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Handgrip strength, chronic physical conditions and physical multimorbidity in middle-aged and older adults in six low- and middle income countries

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ABSTRACT

Purpose: Handgrip strength provides a clinically validated marker of overall health and mortality risk. There are however, no multi-national population-based studies investigating the associations between handgrip strength, chronic physical conditions, and physical multimorbidity (i.e., ≥2 chronic conditions). We aimed to assess these associations among community-dwelling middle-aged and older adults using nationally representative data from six in low- and middle-income countries (LMICs).

Methods: Cross-sectional, community-based data on individuals aged ≥50 years from the World Health Organization's Study on Global Ageing and Adult Health were analyzed. Eleven chronic physical conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, visual impairment) were assessed. Weak handgrip strength was defined as < 30 kg for men and < 20 kg for women. Multivariable logistic regression analysis was conducted.

Results: The final sample included 34,129 individuals (62.4 ± 16.0 years; 52.1% female). After adjustment for potential confounders, when compared to those with no chronic physical conditions, having 1, 2, 3, and ≥4 physical chronic conditions was associated with 1.22 (95%CI = 1.08–1.37), 1.29 (95%CI = 1.11–1.50), 1.41 (95%CI = 1.18–1.68), and 1.78 (95%CI = 1.46–2.18) times higher odds for weak handgrip strength. Similar associations were observed in the analyses stratified by age and sex. There was a moderate level of between-country heterogeneity in the association between weak handgrip strength and physical multimorbidity (Higgin's I^2 = 67.8%) with the pooled estimate being 1.26 (95%CI = 1.06–1.50).

Conclusion: Weaker handgrip strength is associated with a range of chronic physical conditions and multimorbidity. Future research should seek to establish the predictive value of this inexpensive measure for clinical use.

1. Introduction

The prevalence of physical multimorbidity (i.e. two or more chronic physical conditions) is increasing worldwide, partly driven by the increasing life-expectancy [1]. Physical multimorbidity is undoubtedly one of the most significant challenges faced by global health care systems [2]. It is associated with increased health care utilization and costs [3,4], a lower quality of life in patients [5], and ultimately higher risk for premature mortality [6]. Therefore, there is an urgent need to identify modifiable factors that are associated with physical multimorbidity to mitigate its impact at the individual and societal level.

It has been well documented that regular physical activity and associated aerobic fitness levels are protective against future development of physical multimorbidity [7–11]. Furthermore, there is abundant evidence that points to a key role of muscular fitness in the genesis of many common pathologic conditions and chronic physical diseases

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[12]. Indeed, several meta-analyses have shown that muscular weakness in middle-aged and older individuals is strongly related to physical disability and premature mortality, even after adjusting for traditional risk factors [13,14]. A recent population-scale study of the UK Biobank [12] demonstrated that weak handgrip strength was a significant predictor of mortality (including all-cause, cardiovascular and even cancer-related), even after considering other established clinical risk-factors, such as body mass index (BMI), older age, systolic blood pressure, and smoking. Thus, there is increasing recognition that screening of muscle strength in middle-aged and older people is an important prognostic indicator for a range of adverse outcomes in older age. Vice versa, longitudinal data have also demonstrated that for example chronic hyperglycemia [15] and greater fat mass [16] (i.e., two hallmark risk factors for cardio-metabolic diseases) result in diminished muscle quality and strength.

Among the potential measures to capture muscular strength, handgrip strength is a simple, inexpensive risk-stratifying method for cardiovascular diseases, cognitive decline [17], mood disorders [18,19] and all-cause death [12,20]. Handgrip strength correlates closely with measures of muscle strength from other muscle groups, including the lower limbs [21]. 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 risk for physical multimorbidity in low income settings [22].

However, data from population-based studies assessing the relationship between handgrip strength and physical multimorbidity among older men and women are scarce, while conflicting results have been obtained from the very few population-based studies on this topic, especially in terms of gender differences. For example, a cross-sectional study among 1079 German older people [23] demonstrated that weak handgrip strength was significantly associated with an increased odds for physical multimorbidity among women (odds ratio, OR = 2.57 for those for in the lower tertile compared to the upper tertile, 95% CI = 1.30–5.07, $P = 0.007$) but not in men (OR = 1.32; 95%CI = 0.73–2.40; $P = 0.362$), after controlling for confounders. In another cross-sectional study ($n = 1145$) conducted in a high-income setting (Hong Kong), after controlling for age, BMI, history of smoking, educational level and marital status, handgrip strength significantly decreased with an increasing number of chronic physical diseases in men ($P = 0.001$), but not in women, although there was a trend towards statistical significance ($P = 0.06$) [24]. Finally, in the only longitudinal study to date, in 4823 Irish people aged > 50 years, every one kilogram increase in handgrip strength at baseline was significantly associated with a decrease in new onset physical multimorbidity (relative risk, RR = 0.98, CI:0.97–0.99) after 2 years [8]. There was no interaction by sex observed in this study.

To the best of our knowledge, there are no nationally representative population-based studies investigating the associations between handgrip strength, chronic physical conditions, and physical multimorbidity in low- and middle-income countries (LMICs). This is an important research gap given the rapid increase in chronic diseases in these countries, mainly due to increasing rates of physical inactivity, smoking and unhealthy eating habits [25]. In addition, increasing trends of physical multimorbidity in LMICs will have considerable financial implications over the next few decades if health systems are to respond appropriately to this emerging challenge [26]. Also, the association between chronic physical conditions or physical multimorbidity and muscular strength may differ in LMICs due to suboptimal treatment of chronic physical conditions [27,28], less awareness regarding the benefits of physical activity including resistance training [29], or other environmental factors such as unhealthy and unsafe work conditions, household air pollution and unsafe sanitation [30,31].

Given the aforementioned gaps within the literature, we aimed to assess the association between handgrip strength and the presence of chronic physical conditions and physical multimorbidity among community-dwelling middle-aged and older adults using nationally representative data from six LMICs which represent different geographical locations and levels of socio-economic transition.

2. Material and methods

Data from the Global Ageing and Adult Health Survey (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 [32]. 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 World Health Organization Ethical Review Committee and local ethics research review boards. Written informed consent was obtained from all participants.

2.1. Handgrip strength

Handgrip strength was measured twice for both hands with the use of the Smedley's hand 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 < 30 kg for men and < 20 kg for women using the average value of the two handgrip measurements of the dominant hand [33].

2.2. Chronic physical conditions and multimorbidity

We included all 11 chronic physical conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, visual impairment) for which data were available in the SAGE. Chronic back pain was defined as having had back pain everyday during the last 30 days. Respondents who answered affirmatively to the question “Have you lost all of your natural teeth?” were considered to have edentulism. The participant was considered to have hearing problems if the interviewer observed this condition during the survey. Hypertension was defined as having at least one of the following: systolic blood pressure ≥140 mmHg; diastolic blood pressure ≥90 mmHg; or self-reported diagnosis. Visual impairment was defined as having extreme difficulty in seeing and recognizing a person that the participant knows across the road [34]. Diabetes and stroke were solely based on lifetime self-reported diagnosis. For other conditions, the participant was considered to have the condition in the presence of either one of the following: self-reported diagnosis; or symptom-based diagnosis based on algorithms. We used these algorithms, which have been used in previous studies using the same dataset, to detect undiagnosed cases [26,35]. Specifically, the validated Rose questionnaire was used for angina [36], and other previously validated symptom-based algorithms were used for arthritis,

Table 1
Sample characteristics (overall and by country).

Characteristic		Overall	China	Ghana	India	Mexico	Russia	South Africa
Weak handgrip strength[a]	Yes	47.4	44.9	38.9	62.5	42.9	22.4	28.3
Physical multimorbidity[b]	Yes	45.5	39.1	35.1	43.4	43.4	63.3	43.1
Age (years)	Mean (SD)	62.4 (16.0)	62.6 (16.7)	64.4 (19.9)	61.5 (13.7)	63 (18.9)	63.9 (15.4)	61.6 (18.4)
Sex	Female	52.1	50.2	47.6	49.0	53.2	61.1	55.9
Education (years)	Mean (SD)	6.0 (8.9)	5.6 (8.2)	4.2 (9.9)	3.7 (7.4)	5.0 (8.0)	11.1 (5.3)	6.0 (10.1)
Marital status	Married/cohabiting	75.5	85.0	59.3	76.9	73.0	58.3	55.9
	Never married	1.8	1.1	1.3	0.7	7.0	2.7	14.3
	Separated/divorced/widowed	22.8	13.8	39.4	22.3	20.0	39.0	29.8
Body mass index (kg/m^2)	18.5–24.9 (Normal)	47.6	60.4	55.1	48.1	21.4	23.7	23.7
	25.0–29.9 (Overweight)	24.2	29.5	19.7	10.6	49.4	40.8	26.3
	≥30 (Obese)	11.5	5.8	10.0	2.5	28.7	34.5	46.9
	< 18.5 (Underweight)	16.7	4.3	15.2	38.8	0.6	1.1	3.1
Low physical activity[c]	Yes	23.5	24.1	22.1	22.0	33.8	20.2	50.9
Smoking status	Never	58.6	64.1	75.1	45.3	60.7	69.6	66.8
	Current smoker	34.9	29.3	10.7	50.0	20.3	21.3	23.8
	Former smoker	6.6	6.6	14.2	4.7	19.1	9.0	9.4
Depression[d]	Yes	6.0	1.1	7.2	12.9	10.8	3.5	3.0
Chronic physical conditions[e]	Angina	17.6	9.4	12.8	17.0	6.7	37.3	8.9
	Arthritis	29.5	26.7	26.2	27.9	14.5	38.2	30.6
	Asthma	7.9	4.3	5.0	12.5	4.9	6.5	7.7
	Chronic back pain	8.6	5.6	7.5	9.6	8.4	13.0	5.7
	Chronic lung disease	15.8	11.3	3.7	17.2	13.2	24.4	7.4
	Diabetes	6.8	6.6	3.8	6.9	17.6	7.0	9.2
	Edentulism	12.9	9.1	3.0	15.1	21.7	18.1	8.5
	Hearing problem	5.6	5.5	2.9	5.6	9.3	6.1	5.0
	Hypertension	55.0	60.6	59.6	37.5	61.9	72.1	78.3
	Stroke	3.0	3.0	2.8	2.0	4.3	4.8	4.0
	Visual impairment	1.3	0.5	1.0	2.4	0.8	0.9	0.8

Abbreviation: SD Standard deviation. Data are % unless otherwise stated.
[a] Weak handgrip strength referred to < 30 kg for men and < 20 kg for women.
[b] Multimorbidity referred to ≥2 chronic conditions out of 11 conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, and visual impairment).
[c] Low physical activity was defined as < 150 min/week of moderate-to-vigorous physical activity.
[d] Past 12-month DSM-IV depression.
[e] Details on the definition of each chronic condition are presented in e-Table 1.

asthma, and chronic lung disease [35,37]. Further details on the definition of chronic physical conditions can be found in Appendix **eTable 1** (supplementary material). The total number of chronic conditions was calculated and categorized as 0, 1, 2, 3, and ≥4. Multimorbidity was defined as ≥2 chronic conditions, in line with previously used definitions [26].

2.3. Control variables

The selection of control variables was based on past literature [8,23,24,38–42] and included age (years), sex (men versus women), wealth quintiles based on country-specific income, years of education, marital status (married/cohabiting versus never married versus separated/divorced/widowed), smoking status (never versus current versus former), BMI, physical activity level and depression. 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) [43]. Physical activity levels were assessed with the Global Physical Activity Questionnaire [44]. The total amount of moderate to vigorous physical activity in a typical week was calculated based on self-report. Those scoring ≥150 min of moderate to high intensity physical activity were classified as meeting the recommended guidelines (coded = 0), and those scoring < 150 min (low physical activity) were classified as not meeting the recommended guidelines (coded = 1) [45]. Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview [46] were used for the endorsement of past 12-month DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) depression.

2.4. Statistical analysis

The analysis was restricted to those aged ≥50 years. Multivariable logistic regression analysis was conducted to assess the association between the number of chronic physical conditions (0, 1, 2, 3, ≥4) and weak handgrip strength (outcome). Analyses stratifying by age (50–64 and ≥65 years) and sex were also conducted. We also tested for interaction by age and sex by including the interaction terms (age × number of chronic conditions and sex × number of chronic conditions) into the model using the overall sample. The associations between weak handgrip strength and individual chronic physical conditions or multimorbidity (i.e., ≥2 chronic conditions) (outcomes) were also assessed by multivariable logistic regression analyses. In order to assess the between-country heterogeneity that may exist in the association between weak handgrip strength and multimorbidity, we calculated the Higgin's I^2 based on estimates for each country. The Higgin'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 [47]. A pooled estimate was obtained by random-effect meta-analysis. All regression analyses were adjusted for age, sex, wealth, education, marital status, BMI, physical activity, smoking, depression, and country with the exception of the country-wise and sex-stratified analyses which were not adjusted for country and sex, respectively. For the analyses on the individual chronic conditions, we also adjusted for the presence of other illnesses in an attempt to obtain estimates that are less likely to be confounded by comorbid conditions. The variable on other illnesses was a binary variable (Y/N) and included information whether the individual had any other chronic conditions apart from the chronic condition in question. All variables were included in the models as categorical

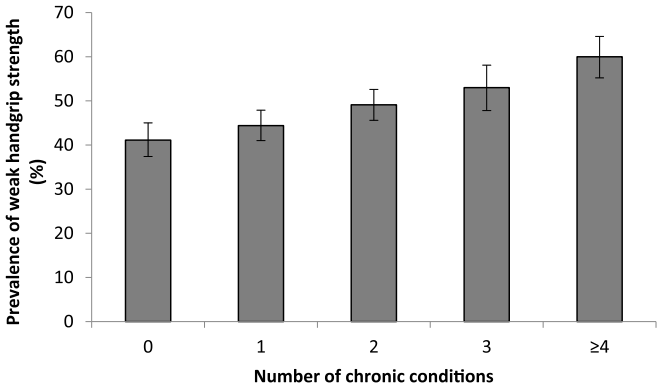

Fig. 1. Prevalence of weak handgrip strength by number of chronic conditions. Bars denote 95% confidence intervals.

variables with the exception of age and years of education (continuous variables). The sample weighting and the complex study design were taken into account in all analyses. Results from the regression analyses are presented as ORs with 95% confidence CIs. The level of statistical significance was set at $P < 0.05$.

3. 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 (SD) of the sample was 62.4 (16.0) and 52.1% were females. The prevalence of weak handgrip strength and physical multimorbidity were 47.4% and 45.5%, respectively. The prevalence of weak handgrip strength increased with increasing number of chronic conditions (Fig. 1). This was also the case even after adjustment for potential confounders where compared to those with no chronic physical conditions, 1, 2, 3, and ≥4 physical chronic conditions were associated with 1.22 (95%CI = 1.08–1.37), 1.29 (95%CI = 1.11–1.50), 1.41 (95%CI = 1.18–1.68), and 1.78 (95%CI = 1.46–2.18) times higher odds for weak handgrip strength in the overall sample (Table 2). Similar associations were observed for analyses stratified by age and sex. No significant interactions by sex and age were found. Angina, arthritis, asthma, chronic back pain, chronic lung disease, edentulism, hearing problems, and stroke were the individual conditions significantly associated with weak handgrip strength (Table 3). There was a moderate level of between-country heterogeneity in the association between weak handgrip strength and physical multimorbidity (Higgin's I^2 67.8%) with the pooled estimate being 1.26 (95%CI = 1.06–1.50) (Fig. 2).

4. Discussion

4.1. General findings

The current multi-national study across six LMICs, demonstrates that weak handgrip strength is associated with a higher prevalence of a wide range of physical conditions and physical co-morbidity. Broadly similar results were observed in middle-aged versus old age people, and in female and male participants. We found that the presence of most chronic conditions (i.e. in eight of 11 chronic conditions) were associated with weak handgrip strength in the overall sample and the odds for weak handgrip strength increased with an increasing number of chronic conditions.

Regarding individual conditions, we found evidence of a relationship between weak handgrip strength and arthritis, chronic low back pain, lung disease and stroke. All of these conditions have previously been associated with impairments in muscle strength. For instance, it is widely established that people following stroke have weaker muscles and consequently benefit from targeted resistance training [48]. Moreover, painful comorbidities such as arthritis and low back pain have also been associated with muscle mass loss and can improve with targeted resistance training [49,50]. We also found evidence of an association between muscle weakness and some chronic conditions whereby the underpinning mechanism is less clear such as hearing problems. In this instance, it might be hypothesized that the association between hearing problems and muscular weakness is more likely mediated by lack of physical activity, a known risk factor for declines in muscle mass and function [51]. Indeed, previous research has shown that hearing problems may be an important barrier for being physically active in LMICs [52]. Stigma and discrimination associated with hearing problems and a lack of social support may complicate physical activity participation. We also found a relationship between edentulism and weak handgrip strength. Similarly, negative self-perceptions associated with edentulism might be a barrier for participation in physical activity [53] and result in muscular weakness. Finally, diabetes, hypertension, and visual impairment were not significantly associated with weak handgrip strength in our study. At least for diabetes and hypertension, previous studies have found mixed results [54,55]. Future studies from more diverse settings are warranted to assess whether these conditions are associated with weak handgrip strength. In particular, the fact that we had no blood glucose measurement is a limitation and the association between diabetes and weak handgrip strength may have differed if this measure was available.

The observed strong association between weak handgrip strength and the presence of individual chronic physical conditions and multimorbidity among middle-aged and older 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 functional limitations, disability and mortality in older people, also in LMICs [56]. Research suggests that skeletal muscle release 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 of several chronic diseases [57,58]. In addition, it is established that both frailty [59] and sarcopenia [60] are associated with an adverse inflammatory profile in middle and older age, which may increase risk for a variety of physical diseases. Underlying inflammatory mechanisms might also explain the role of physical inactivity [61] and the presence of depression [62,63] in the association between weak handgrip strength and physical morbidity in middle-aged and older people. Moreover, chronic oxidative stress, which is associated with a higher risk for chronic obstructive pulmonary disease, chronic cardio-metabolic diseases, arthritis and consequently physical multimorbidity [64,65], might partially explain the observed associations between angina, asthma, chronic lung disease, stroke, and arthritis with muscle weakness. It is known that resistance training lowers oxidative stress in people with these diseases [66,67].

In our study, we did not find any gender differences in the association between reduced handgrip strength and physical multimorbidity. This is in contrast with one previous study which found gender differences [23], and this discrepancy may be related with the different diseases included. For example, some chronic conditions known to be more prevalent in men such as Parkinson's disease [68] were not assessed in our study. Another reason might be that 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 [56]. Unlike Western populations, most elderly people, in particular women, in low-income countries engage in lifelong physical exercise. Manual labor in farming and housekeeping is necessary for subsistence up to the highest ages, while mechanical means of farming and transportation are lacking [56]. However, clearly, more research is

Table 2
Association of number of chronic conditions and other covariates with weak handgrip strength (outcome) estimated by multivariable logistic regression.

Characteristic	Category	Overall		Age 50–64 years		Age ≥ 65 years		Female		Male	
Number of chronic conditions[a]	0	1.00		1.00		1.00		1.00		1.00	
	1	1.22**	[1.08,1.37]	1.23**	[1.06,1.43]	1.20	[0.95,1.51]	1.12	[0.94,1.34]	1.30**	[1.08,1.57]
	2	1.29***	[1.11,1.50]	1.32**	[1.11,1.56]	1.28	[0.97,1.70]	1.29*	[1.04,1.61]	1.25*	[1.01,1.55]
	3	1.41***	[1.18,1.68]	1.19	[0.92,1.54]	1.69***	[1.30,2.20]	1.44**	[1.12,1.85]	1.36*	[1.06,1.73]
	≥4	1.78***	[1.46,2.18]	1.63**	[1.21,2.20]	1.89***	[1.40,2.55]	1.68***	[1.27,2.23]	1.90***	[1.35,2.66]
Age (years)		1.06***	[1.05,1.07]	1.06***	[1.05,1.08]	1.07***	[1.05,1.08]	1.06***	[1.05,1.07]	1.06***	[1.05,1.07]
Sex	Female vs. Male	1.08	[0.95,1.23]	1.05	[0.89,1.24]	1.17	[0.99,1.39]				
Wealth	Poorest	1.00		1.00		1.00		1.00		1.00	
	Poorer	0.92	[0.77,1.10]	0.95	[0.77,1.18]	0.87	[0.67,1.14]	0.94	[0.76,1.15]	0.92	[0.74,1.14]
	Middle	0.88	[0.72,1.08]	0.95	[0.74,1.23]	0.75*	[0.58,0.97]	0.92	[0.74,1.14]	0.84	[0.66,1.08]
	Richer	0.75**	[0.61,0.93]	0.77*	[0.60,1.00]	0.73*	[0.55,0.97]	0.82	[0.66,1.03]	0.69**	[0.54,0.89]
	Richest	0.70**	[0.56,0.88]	0.67**	[0.52,0.86]	0.82	[0.59,1.13]	0.83	[0.65,1.07]	0.60***	[0.46,0.78]
Education (years)		1.00	[0.98,1.01]	1.00	[0.98,1.02]	0.99	[0.97,1.02]	1.01	[0.99,1.04]	0.98	[0.97,1.00]
Marital status	Married/cohabiting	1.00		1.00		1.00		1.00		1.00	
	Never married	1.05	[0.76,1.45]	1.28	[0.94,1.75]	0.61	[0.33,1.14]	0.95	[0.57,1.58]	1.27	[0.86,1.87]
	Separated/divorced/ widowed	1.07	[0.92,1.24]	1.21*	[1.00,1.45]	0.91	[0.75,1.12]	1.15	[0.96,1.37]	0.98	[0.78,1.24]
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)	0.90	[0.78,1.03]	0.86	[0.73,1.03]	0.96	[0.80,1.16]	0.87	[0.72,1.05]	0.93	[0.79,1.11]
	≥30.0 (Obese)	0.90	[0.71,1.13]	0.96	[0.73,1.27]	0.86	[0.63,1.17]	0.83	[0.63,1.11]	1.02	[0.67,1.56]
	< 18.5 (Underweight)	1.64***	[1.42,1.89]	1.61***	[1.35,1.93]	1.71***	[1.36,2.15]	1.35**	[1.10,1.65]	1.93***	[1.55,2.40]
Low physical activity[b]	Yes vs. No	1.48***	[1.30,1.68]	1.45***	[1.23,1.71]	1.49***	[1.26,1.76]	1.55***	[1.31,1.83]	1.41***	[1.19,1.67]
Smoking status	Never	1.00		1.00		1.00		1.00		1.00	
	Current smoker	0.87	[0.76,1.00]	0.90	[0.76,1.06]	0.83*	[0.70,0.99]	1.13	[0.92,1.39]	0.75**	[0.63,0.91]
	Former smoker	0.88	[0.73,1.06]	0.77*	[0.60,1.00]	1.03	[0.80,1.32]	1.06	[0.64,1.76]	0.80*	[0.65,0.98]
Depression[c]	Yes vs. No	1.47**	[1.14,1.90]	1.44*	[1.03,2.00]	1.63*	[1.12,2.37]	1.49*	[1.08,2.05]	1.46*	[1.04,2.06]

Data are odds ratio [95% confidence interval].
Models are adjusted for all variables in the respective column and country.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
[a] A total of 11 conditions were assessed (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, and visual impairment).
[b] Low physical activity was defined as < 150 min/week of moderate-to-vigorous physical activity.
[c] Past 12-month DSM-IV depression.

Table 3
Association between individual chronic conditions and weak handgrip strength (outcome) estimated by multivariable logistic regression.

Chronic condition	OR	95%CI
Angina	1.30**	[1.10,1.52]
Arthritis	1.11*	[1.01,1.22]
Asthma	1.30***	[1.11,1.51]
Chronic back pain	1.31*	[1.06,1.63]
Chronic lung disease	1.19*	[1.02,1.38]
Diabetes	1.10	[0.91,1.34]
Edentulism	1.23*	[1.03,1.47]
Hearing problems	1.40***	[1.16,1.70]
Hypertension	1.00	[0.90,1.11]
Stroke	1.62***	[1.29,2.04]
Visual impairment	1.33	[0.83,2.13]

Abbreviation: OR Odds ratio; CI Confidence interval.
Models are adjusted for age, sex, wealth, education, marital status, body mass index, physical activity, smoking, depression, other chronic conditions, and country.
Details on the definition of each chronic condition can be found in e-Table 1.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

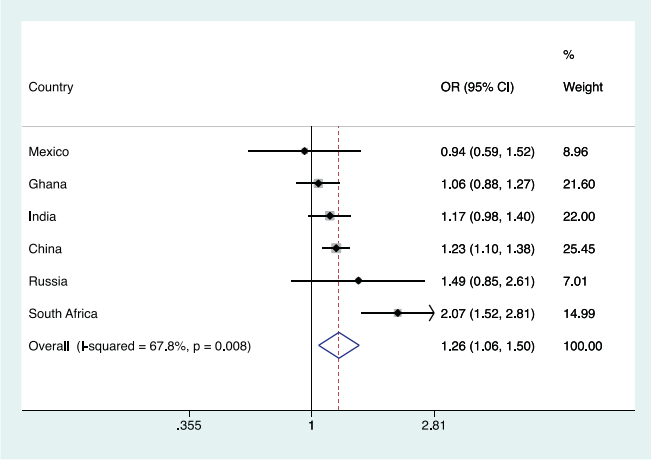

Fig. 2. Country-wise association between weak handgrip strength and physical multimorbidity (outcome) estimated by multivariable logistic regression.
Abbreviation: OR Odds ratio; CI Confidence interval.
[b]Multimorbidity referred to ≥2 chronic conditions out of 11 conditions (angina, arthritis, asthma, chronic back pain, chronic lung disease, diabetes, edentulism, hearing problems, hypertension, stroke, and visual impairment).
Models are adjusted for age, sex, wealth, education, marital status, body mass index, physical activity, smoking, and depression.
Overall estimate was obtained by meta-analysis with random effects.

needed to understand whether gender differences are context-specific, and if so, what factors can lead to such differences.

Future research should also explore the observed country-wise differences. For example, the ORs for physical multimorbidity in those with muscle weakness ranged from 0.94 in Mexico to 2.07 in South Africa. 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 the elderly in different countries. For example, a previous SAGE study [69] demonstrated that access to basic chronic care is lowest in Mexico with only 20.6% (95%

CI = 15.1–27.4) of those aged 50 or older having access. 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.

Despite between-country 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 ageing, and by extension reduce the risk for physical chronic diseases or multimorbidity 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 physical multimorbidity. Preventing and treating physical conditions and physical co-morbidity might be a unique challenge in LMICs, where resources are often sparse and care may be fragmented. An important first step will be raising awareness of the importance of considering chronic conditions and physical comorbidity among health care providers in LMICs. Low cost, population level screening interventions, such as assessing handgrip strength to identify people at risk may play a pivotal role in the prevention and but also management of chronic physical conditions and ultimately physical multimorbidity. 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 clinically utility of handgrip strength as a predictor of mortality/morbidity risk in LMICs. Furthermore, interventional research should explore the efficacy and effectiveness of low-cost screening programs based on handgrip strength assessment.

4.2. Limitations

Although the strength of the study includes the large sample size and the use of nationally representative samples from six countries, our results should be interpreted in the light of several limitations. First, because this was a cross-sectional study, causality cannot be inferred. Therefore, it remains unclear whether weak handgrip strength was caused by chronic conditions or vice versa. Second, whilst we included all physical health conditions which were assessed within the SAGE, other physical conditions such as cancer, HIV, Parkinson's disease or dementia may have been present and not identified in the study. Therefore, the prevalence of physical multimorbidity is likely to be an underestimation and it is possible that the association between physical multimorbidity and weak handgrip strength could have differed if data on more chronic physical conditions were available. Third, since some of the information on chronic physical conditions was based on self-report, reporting bias may exist. Finally, the present study did not include institutionalized people, which may limit generalizability at a national level. Nonetheless, the strengths of the study include the multinational scope focused on LMICs, countries for which no data exist in prior literature.

5. Conclusions

The current study shows that the prevalence of chronic physical conditions and physical multimorbidity is higher among those with weak handgrip strength. Future research should explore whether handgrip strength may be an early, indirect marker of subsequent health risks in LMICs, as it has many advantages over other biological measurements making it very attractive to use within LMIC settings. Handgrip dynamometers are inexpensive, easily portable, non-invasive, fast, reliable, and do not require extensive training. Additionally, increasing our understanding of the connection between muscular fitness and disability in low income settings could ultimately lead to the development and potential broader implementation of resistance-training interventions.

Competing interests

There are no competing interests to report.

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Authors' contributions

Analyses were performed by Dr. Ai Koyanagi and Dr. Brendon Stubbs. Dr. Davy Vancampfort wrote a first draft which was reviewed and revised in several rounds by the other co-authors. All authors approved the final version and all authors certify that they have participated sufficiently in the work to believe in its overall validity and to take public responsibility for appropriate portions of its content.

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Appendix A. Supplementary data

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