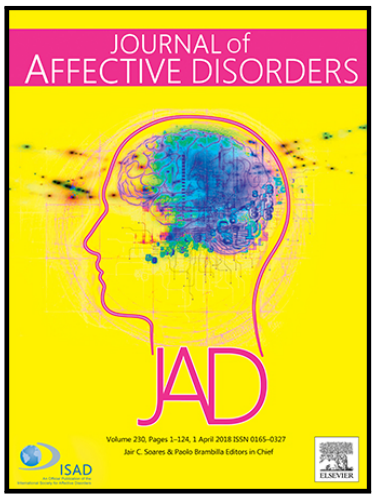

Handgrip strength and depression among 34,129 adults aged 50 years and older in six low- and middle-income countries

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HIGHLIGHTS

- Little is known about the relationship between handgrip strength and depression
- Our data across 6 LMICs suggests weak handgrip strength is associated with depression.
- Across all countries, weak handgrip strength was associated with a 1.45 (95%CI=1.12-1.88) times higher odds for depression.
- Future research should seek to establish the predictive value of this inexpensive measure for clinical use.

Handgrip strength and depression among 34,129 adults aged 50 years and older in six low- and middle-income countries

Submission to Journal of Affective Disorders

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Abstract (250/250)

Introduction: Handgrip strength is a simple and inexpensive marker of health and mortality risk. It presents an ideal risk-stratifying method for use in low and middle-income countries (LMICs). There are, however, no population-based studies investigating the associations between handgrip strength and depression in LMICs. We aimed to assess these associations among community-dwelling middle-aged and older adults using nationally representative data from six LMICs.

Method: Cross-sectional data on individuals aged ≥50 years from the World Health Organization's Study on Global Ageing and Adult Health were analyzed. Depression was based on the Composite International Diagnostic Interview. Weak handgrip strength was defined as <30kg for men and <20 kg for women using the average value of two handgrip measurements of the dominant hand. Multivariable logistic regression analysis was conducted.

Results: The sample included 34,129 individuals (62.4±16.0 years; 52.1% female). The prevalence of weak handgrip strength and depression were 47.4% and 6.2%, respectively. Individuals with weak handgrip strength had a higher prevalence of depression than those without this condition (8.8% vs. 3.8%; p<0.001). Across all countries, after adjustment for potential confounders, weak handgrip strength was associated with a 1.45 (95%CI=1.12-1.88) times higher odds for depression, although some between-country differences were noted.

Discussion: Weaker handgrip strength is associated with higher odds for depression in LMICs. Future research should seek to establish the predictive value of this inexpensive measure for clinical use. Furthermore, interventional studies should examine if muscular strength can be a target of resistance-training interventions to address depressive symptoms in low-resourced settings.

Key words: hand grip strength, depression, older adults, health, mental health

Introduction

Depression is an important public health problem, particularly among older adults in low- and middle- income countries (LMICs) (Guerra et al., 2016a) where a demographic transition, with an increasing number of older people, is rapidly occurring (Christensen et al., 2009). Not only does depression carry an immense mental health burden, but those with depressive disorders are also at a higher risk for various physical health co-morbidities such as hearing problems, arthritis and angina, among others (Stubbs et al., 2017a; Stubbs et al., 2017b; Vancampfort et al., 2016; Vancampfort et al., 2014; Vancampfort et al., 2015) and associated premature mortality (Corrrell et al., 2017; Walker et al., 2015). Despite the clear negative consequences of depression, only between 7-21% of patients are treated for depressive disorders in LMICs (Chisholm et al., 2016). While high-income countries spend an average of US$50 per year per person on the prevention and treatment of mental disorders, LMICs spend less than US$2 per year per person (World Health Organization, 2015).

Engagement in physical activity has been associated with the prevention of depression in middle-aged and old age people (Schuch et al., 2018). Furthermore, in older people with depression (≥ 60 years), physical activity has a large antidepressant effect (Standardized Mean Difference (SMD) = -0.90 [95%CI -0.29 to -1.51]) (Schuch et al., 2016c). However, most research on the protective and antidepressant effects of physical activity has focused on aerobic exercise (e.g., walking) and not on resistance training (Schuch et al., 2018; Schuch et al., 2016b). Whilst there is evidence on the relationship between physical activity and depression in older age, there is increasing recognition that objective measures of physical fitness may be an important associated factor (Bouchard et al., 1994). For example, people free from depression with low cardiorespiratory fitness are at increased risk of developing depression (n=1,128,290, hazard ratio=1.76, 95% CI 1.61-1.91, p<0.001) (Schuch et al., 2016d). Furthermore, there is increasing evidence suggesting that objective tests of muscular fitness may be useful to identify people with depression (Veronese et al., 2017a; McDowell et al., 2018).

Among the potential measures to capture muscular strength, handgrip strength is a simple, inexpensive risk-stratifying method that correlates closely with measures of muscle strength from other muscle groups, including the lower limbs (Samuel et al., 2012). Handgrip strength is associated with cardiovascular diseases, cognitive decline (Veronese et al., 2016), mood disorders (Veronese et

al., 2017a; Veronese et al., 2017b) and all-cause death (Celis-Morales et al., 2018; Leong et al., 2015). Its prognostic value, the simplicity of measurement with minimal training, portability, and low cost could make it an attractive clinical test to evaluate an individual's health risk in low-income settings (Leong et al., 2016).

Data from population-based studies assessing the relationship between handgrip strength and depression among older men and women is scarce, and limited to higher-income countries. In a longitudinal Italian study in people aged 65 years or older, handgrip strength has been shown to predict depression based on the Geriatric Depression scale four years later (Veronese et al., 2017). Next to this, in a longitudinal Irish study in people aged 50 years or older, prospective models adjusted for age, sex, waist circumference, social class, smoking, and health status among 2554 men, showed that the middle and high muscle strength tertiles were non-significantly associated with 32.9% (p=0.21) and 9.9% (p=0.74) reduced odds of developing depression, respectively. Among 1961 women, the middle and high strength tertiles were non-significantly associated with 28.5% (p=0.13) and significantly associated with 43.4% (p=0.01) reduced odds of developing depression, respectively (McDowell et al., 2018a). Finally, among a Japanese sample of older adults, those with lower hand-grip strength had increased odds of having depressive symptoms at baseline. Furthermore, lower hand-grip strength was associated with the development of depressive symptoms after 1 year (Fukumori et al., 2015).

Furthermore, while a Brazilian study found that among a small sample (N=180) of adults 60 years or older, depression was independently associated with (p=0.03) low grip strength, (Lino et al., 2016), there are no nationally representative population-based studies investigating the associations between handgrip strength and depression in LMICs. This is an important research gap given the rapid increase in chronic diseases including depression (Guerra et al., 2016b) in LMICs. In addition, increasing rates of chronic conditions in LMICs will have considerable financial implications over the next few decades if health systems are to respond appropriately to the emerging mental and physical health burden (Garin et al., 2016). The association between depression and muscular strength may also differ in LMICs due to the suboptimal treatment of depression (Arokiasamy et al., 2017) and other chronic physical conditions (Chow et al., 2013; Patel et al., 2007), and/or due to differences in knowledge regarding the benefits of physical activity including resistance training (Pengpid et al.,

2015), or different occupational and socio-cultural structures, methods of transportation, and environmental factors (e.g., safety, climate) (Atkinson et al., 2016).

Given the aforementioned gaps within the literature, we aimed to assess the association between handgrip strength and the presence of depression among community-dwelling middle-aged and older adults using nationally representative data from six LMICs (China, Ghana, India, Mexico, Russia, South Africa) which represent different geographical locations and levels of socio-economic transition. Given the previously reported links between handgrip strength and adverse mental health outcomes, we hypothesized that weaker handgrip strength would be associated with higher depression, and that this would hold true across all six countries.

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. These countries broadly represent different geographical locations and levels of socio-economic and demographic transition. Based on the World Bank classification at the time of the survey, Ghana was the only low-income country, and China and India were lower middle-income countries although China became an upper middle-income country in 2010. The remaining countries were upper middle-income countries.

Details of the survey methodology have been published elsewhere (Kowal et al., 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.

Depression (outcome)

Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview (Kessler and Ustun, 2004) were used for the endorsement of past 12-month DSM-IV depression based on the same algorithm used in previous studies using the same dataset (Garin et al., 2016; Koyanagi et al., 2014) (Details provided in **eTable 1**).

Handgrip strength (exposure)

Handgrip strength was measured twice for both hands with the use of the Smedley's handgrip dynamometer. If the participant had any surgery in the last three months or arthritis or pain in the

hand/wrist/arm, handgrip strength was not measured for that hand. Weak handgrip strength was defined as <30kg for men and <20 kg for women using the average value of the two handgrip measurements of the dominant hand (Cruz-Jentoft et al., 2010).

Control variables

The selection of control variables was based on past literature and included age, sex, wealth quintiles based on country-specific income, years of education, physical activity, smoking status (never, current smoker, former smoker), body mass index (BMI), and number of chronic physical conditions (McDowell et al., 2018b). Physical activity levels were assessed with the Global Physical Activity Questionnaire (Bull et al., 2009). The total amount of moderate-to-vigorous physical activity in a typical week was calculated based on self-report. Those scoring ≥150 minutes of moderate-to-vigorous intensity physical activity were classified as meeting the recommended guidelines (coded=0), and those scoring <150 minutes (low physical activity) were classified as not meeting the recommended guidelines (coded=1) (Organization, 2010). BMI was calculated as weight in kilograms divided by height in meters squared based on measured weight and height, and categorized as <18.5 kg/m^2 (underweight), 18.5-24.9 kg/m^2 (normal weight), 25.0-29.9 kg/m^2 (overweight), and ≥30 kg/m^2 (obese) (World Health Organization). The total number of 11 chronic physical conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, visual impairment) was summed per individual. These conditions were assessed by self-report of diagnosis, symptoms, or blood pressure measurement (See **eTable 2** of the Appendix for details).

Statistical analysis

The analysis was restricted to those aged ≥50 years. The difference in sample characteristics among those without and without weak handgrip strength was tested by Chi-squared tests and Student's *t*-tests for categorical and continuous variables, respectively. Multivariable logistic regression analysis was conducted to assess the association between weak handgrip strength (exposure) and depression (outcome). Analyses stratifying by age (50-64 and ≥65 years), sex, and country were also conducted. All regression analyses were adjusted for age, sex, wealth, education, physical activity, smoking status, BMI, number of chronic diseases, and country with the exception of the country-wise and sex-stratified analyses which were not adjusted for country and sex, respectively. 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 all analyses. In order to assess the between-country heterogeneity that may exist in the association between weak handgrip strength and depression, we calculated the Higgins' I^2 based on estimates for each country. The Higgins' I^2 represents the degree of heterogeneity that is not explained by sampling error with values of 25%, 50%, and 75% often considered to represent low, moderate, and high levels of heterogeneity (Higgins et al., 2003). 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 34,129 individuals aged ≥50 years (China 13,175; Ghana 4305; India 6560; Mexico 2313; Russia 3938; South Africa 3838). The sample characteristics are provided in **Table 1**. Overall, the mean age of the sample was 62.4 years and 51.4% were females. The prevalence of weak handgrip strength and depression were 47.4% and 6.2%, respectively. Individuals with weak handgrip strength had a higher prevalence of depression than those without this condition (8.8% vs. 3.8%; p<0.001). Overall, after adjustment for potential confounders, weak handgrip strength was significantly associated with a 1.45 (95%CI=1.12-1.88, p<0.01) times higher odds for depression (**Table 2**). Age and sex-stratified analyses showed similar results. Weak grip strength was significantly associated with greater odds for depression when restricting analyses to entirely female samples (OR=1.45, 95 CI= 1.05 to 2.00, p<0.05) or entirely male samples (OR=1.48, 95 CI=1.03 to 2.11, p<0.05). Furthermore, the significant relationships between weak grip and depression were observed in subgroups of individuals aged over 65 (OR=1.55, 95 CI=1.09 to 2.21, p<0.05) and those aged under 65 (OR=1.43, 95CI=1.01 to 2.03, p<0.05). Country-wise analyses showed that there is a high level of heterogeneity between countries (I^2=84.3%) with the association being particularly strong in Ghana (OR=4.25; 95%CI=2.83-6.38, p<0.001) (**Figure 1**).

Discussion

To the best of our knowledge, this study is the first to explore the multi-country relationship between handgrip strength and depression in older adults across LMICs and contains a number of novel results. Our data suggest that those with weak handgrip strength have a higher prevalence of depression than those with stronger handgrip strength. Specifically, weak handgrip strength was significantly associated with a 1.45 (95%CI=1.12-1.88, p<0.01) times higher odds for depression. There was considerable variation in the relationship between weak handgrip and depression between the countries, with the association being strongest in Ghana (OR=4.25; 95%CI=2.83-6.38, p<0.001). There were no significant differences between age groups (50-64 and 65+) or between males and females, in the relationship between handgrip strength and depression.

This study did not find any gender differences in the associations between reduced handgrip strength and the presence of depression. This is contrary to the findings of McDowell et al. (2018) which found that the prospective association between handgrip strength and depressive symptoms were stronger among females than males. The findings of McDowell et al. (2018) are in line with those of Veronese et al. (2017) and Smith et al. (2018) which also found the association to be stronger among females than males. A possible reason for these discrepancies with our study might be due to the differences in contexts between higher income countries (i.e. Ireland, Italy, United States) and LMICs. For example, compared to age- and BMI-matched older people in high-income countries, it has been reported that women but not men in LMICs have higher handgrip strength (Koopman et al., 2014). Unlike Western populations, most old age people and in particular women in low-income countries engage in lifelong physical exercise (Koopman et al., 2014). Manual labor in farming and housekeeping is necessary for subsistence up to the highest ages, while mechanical means of farming and transportation are lacking (Koopman et al., 2014). However, more research is needed to understand whether gender differences are context-specific, and if so, what factors can lead to such differences.

Our data also suggest that there is considerable variation across countries in the association between grip strength and depression. For example, the mean ORs for depression in those with muscle weakness ranged from 0.61 in Mexico to 4.25 in Ghana. Although the reasons for the between-country differences are unknown, it may partly be explained by differences in access to prevention and treatment programs for elderly in the different countries. For example, a previous

SAGE study (Goeppel et al., 2016) demonstrated that access to basic chronic care for older people, of which a majority will likely present with muscle weakness, is lowest in Mexico with only 20.6% (95% CI=15.1-27.4) while in the other countries, these rates ranged from 30.5% (95%CI:27.8 -33.4) in China to 47.6% (95%CI=43.3-51.9) in South Africa. However, there was a protective effect of muscle weakness on depression in Mexico, suggesting other factors may be at play and need to be examined. For example, also the proportion of untreated depression in our nationally representative samples ranged from 69.5% (95% CI: 57.1, 81.9) in South-Africa to 93.2% (95% CI: 90.1, 95.7) in India (Arokiasamy et al., 2017). Furthermore, in Ghana, only 1.4% of health care expenditures are spent on mental health, and only 2.8% of those with a diagnosed mental illness received treatment in 2011 (Roberts et al., 2014). Across LMICs in Africa, it has been estimated that 76-99% of individuals with serious mental illness do not have access to the treatment they require (Faydi et al., 2011; World Health Organization, 2008).

Cultural and historical differences in the ways that mental illnesses are viewed and treated may also play a role in these country-wise differences. For example, in South Africa, significant delays in treating patients with mental illness have been reported as individuals chose to seek out traditional healers as their first contact (Owakwe & Otakpor, 2014). In various African countries, historical and symbolic practices such as beliefs in supernatural causes, influence social and traditional norms and thereby people's attitudes towards individuals with mental illness (Gureje & Alem, 2000; Read et al., 2009). This can be seen in Ghana for example, where such stigma leads to beliefs that individuals with mental illness are dangerous or unpredictable, and the difficulty in accessing psychiatric treatment further perpetuates these attitudes (Barke et al., 2011; Dako-Gyeke & Asumang, 2013). More broadly, LMICs are contexts in which adverse social conditions, such as poverty and human rights abuses, increase vulnerability to poor mental health outcomes (Tomlinson, 2013; Becker & Kleinman, 2013). These conditions, compounded by mental health care shortages and lack of professionals can make treatment in these contexts highly inaccessible (Kakuma et al., 2011). However, these findings do not necessarily explain the country-wise differences in our study, and thus future research should explore the observed country-wise differences in more detail.

The observed strong association between weak handgrip strength and the presence of depression among middle-aged and old age men and women in LMICs may be explained by several physiological mechanisms. For example, regularly performed resistance exercises such as carrying

heavy weights (water, firewood) and digging might counteract the age-related decline in muscle mass and strength (sarcopenia), which is strongly associated with mental and physical functioning also in LMICs (Koopman et al., 2014). Vice versa, people with depression are less likely to perform these heavy household chores. Handgrip strength is also a core component for the identification of frailty syndrome (Fried et al., 2011). A recent meta-analysis in older adults has identified that 40% of people with depression have frailty (OR 4.07, 95%CI 1.93-8.55, k=8) whilst the prevalence of depression in frailty was equally high (38.60%, OR 4.42, 95%CI 2.66-7.35, k=11, Soysal et al., 2017). Furthermore, among depressed older adults (Mean age=75), greater impairments in four frailty characteristics have been observed: gait speed, handgrip strength, physical activity levels, and fatigue (Brown et al., 2014). Thus, it may be that weak handgrip strength, which was particularly high in this sample (47.4%), is an indicator of frailty in our sample and this identifies those at risk of depression. Research also suggests that skeletal muscle releases several cytokines and peptides (myokines) into the circulation in response to muscle contractions and that the anti-inflammatory and anti-atherogenic properties of these myokines protect against the risk for depression (Köhler et al., 2017; Martínez-Cengotitabengoa et al., 2016). In addition, it is established that both frailty (Soysal et al., 2016) and sarcopenia (Bano et al., 2017) are associated with an adverse inflammatory profile, which may increase risk for depression (Buigues et al., 2015; Chang et al., 2017). Underlying inflammatory mechanisms might also explain the role of other chronic conditions in the association between weak handgrip strength and depression in middle-aged and old age persons (Pedersen, 2013). Moreover, chronic oxidative stress, which is associated with a higher risk for depression (Diniz et al., 2018; Maurya et al., 2016) and other chronic conditions (Barnes, 2015; Quiñonez-Flores et al., 2016) may play a role. It is known that resistance training lowers oxidative stress (Franzke et al., 2018; Padilha et al., 2015; Ribeiro et al., 2017), although evidence that this also clarifies the antidepressant effects of exercise is to the best of our knowledge currently lacking (Schuch et al., 2016a). Nonetheless, the relationship between muscular strength with overall neurological health and brain function has recently been confirmed by population-scale studies demonstrating that greater handgrip strength is positively associated with greater white-matter integrity, hippocampal volume, and neurocognitive functioning in the general population, and in people with major depression (Stubbs et al., in press; Firth et al., 2018).

Also psychosocial mechanisms may be at play in the relationship between handgrip weakness and depression. For example, in old age, muscle strength is a key factor in maintaining independence and thereby quality of life (Musalek & Kirchengast, 2017). In addition, higher handgrip strength has been linked to preserved mobility (Sallinen et al., 2010), greater engagement in activities of daily living (Taekema et al., 2010; Kozakai, 2017) and decreased disability (Frederiksen et al., 2002; Dato et al., 2012). If, as suggested, an individual with higher handgrip strength has greater mobility and less disability, it may also be that they are engaging in more social activities and receiving more social support, and this social support may lead to lower risks of developing depression (Grav et al., 2012). Future research should look to elucidate the exact physiological and psychosocial mechanisms that underpin the relationship between muscular strength and depression.

The current findings should be interpreted in light of some limitations. First, the study is cross-sectional, therefore the directionality of the relationships cannot be deduced with certainty. Although our data provides some potential hypotheses to address the weak muscle strength and depression relationship, longitudinal studies are required to better disentangle the relationships we observed. Second, due to the 12-month timeframe for a depression diagnosis, participants without current depressive symptoms might have been included and consequently some level of misclassification may have affected the results. Furthermore, the cut-off used to define weak handgrip strength was based on a European consensus to identify sarcopenia (Cruz-Jentoft et al., 2010), thus it may be that this cut-off is not applicable to all six countries included in our study. A further limitation is that dementia/poor cognitive status were not examined as factors in the association between depression and weakness. Finally, the present study did not include institutionalized people, which may limit generalizability at a national level. Nonetheless, the strengths of the study include objectively measured strength, and the multi-national scope focused on LMICs, countries for which no data exist in prior research literature.

Despite country-wise differences, our data provide a platform to investigate whether preserving a sufficient level of muscle mass and strength can counteract the catabolic and inflammatory adverse effects of aging, and help maintain individuals' mobility and independence, and by extension reduce the risk for depression among older adults in LMICs. Such research might be of great interest from a public health perspective since muscular strength is a modifiable risk factor, which may substantially influence the risk for depression. Preventing and treating depression might be

a unique challenge in LMICs, where resources are often sparse and care may be fragmented (Chisholm et al., 2016; World Health Organization, 2015; Ariokiasamy et al., 2017; Kakuma et al., 2011). Strong cultural and traditional views also call for prevention and treatment to be culturally-sensitive. An important first step will be raising awareness of the importance of considering depressive symptoms among health care providers in LMICs. Additionally, low cost, population level screening interventions, such as assessing handgrip strength to identify people at risk, may play a pivotal role in the prevention but also management of depression and associated chronic physical conditions. Given the cross-sectional nature of our work, prospective research should also attempt to disentangle the directionality of the relationships we observed and determine the clinical-utility of handgrip strength as a predictor of depression and associated morbidity and mortality risk in LMICS. Furthermore, interventional research should explore the efficacy and effectiveness of low-cost screening programs based on handgrip strength assessment.

Contributors:
BS, GAF, NV, AK, DV devised the study
AK, BS, DV analysed the data
All authors interpreted the data
GAF, BS, DV, AK wrote the manuscript and all authors provided critical comments and approved the final version

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Table 1 Sample characteristics (overall and by weak handgrip strength)

Characteristic	Category	Overall	Weak handgrip strength		
			No	Yes	P-value[a]
Depression	No	93.8	96.2	91.2	<0.001
	Yes	6.2	3.8	8.8	
Age (years)		62.4 (0.16)	59.9 (0.16)	64.5 (0.26)	<0.001
Sex	Male	48.6	50.1	47.0	0.002
	Female	51.4	49.9	53.0	
Wealth	Poorest	17.1	14.2	20.3	<0.001
	Poorer	18.6	17.3	20.0	
	Middle	19.7	19.1	20.3	
	Richer	21.7	23.7	19.5	
	Richest	22.9	25.7	19.8	
Education (years)		6.0 (0.15)	6.8 (0.19)	4.5 (0.13)	<0.001
Low physical activity	No	77.9	82.7	72.6	<0.001
	Yes	22.1	17.3	27.4	
Smoking status	Never	57.4	58.1	56.6	0.091
	Current smoker	36.2	35.1	37.4	
	Former smoker	6.4	6.8	6.0	
Body mass index (kg/m^2)	18.5-24.9 (Normal)	48.2	48.1	48.4	<0.001
	25.0-29.9 (Overweight)	24.0	28.2	19.3	
	≥30.0 (Obese)	10.6	13.9	6.9	
	<18.5 (Underweight)	17.2	9.8	25.4	
No. of chronic diseases		1.6 (0.03)	1.4 (0.03)	1.7 (0.03)	<0.001

Data are % or mean (standard error).
[a] P-values were calculated with Chi-squared tests and Student's *t*-tests for categorical and continous variables respectively.

Table 2 Association of weak handgrip strength and other covariates with depression (outcome) estimated by multivariable logistic regression

Characteristic	Category	Overall		Age 50-64 years		Age ≥65 years		Female		Male	
Weak handgrip strength	Yes vs. No	1.45**	[1.12,1.88]	1.43*	[1.01,2.03]	1.55*	[1.09,2.21]	1.45*	[1.05,2.00]	1.48*	[1.03,2.11]
Age (years)		0.99	[0.98,1.00]	0.99	[0.95,1.03]	1.00	[0.98,1.03]	0.99	[0.97,1.00]	0.99	[0.97,1.01]
Sex	Female vs. Male	1.51**	[1.16,1.96]	1.50*	[1.08,2.08]	1.54*	[1.04,2.27]				
Wealth	Poorest	1.00		1.00		1.00		1.00		1.00	
	Poorer	0.91	[0.68,1.22]	1.05	[0.79,1.40]	0.75	[0.45,1.25]	0.93	[0.66,1.31]	0.92	[0.59,1.44]
	Middle	0.76	[0.50,1.15]	0.86	[0.56,1.33]	0.63	[0.36,1.11]	0.76	[0.49,1.18]	0.76	[0.43,1.34]
	Richer	0.78	[0.60,1.03]	0.88	[0.53,1.46]	0.65	[0.39,1.10]	0.85	[0.59,1.22]	0.74	[0.47,1.14]
	Richest	0.49***	[0.34,0.69]	0.53**	[0.34,0.85]	0.41**	[0.21,0.79]	0.52**	[0.33,0.81]	0.48*	[0.27,0.85]
Education (years)		0.98	[0.95,1.01]	0.98	[0.94,1.02]	0.98	[0.93,1.03]	0.99	[0.95,1.03]	0.97	[0.92,1.02]
Low physical activity	Yes vs. No	0.99	[0.77,1.26]	0.88	[0.58,1.33]	1.15	[0.86,1.55]	0.93	[0.66,1.31]	1.06	[0.75,1.51]
Smoking status	Never	1.00		1.00		1.00		1.00		1.00	
	Current smoker	1.11	[0.86,1.45]	1.04	[0.75,1.42]	1.29	[0.90,1.84]	1.04	[0.70,1.56]	1.31	[0.87,1.98]
	Former smoker	1.41	[0.94,2.12]	1.44	[0.82,2.53]	1.45	[0.86,2.45]	1.68	[0.88,3.20]	1.58	[0.95,2.63]
Body mass index (kg/m^2)	18.5-24.9 (Normal)	1.00		1.00		1.00		1.00		1.00	
	25.0-29.9 (Overweight)	0.80	[0.61,1.05]	0.88	[0.63,1.23]	0.63	[0.38,1.05]	0.88	[0.60,1.29]	0.68	[0.38,1.23]
	≥30.0 (Obese)	0.96	[0.59,1.57]	1.22	[0.62,2.41]	0.59	[0.31,1.15]	1.07	[0.61,1.89]	0.59	[0.24,1.47]
	<18.5 (Underweight)	1.17	[0.92,1.49]	1.31	[0.93,1.87]	0.97	[0.71,1.34]	1.31	[0.96,1.79]	0.99	[0.67,1.45]
No. of chronic diseases		1.47***	[1.37,1.58]	1.58***	[1.43,1.76]	1.34***	[1.23,1.47]	1.45***	[1.33,1.59]	1.49***	[1.34,1.66]

Data are odds ratio [95% confidence interval].
Models are adjusted for all variables in the respective column and country.
* p<0.05, ** p<0.01, *** p<0.001

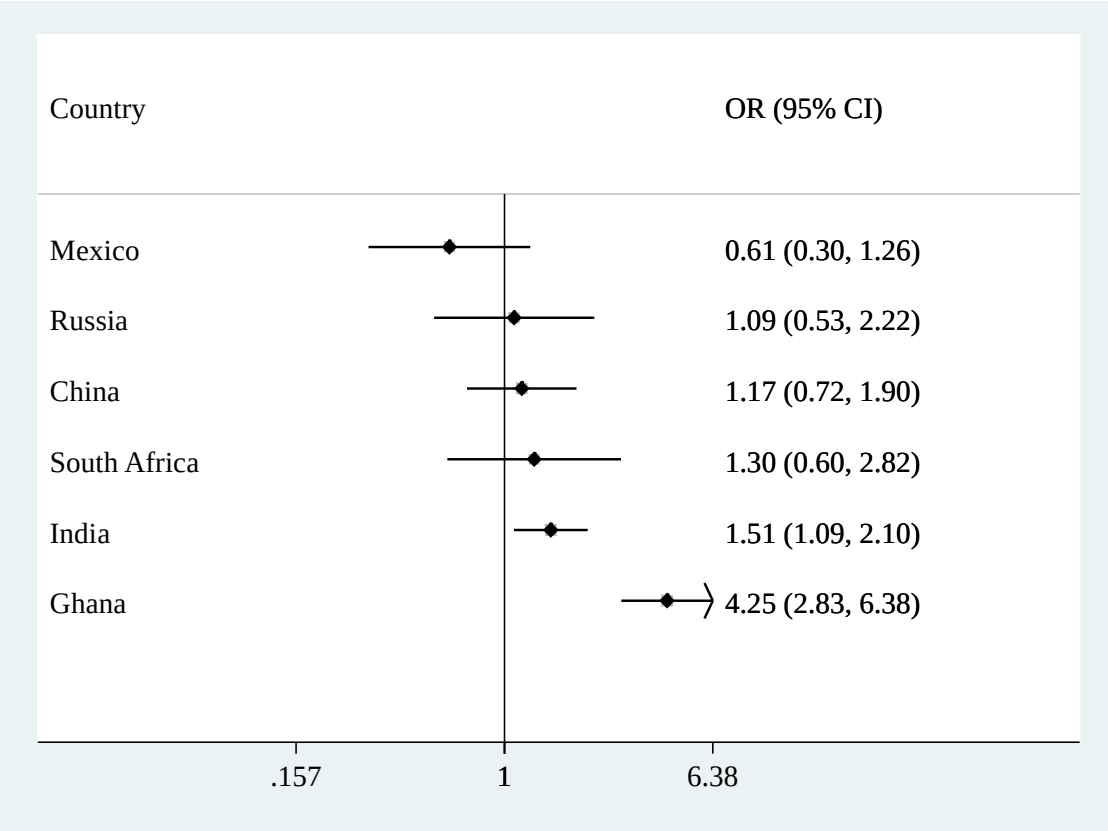

Figure 1 Country-wise association between weak handgrip strength and depression (outcome) estimated by multivariable logistic regression
Abbreviation: OR Odds ratio; CI Confidence interval
Models are adjusted for age, sex, wealth, education, body mass index, physical activity, smoking and number of chronic physical conditions.
Overall estimate was obtained by meta-analysis with random effects.

eTable 1 Questions and answer options used for endorsement of DSM-IV depression

1. At least one of the two following symptoms in the last 12 months:
(a) A period, lasting several days, of feeling sad, empty or depressed
(b) A period lasting several days with a loss of interest in most things the participant usually enjoys such as personal relationships, work or hobbies/recreation
AND
2. The period of sadness/loss of interest/low energy lasted for more than two weeks and was most of the day and nearly every day
AND
3. Five or more of the following symptoms:
(a) Loss of appetite
(b) Insomnia (problems falling asleep or waking up too early)
(c) Decreased energy or tiredness all the time
(d) Slowing down in moving around or restless/jittery
(e) Negative feelings/loss of confidence or frequent feelings of hopelessness.
(f) Slowed thinking or difficulties concentrating (e.g., listening to others, working, watching TV, listening to the radio)
(g) Thoughts of death, wishes of own death or suicide attempt
(h) Feelings of sadness, emptiness or depression lasting several days
(i) Anhedonia: loss of interest in things the participant usually enjoys

eTable 2 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)?	Affirmative answers to all four of the following: 1. During the last 12 months, have you experienced pain, aching, stiffness or swelling in or around the joints (e.g., in arms, hands, legs or feet) which were not related to an injury and lasted for more than a month? 2. During the last 12 months, have you experienced stiffness in the joint in the morning after getting up from bed, or after a long rest of the joint without movement? 3. Did this stiffness last for less than 30 minutes? 4. Did this stiffness go away after exercise or movement in the joint?
Asthma	Have you ever been diagnosed with asthma (an allergic respiratory disease)?	1. During the last 12 months, have you experienced attacks of wheezing or whistling breathing? (Yes) **AND** 2. "Yes" to at least one of the following (past 12 months): (a) Have you experienced an attack of wheezing that came on after you stopped exercising or some other physical activity? (b) Have you had a feeling of tightness in your chest? (c) Have you woken up with a feeling of tightness in your chest in the morning or any other time? (d) Have you had an attack of shortness of breath that came on without an obvious cause when you were not exercising or doing some physical activity?
Chronic lung disease	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?
Chronic back pain	Back pain everyday during the last 30 days based on the following questions: Have you experienced back pain during the last 30 days? On how many days did you have this back pain during the last 30 days?	NA
Diabetes	Have you ever been diagnosed with diabetes (high blood sugar)? (not including diabetes associated with a pregnancy)	NA
Edentulism	Respondents who answered affirmatively to the question "Have you lost all of your natural teeth?" were considered to have edentulism.	NA
Hearing problems		Interviewers impression at the conclusion of 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 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] These algorithms have been used in previous publications [2, 3] and those of arthritis, asthma, and chronic lung disease have been validated [2, 4].

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