I^2 based on estimates from each country. The Higgins's I^2 represents 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 (Higgins and Thompson 2002). A pooled estimate was obtained by random-effect meta-analysis. All variables were included in the models as categorical variables with the exception of age, years of education, and number of chronic conditions (continuous variables). The sample weighting and the complex study design were taken into account in the analyses. Results from the regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CIs). The level of statistical significance was set at $P<0.05$.

RESULTS

The final sample included 13,101 individuals aged ≥65 years (China n=5,360; Ghana n=1,975; India n=2,441; Mexico n=1,375; Russia n=1,950). Overall, the mean (SD) age of the sample was 72.6 (11.3) years and 45.2% were males, while the prevalence of sarcopenia and fall-related injuries was 13.5% and 4.9%, respectively. The sample characteristics by country are provided in **Table 1**. The prevalence of fall-related injury ranged from 2.3% (Russia) to 7.2% (India), while that of sarcopenia ranged from 12.7% (Russia) to 14.8% (Mexico).

Table 1

Sample characteristics by country

Characteristic		China (n=5360)	Ghana (n=1975)	India (n=2441)	Mexico (n=1375)	Russia (n=1950)
Fall-related injury	Yes	4.4	3.1	7.2	4.6	2.3
Sarcopenia	Yes	13.0	13.1	14.6	14.8	12.7
Sex	Male	46.6	52.0	52.0	45.1	31.8
Age (years)	Mean (SD)	72.3 (11.0)	74.1 (14.1)	71.6 (10.0)	74.7 (15.9)	74.2 (10.4)
Education (years)	Mean (SD)	4.5 (9.2)	2.7 (8.7)	3 (7.0)	4.0 (9.0)	9.6 (6.2)
Living arrangement	Alone	14.9	10.6	3.1	5.1	40.1
Alcohol consumption	Yes	17.1	26.6	5.5	11.4	20.7
Smoking	Never	67.8	73.5	42.8	60.1	80.3
	Current	23.4	11.7	51.0	17.7	9.3
	Former	8.9	14.8	6.2	22.2	10.4
Physical activity	High	32.0	53.5	35.9	25.2	40.8
	Moderate	30.3	12.7	25.5	24.1	18.4
	Low	37.6	33.8	38.6	50.7	40.9
Body mass index	Underweight	6.3	20.8	46.0	1.1	1.7
	Normal	60.1	55.6	44.0	31.9	27.1
	Overweight	28.3	16.5	7.8	43.8	42.4
	Obese	5.4	7.2	2.2	23.2	28.8
No. of chronic conditions	Mean (SD)	1.9 (2.6)	1.4 (2.0)	1.9 (2.4)	2.0 (2.9)	2.9 (2.7)
Disability	Yes	3.2	11.7	19.0	11.2	15.9

Abbreviation: SD Standard deviation
Data are % unless otherwise stated.

Overall, the prevalence of fall-related injury was higher among those with sarcopenia than in those without this condition (7.9% vs. 4.3%). The country-wise figures are shown in **Figure 1**. In all countries, the prevalence of fall-related injury was higher among those with sarcopenia with the contrast being particularly pronounced in Mexico (no sarcopenia 2.7% vs. sarcopenia 9.8%).

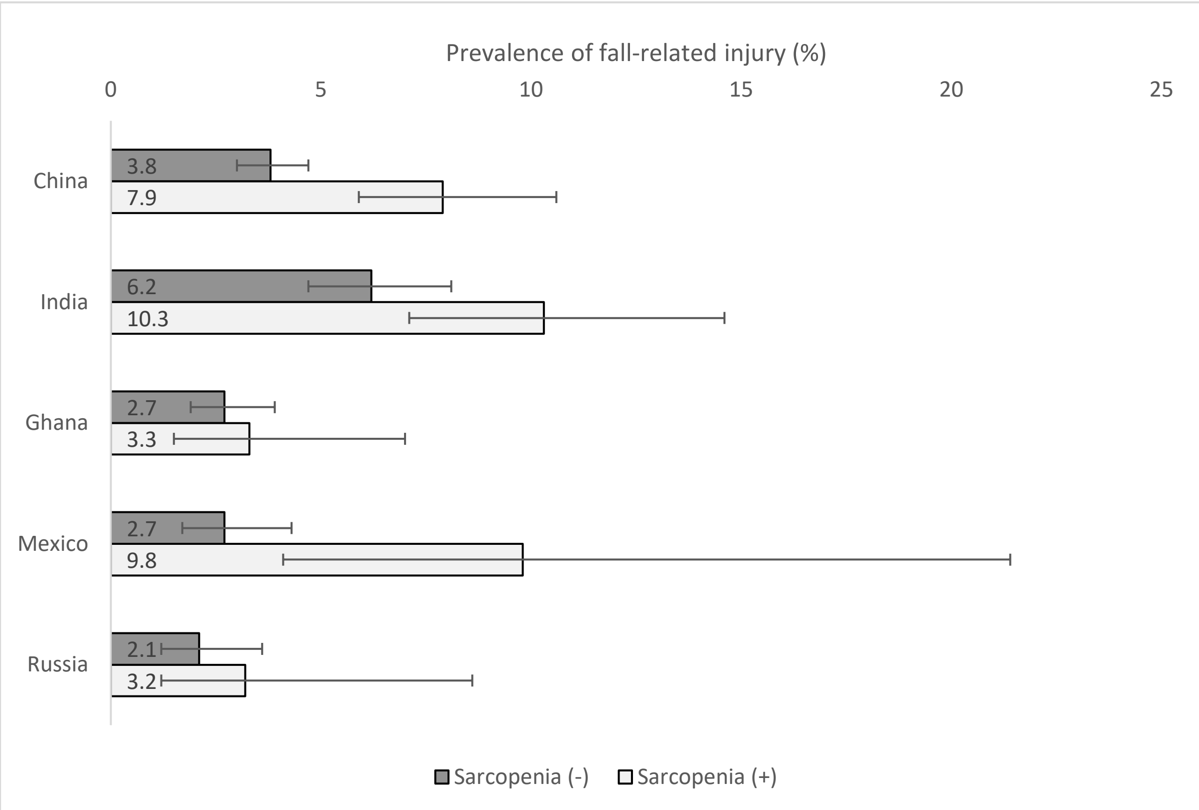


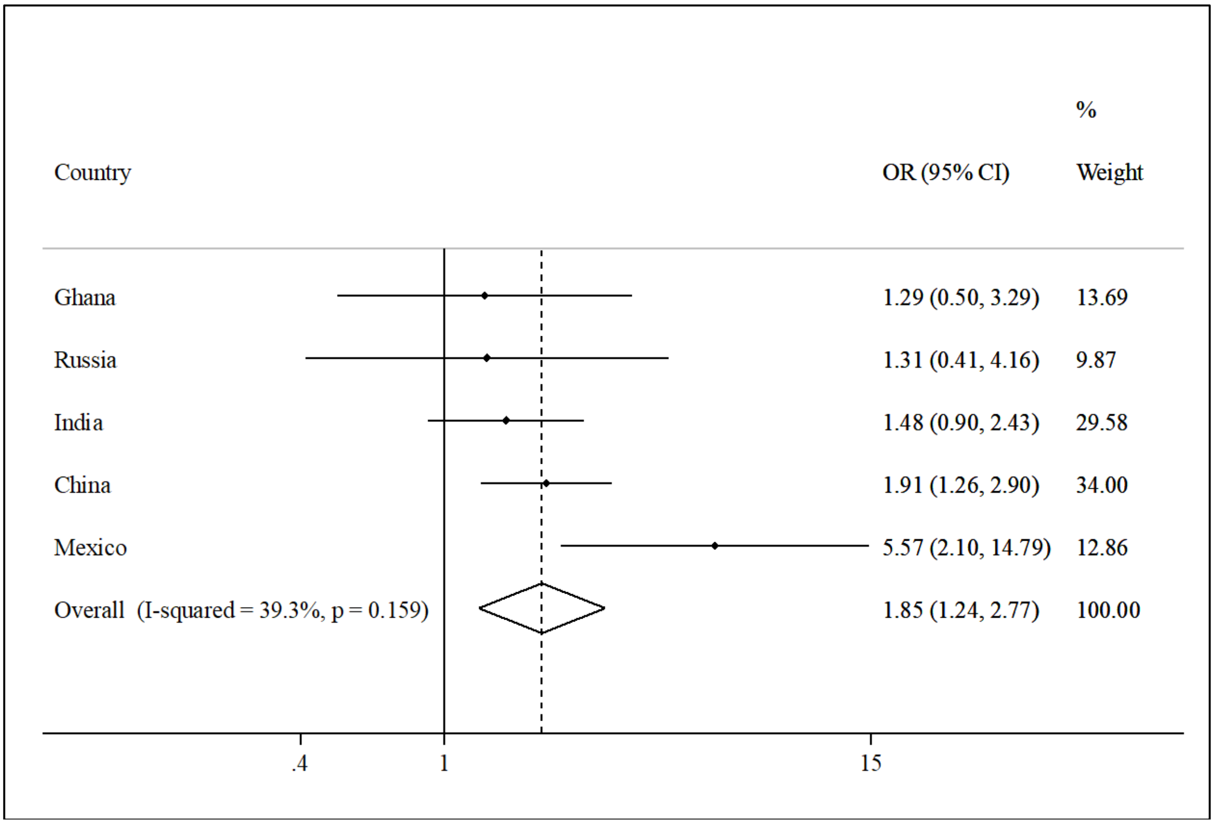
Figure 1

Prevalence of fall-related injury by sarcopenia status
Bars denote 95% confidence interval.

The country-wise association between sarcopenia and fall-related injuries estimated by multivariable logistic regression is shown in **Figure 2**. There was a positive association (OR>1) between sarcopenia and fall-related injuries in all countries although statistical significance was reached only in China and Mexico. Overall, sarcopenia was associated with a 1.85 (95%CI=1.24-2.77) times higher odds for fall-related injury, with a low level of between-country heterogeneity (I^2=39.3%).

Figure 2

Country-wise association between sarcopenia and fall-related injury estimated by multivariable logistic regression



Abbreviation: OR Odds ratio; CI Confidence interval
Models are adjusted for sex, age, wealth, education, living arrangement, alcohol consumption, smoking, physical activity, body mass index, number of chronic conditions, and disability.
Overall estimate was based on meta-analysis with random effects.

DISCUSSION

In this research, we found that sarcopenia is significantly associated with higher odds for fall-related injuries among adults aged ≥65 years in LMICs. To the best of our knowledge, this is the largest study on this topic to date and also the first study from LMICs.

The topic of sarcopenia and falls has previously been examined in high-income countries. A meta-analysis, published about 15 years ago, showed a significant, but weak association between low muscle strength and falls (Moreland and others 2004). Of importance is that two more recent systematic reviews and meta-analyses reported that multidimensional assessment of sarcopenia (i.e., evaluating muscle strength, physical performance and body composition parameters) predicts the onset of falls and fractures in older people much more accurately. (Beaudart and others 2017; Yeung and others 2019). Our investigation, including all the dimensions needed for the diagnosis of sarcopenia, further confirmed the hypothesis that sarcopenia is significantly associated with falls.

The association between sarcopenia and falls can be mediated by several factors. First, sarcopenia is characterized by slow gait speed (Cruz-Jentoft and others 2010) that, in turn, is a strong factor for falls (Veronese and others 2014). Second, sarcopenia may impair balance in older people that is, again, a strong risk factor for falls.(Gadelha and others 2018) Finally, the hormonal dysregulations typical of sarcopenia (e.g., low testosterone and low insulin growth factor [IGF] levels) (Morley and Malmstrom 2013) are also associated with an increased risk of falls (Stewart 2006). In this sense, for example, low testosterone is associated with falls, since sexual hormones are strongly associated with low muscle mass and physical performance such as neuromuscular coordination, poor vision and impairment in balance. (Vandenput and others 2017) A similar evidence is available for low IGF levels. Again, the impairment in physical performance and strength seems the most important mechanism explaining the association between low IGF levels and increased risk of falls.(Iolascon and Moretti 2018) Future basic research is however needed to explain, from a pathophysiological point of view, the association between these hormonal alterations and falls.

Our findings further stress the importance and the urgency for a timely and early identification of sarcopenia, for preventing falls and fractures, through tailored interventions. In this sense, current literature suggests that among all the interventions that we can consider for older people affected by sarcopenia, progressive resistance training may improve risk factors for falls and fractures such as muscle function, balance, and functional mobility (Papa and others 2017). Unfortunately, it is still not clear if progressive resistance training translates directly into a reduction in incidence of falls and fractures (Hopewell and others 2018). Therefore, future randomized controlled trials examining the effect of progressive resistance training on falls in sarcopenic people are needed (Yeung and others 2019). At the same time, another important intervention that we may suggest is the nutritional approach. Sarcopenic subjects are often affected by poor nutritional status particularly in terms of proteins and some micronutrients (such as vitamin D) (Schneider and Trence 2019), and some multinutrient interventions may improve physical performance and muscle strength in sarcopenia (Veronese and others 2019b), possibly leading to a decreased risk of falls.

The large sample size and the use of nationally representative datasets from LMICs are clear strengths of the study. However, the results of this study must be interpreted in the light of its limitations. First, several data were self-reported, which is subject to bias (e.g., recall, social desirability bias). For example, falls were self-reported and it is known that for this condition, this can lead to an important underestimation (Mackenzie and others 2006). Second, the estimation of muscle mass was not based on a direct assessment, e.g., with dual-energy X-ray absorptiometry (DXA). However, this estimation has been validated against gold standard methods (magnetic resonance imaging and DXA), with good concordance rates (Lee and others 2000a). These radiological methods (i.e., DXA), however, are expensive and often impractical for population-based surveys especially from LMICs. Third, for sarcopenia, there are still no universal operative definitions. Our definition was based on that proposed by international groups of experts and already used in this study (Koyanagi and others 2020), but it is possible that the results may differ if a different definition for sarcopenia was used. Finally, given the cross-sectional nature of the study, causality and temporal associations cannot be established and reverse causality is also possible, i.e., people falling more frequently may experience a higher risk of sarcopenia.

In conclusion, the present study found that sarcopenia is associated with higher odds fall-related injury among adults aged ≥65 years in five LMICs. Confirmatory studies with a longitudinal design are necessary to examine whether sarcopenia can be considered as a potential risk factor for falls in older people living in LMICs, since this population is exponentially increasing.

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Table S1

Table S1 Details on the diagnosis of chronic conditions

Condition	(a) Self-reported diagnosis	(b) Symptom-based algorithm or other method of diagnosis[a]
Angina	Have you ever been diagnosed with angina or angina pectoris (a heart disease)?	Rose questionnaire [1]
Arthritis	Have you ever been diagnosed with/told you have arthritis (a disease of the joints, or by other names rheumatism or osteoarthritis)?	NA
Asthma	Have you ever been diagnosed with asthma (an allergic respiratory disease)?	NA
Chronic back pain	Chronic back pain was defined as having had back pain everyday during the last 30 days.	NA
Chronic lung disease[a]	Have you ever been diagnosed with chronic lung disease (emphysema, bronchitis, COPD)?	1. During the last 12 months, have you experienced any shortness of breath at rest (while awake)? (Yes) **OR** 2. "Yes" to both of the following (past 12 months): (a) Have you experienced any coughing or wheezing for 10 minutes or more at a time? (b) Have you experienced any coughing up of sputum or phlegm on most days of the month for at least 3 months?
Diabetes	Have you ever been diagnosed with diabetes (high blood sugar)? (not including diabetes associated with a pregnancy)	NA
Edentulism	Have you lost all of your natural teeth?	NA
Hearing problems	NA	The interviewer observed this condition during the survey
Hypertension	Have you ever been diagnosed with high blood pressure (hypertension)?	Blood pressure was measured three times with a one-minute interval with the use of a wrist blood pressure monitor (Medistar Wrist Blood Pressure Model S) and the mean value of the three measurements was calculated. Hypertension was defined as having at least one of the following: systolic blood pressure ≥140 mmHg; diastolic blood pressure ≥90 mmHg.
Stroke	Have you ever been told by a health professional that you have had a stroke?	NA
Visual impairment	Visual impairment was defined as having severe/extreme difficulty in seeing and recognizing a person that the participant knows across the road	NA

For all chronic conditions, we assumed that the individual had the condition if they fulfilled at least one of the following: (a) affirmative answer to self-reported diagnosis or (b) symptom-based algorithm or other method of diagnosis.

[a] This algorithm has been used in previous publications [2, 3] and have been validated [2, 4].

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