Title: Multimorbidity and subjective cognitive complaints: Findings from 48 low- and middle-income countries of the World Health Survey 2002-2004

Running title: Multimorbidity and cognition

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ABSTRACT

Background: Data on the association between multimorbidity and subjective cognitive complaints (SCC) are lacking from low- and middle-income countries (LMICs).

Objective: To assess the association between multimorbidity and SCC among adults from 48 LMICs.

Methods: Cross-sectional, community-based data were analyzed from the World Health Survey 2002-2004. Ten chronic conditions (angina, arthritis, asthma, chronic back pain, depression, diabetes, edentulism, hearing problems, tuberculosis, visual impairment) were assessed. Two questions on subjective memory and learning complaints in the past 30 days were used to create a SCC scale ranging from 0 (No SCC) to 100 (worse SCC). Multivariable linear regression and mediation analyses were conducted to explore the associations.

Results: A total of 224,842 individuals aged ≥18 years [mean (SD) age 38.3 (16.0) years; 49.3% males] constituted the final sample. Compared to no chronic conditions, the mean SCC score was higher by 7.13 (95%CI=6.57-7.69), 14.84 (95%CI=13.91-15.77), 21.10 (95%CI=19.49-22.70), 27.48 (95%CI=25.20-29.76), and 33.99 (95%CI=31.45-36.53) points for 1, 2, 3, 4, and ≥5 chronic conditions. Estimates by sex and age groups (18-44, 45-64, ≥65 years) were similar. Nearly 30% of the association between multimorbidity (i.e., ≥2 chronic conditions) and SCC was explained by psychological factors (i.e., perceived stress, sleep problems, anxiety symptoms).

Conclusion: Multimorbidity is associated with SCC among adults in LMICs. Future studies should investigate whether addressing psychological factors in people with multimorbidity can improve cognitive function, and whether screening for SCC in individuals with multimorbidity can be a useful tool to identify individuals at particularly high risk for future cognitive decline.

Keywords: Subjective cognitive complaints; Multimorbidity; Chronic physical conditions; Low- and middle-income countries

INTRODUCTION

Subjective cognitive complaints (SCC) are everyday cognitive problems (e.g., problems in concentration, memory, decision making) reported by people who may or may not have deficits on objective testing, and are common in all age groups [1]. One general population study conducted in the UK showed that the prevalence of SCC is between 7.6%-9.4% among adults [1]. SCC can be a meaningful indicator of an individual's cognitive function, and among older adults, SCC without evidence of objective neurocognitive impairment have been associated with substantially increased risk for developing dementia [2]. Furthermore, SCC have also been associated with lower quality of life [3], fractures, falls, increased health care utilization [4], and premature mortality [5].

Recently, there has been a growing interest in the association between multimorbidity (often defined as two or more chronic conditions in an individual) [6] and cognition, with longitudinal data showing that multimorbidity may precede mild cognitive impairment [7]. Multimorbidity is an important risk concept as it is associated with high health care costs [8], lower quality of life [9], disability [10], and premature mortality [11], and is one the most significant health-related issues globally [8]. Multimorbidity is increasing rapidly due to population aging and longer survival of people with chronic conditions, but it is not a problem exclusively among the older population. Indeed, one study showed that up to 20% of people experience multimorbidity before the age of 40 years [12]. It is possible for multimorbidity to lead to cognitive decline via factors such as atherosclerosis, microvascular changes, and inflammatory processes [13], or psychological factors (e.g., sleep problems, perceived stress) [14], while cognitive impairment in turn, can potentially impact the severity and burden of multimorbidity by reducing response capacities (e.g., fragmented care, suboptimal health care use, lower treatment adherence), and this can result in a vicious cycle [15].

Although several studies on multimorbidity and objective cognitive function exist, there are only a few studies on multimorbidity and SCC to date, all of which have been conducted in high-income countries [11, 14, 16, 17]. This is an important research gap for several reasons. First, SCC can identify subtle changes in everyday functioning that could be a precursor for more serious cognitive decline and functioning, which may not be detected otherwise, and can much more easily be measured than objective cognitive function [18]. Second, studies from low- and middle-income countries (LMICs) are important as the prevalence of multimorbidity is increasing rapidly in this setting due to increments in non-communicable diseases, while the multimorbidity-SCC association may differ from that of high-income countries due to different disease profiles and population age structure as well as higher prevalence of poverty and low education, and suboptimal treatment for chronic conditions [19].

Given that SCC and multimorbidity are both associated with adverse health outcomes, while they may mutually affect each other and lead to the exacerbation of the other condition, it is crucial to understand their association. Thus, the aims of the current study were to assess the association between multimorbidity and SCC among adults aged ≥18 years in 48 LMICs, and to determine the extent to which the association can be explained by psychological factors (i.e., perceived stress, anxiety symptoms, sleep problems).

METHODS

The World Health Survey (WHS) was a cross-sectional survey carried out in 2002-2004. Survey details are available elsewhere (http://www.who.int/healthinfo/survey/en/). Briefly, a single stage random sampling approach was employed in 10 countries, while a stratified multi-stage random cluster sampling method was used in 60 countries. Individuals with a valid home address aged ≥18 years were eligible to participate. Kish tables were used so that

all household members had an equal chance of being selected. A standardized questionnaire to collect data for the WHS was developed and a consistent translation procedure was employed to ensure cross-country comparability. Information was obtained through face-to-face interviews conducted by trained interviewers who received training before going to the field and who followed standard protocols. Across all countries, the individual response rate was 98.5%. To adjust for non-response, sampling weights were generated using the population distribution as reported by the United Nations Statistical Division. Ethical approval for the survey was provided by ethical boards at each study site. All participants gave their informed consent. The study was done in accord with the Helsinki Declaration of 1975.

Chronic conditions and multimorbidity (exposure)

Ten chronic conditions were assessed in our study. *Arthritis*, *asthma*, and *diabetes* were based on self-reported lifetime diagnosis. For *angina*, in addition to a self-reported diagnosis, a symptom-based diagnosis based on the Rose questionnaire was also used [20]. *Chronic back pain* was defined as having had back pain (including disc problems) everyday during the last 30 days. *Visual impairment* was defined as having severe/extreme difficulty in seeing and recognizing a person that the participant knows from across the road (i.e., from a distance about 20 meters) [21]. The participant was considered to have *hearing problems* if the interviewer observed this condition. Those who have lost all their natural teeth were considered to have *edentulism*. A *tuberculosis* diagnosis was based on past 12-month symptoms and was defined as: (a) having had a cough that lasted for three weeks or longer; and (b) having had blood in phlegm or coughed up blood [22]. Past 12-month *depression* was defined using the Diagnostic and Statistical Manual of Mental Disorders-IV algorithm [23]. Multimorbidity was defined as having at least two chronic conditions, in line with previously

used definitions [14]. The number of chronic conditions was also classified as 0, 1, 2, 3, 4, and ≥5 conditions.

Subjective cognitive complaints (SCC) (outcome)

SCC were assessed with two questions: (a) "Overall in the last 30 days, how much difficulty did you have with concentrating or remembering things?"; and (b) "In the last 30 days, how much difficulty did you have in learning a new task (for example, learning how to get to a new place, learning a new game, learning a new recipe etc.)?" Each item was scored on a five-point scale: none (score=1), mild (score=2), moderate (score=3), severe (score=4), and extreme/cannot do (score=5). Since these answer options were an ordered categorical scale, as in previous WHS studies, we conducted factor analysis with polychoric correlations to incorporate the covariance structure of the answers provided for individual questions measuring a similar construct [22, 24]. The principal component method was used for factor extraction, while factor scores were obtained using the regression scoring method. These factor scores were later converted to scores ranging from 0-100 to create a SCC scale with higher values representing worse subjective cognitive function.

Mediators

The potential mediators (perceived stress, anxiety symptoms, sleep problems) were selected based on past literature [14]. Stress over the month prior to the interview was assessed by two questions from the Perceived Stress Scale: "How often have you felt that you were unable to control the important things in your life?"; and "How often have you found that you could not cope with all the things that you had to do?" The answer options to these questions were: never (score=1), almost never (score=2), sometimes (score=3), fairly often (score=4), very often (score=5). The scores of the two questions were added to create a scale ranging from 2

to 10 [25]. Anxiety symptoms was assessed by the question "Overall in the past 30 days, how much of a problem did you have with worry or anxiety?" and sleep problems by the question "Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?" Those answering "severe" or "extreme" were considered to have anxiety symptoms [24] and sleep problems [26], respectively. Data on perceived stress were not available from Brazil, Hungary, and Zimbabwe, while data on anxiety symptoms were not available from Morocco. These countries were excluded from the analyses which include perceived stress and/or anxiety.

Control variables

Control variables included age, sex, education (no formal education, primary education, secondary or high school completed, or tertiary education completed), and wealth [14]. Principal component analysis based on 15-20 assets (e.g., cars, washing machine, television, computer) was conducted to create country-wise wealth quintiles. Although lifestyle factors such as physical activity, smoking, alcohol consumption, and obesity could also be confounders [27], since preliminary analysis showed that they have almost no influence in the association between multimorbidity and SCC, they were not included in the models in order to maximize sample size (See Supplementary material **eTable 1** for details of these additional covariates and **eTable 2** for results of regression models including these variables).

Statistical analysis

The statistical analysis was done with Stata 14.2 (Stata Corp LP, College station, Texas). Of the 69 countries with publicly available data, 10 countries were excluded due to lack of sampling information, and so were 10 high-income countries in order to focus on LMICs.

Moreover, Turkey was deleted due to lack of data on education. Thus, the final sample consisted of 48 LMICs according to the World Bank classification at the time of the survey (2003). The data were nationally representative for all countries with the exception of China, Comoros, the Republic of Congo, Ivory Coast, India, and Russia. The list of included countries and their sample size are provided in **eTable 3** of the supplementary material.

In our study, we excluded individuals who reported a lifetime diagnosis of schizophrenia (psychosis) (n=2424) and those who were missing information on this variable (n=15686) to obtain a sample free of schizophrenia (psychosis) as it has been previously reported that SCC among individuals with schizophrenia may be unreliable [28]. The association between the number of chronic conditions or individual chronic conditions (exposures) and SCC score (outcome) was estimated by multivariable linear regression. Next, we conducted country-wise analysis with multimorbidity (i.e., ≥2 chronic conditions) as the exposure variable. Furthermore, to assess whether there is between-country heterogeneity in the association between multimorbidity and SCC, the Higgins's I^2 statistic was calculated. This represents the degree of heterogeneity that is not explained by sampling error with values of 25%, 50%, and 75% often being considered low, moderate, and high level of heterogeneity, respectively [29]. A pooled estimate was obtained by combining the estimates for each country into a random effect meta-analysis. Finally, using the overall sample, we conducted mediation analysis to assess the degree to which perceived stress, sleep problems, and anxiety symptoms explain the association between multimorbidity and SCC. We used the *khb* (Karlson Holm Breen) command in Stata [30] for this purpose. This method decomposes the total effect of a variable into direct and indirect effects (i.e., the mediational effect). Using this method, the percentage of the main association explained by the mediator can also be calculated (mediated percentage). Each potential influential factor was included in the model

individually apart from the analysis where all mediators were included simultaneously in the model.

All analyses including the mediation analysis were stratified by age groups, and the analysis on the number of chronic conditions and SCC was also stratified by sex. The regression and mediation analyses were all adjusted for age, sex, education, wealth, and country with the exception of the sex-wise and country-wise analysis which were not adjusted for sex and country, respectively. Adjustment for country was done by including dummy variables for each country as in previous WHS publications [22, 26]. The analysis on the individual chronic conditions was mutually adjusted for all 11 chronic conditions. The number of chronic conditions was included in the model as dummy variables. The sample weighting and the complex study design were taken into account in all analyses. Results from the linear regression models are presented as b-coefficients with 95% confidence intervals (CIs). The level of statistical significance was set at $P<0.05$.

RESULTS

The final sample included 224,842 individuals aged ≥18 years without schizophrenia (psychosis) [mean (SD) age 38.3 (16.0) years; 49.3% males] (**Table 1**). Overall, the prevalence of 1, 2, 3, 4, and ≥5 chronic conditions was 9.4%, 3.8%, 1.6%, and 0.8%, respectively. The mean SCC score increased sharply with increasing number of chronic conditions regardless of age group (**Figure 1**). After adjustment for potential confounders, overall, compared to no chronic conditions, the mean SCC score was higher by 7.13 (95%CI=6.57-7.69), 14.84 (95%CI=13.91-15.77), 21.10 (95%CI=19.49-22.70), 27.48 (95%CI=25.20-29.76), and 33.99 (95%CI=32.45-36.53) points for 1, 2, 3, 4, and ≥5 chronic conditions (**Table 2**). The results in samples stratified by sex and age were similar. All individual chronic conditions were significantly associated with greater SCC scores in the

overall sample (**Figure 2**) although age-stratified analysis showed that some individual chronic conditions are not significantly associated with SCC in some age groups (**eTable 4** of supplementary material). Country-wise analysis showed that multimorbidity (i.e., ≥2 chronic conditions) was significantly associated with greater SCC scores in all countries with the exception of Slovakia in the overall sample (**Figure 3**). Overall, multimorbidity (versus no multimorbidity) was associated with a higher SCC score by 13.44 (95%CI=12.35-14.52) points on average with a high level of between-country heterogeneity (I^2=76.7%). The country-wise analyses by age groups are shown in **eFigure 1** (age 18-44 years), **eFigure 2** (45-64 years), and **eFigure 3** (≥65 years) of the supplementary material. The overall estimates for age 18-44, 45-64, and ≥65 years were 12.59 (95%CI=11.18-14.00; I^2=69.9%), 12.60 (95%CI=11.31-13.89; I^2=59.7%), and 13.30 (95%CI=11.67-14.94; I^2=56.4%), respectively. Finally, mediation analysis showed that 9.7%, 14.6%, and 17.1% of the association between multimorbidity and SCC was explained by perceived stress, anxiety symptoms and sleep problems, respectively, with all three mediators collectively explaining 29.0% of the association (**eTable 5** of supplementary material). The mediated percentages were similar between age groups (**eTable 6** of supplementary material).

DISCUSSION

Main findings

In our large study including 224,842 adults from 48 LMICs, an increase in the number of chronic conditions was associated with a substantial worsening in SCC. Associations were similar between sex and age groups. Country-wise analysis showed that the association between multimorbidity (i.e., ≥2 chronic conditions) and SCC holds in the vast majority of countries. Finally, nearly 30% of the association between multimorbidity and SCC was explained collectively by psychological factors [i.e., perceived stress (9.7%), anxiety

symptoms (14.6%), sleep problems (17.1%)]. To the best of our knowledge, this is the first multi-country study on the association between multimorbidity and SCC, while it is also the first study on this topic from LMICs.

Interpretation of the findings

All individual chronic conditions assessed in our study were significantly associated with greater SCC with particularly strong associations being observed for sensory impairments and depression. Sensory impairments such as visual impairment and hearing loss may lead to cognitive impairment via lack of stimulating activities that may result in reduced brain reserve [31]. Alternatively, SCC has been linked to higher anxiety symptoms [1]. Thus, it is possible that people with SCC are more likely to report complaints for other symptoms such as visual impairment, as there may be a tendency for anxious people to over-report their symptoms. For depression, underlying central nervous system alterations or high cortisol levels may cause both depression and cognitive decline [32].

As for other conditions, angina may lead to cognitive decline via vascular factors underlying both conditions or co-existing heart failure via reduced cardiac output and cerebral hypoperfusion [33]. Due to the close link between neural systems involved in cognition and pain processing, they may mutually modulate each other [34], and this may explain our findings on chronic back pain and greater SCC. Respiratory diseases such as asthma and tuberculosis may lead to cognitive decline via hypoxia and subsequent neural abnormalities [35], while systemic inflammation in tuberculosis may also increase risk for cognitive decline [36]. Arthritis may be linked with cognitive decline via comorbid cardiovascular risk factors or systemic inflammatory processes [37]. Inefficient mastication in edentulism may lead to a reduced activation of brain regions related with memory and learning processes [38]. Finally, cognitive decline in diabetes is common and it has been

suggested that brain structural changes due to factors such as poor glycemic control, vascular disease, and oxidative stress may be implicated [39].

The findings of our study that multimorbidity is associated with greater SCC are in line with previous studies on this topic from high-income countries [11, 14, 16, 17]. For example, one study including individuals aged ≥65 years conducted in Spain found that the prevalence of subjective memory complaints increases linearly with increasing number of diseases [11]. Furthermore, another study from Sweden found that multimorbidity is associated with 2.1 times higher odds for SCC among adults aged ≥65 years [16]. Finally, one study including adults aged ≥16 years from the UK found that multimorbidity is associated with 2.58 and 2.34 times higher odds for subjective cognitive complaints and memory complaints, respectively [14].

Apart from the accumulating effects of individual chronic conditions on cognition, it is also possible that multimorbidity is a proxy of an age-related multisystem failure which co-exists with neurodegeneration or cognitive impairment [40]. Furthermore, it is also possible for polypharmacy and drug interactions in multimorbidity to induce cognitive decline [7]. Finally, multimorbidity can lead to increased burden on the individual (in terms of costs, mobility, complexity of care), and this may lead to suboptimal and/or fragmented care or treatment non-adherence, rendering the optimal treatment of all co-existing chronic conditions difficult. This can lead to aggravation of chronic conditions, and increase risk for cognitive decline.

In our study, approximately 30% of the association between multimorbidity and SCC was explained by psychological factors such as perceived stress, anxiety symptoms, and sleep problems. This finding aligns with a previous study conducted in the UK [14]. Multimorbidity may induce sleep problems via, for example, the nocturnal symptoms of some chronic condition that may interrupt sleep (e.g., breathing problems in asthma, chest

pain in angina, nocturia in diabetes) [41]. In turn, sleep problems may induce structural changes in the brain (e.g., frontotemporal region atrophy, ventricular enlargement, hippocampal degeneration) and consequent cognitive decline [42]. Next, psychotropic medication use and increased inflammatory profiles among people with anxiety may increase risk for multimorbidity [43, 44], while the burden of the illness including those related to the symptoms, prognosis, and the costs for treatment may increase levels of anxiety among those with multiple chronic conditions. Anxiety in turn, may increase risk for cognitive decline via reduction in intellectually stimulating activities, sleep problems, or use of benzodiazepines [42, 45]. Multimorbidity may increase risk for perceived stress via mechanisms similar to those of anxiety (e.g., symptoms, long-term prognosis, treatment costs) or the complexity of treating multiple conditions. Perceived stress may increase risk for cognitive decline via several physiological pathways pertaining to the central nervous, neuroendocrine, and immune systems. In particular, prolonged elevation of cortisol (a hypothalamic-pituitary-adrenal axis response to chronic stress) may increase risk for stress-related cognitive decline by causing alterations in brain structure and function in the prefrontal cortex, hippocampus, and amygdala [46].

The reason for the high level of between-country heterogeneity in the association between multimorbidity and SCC observed in our study is unknown, but it may be attributable to different disease profiles or availability of health care. However, clearly, more research is needed to understand the reasons for the between-country heterogeneity. Furthermore, in our study, the association between multimorbidity and SCC were similar between age groups (i.e., 18-44, 45-64, ≥65 years). Although a more pronounced association in older adults could have been expected due to the long-term effects of the chronic conditions, younger individuals may become more concerned even by a subtle cognitive decline than in older adults who may consider it to be normal, and this may explain the

similar strength of associations between age groups. Alternatively, it is possible for younger individuals to feel more stressed or anxious about having multiple chronic conditions, as they may have a more profound negative effect on life (e.g., loss of job, dim future prospects) than in older people, and this may lead to greater SCC.

Clinical implications and areas for future research

One previous study from six LMICs found that multimorbidity is associated with increased odds for mild cognitive impairment (MCI) among middle-aged and older adults, suggesting that prevention of multimorbidity may reduce future cognitive decline and dementia onset in these countries [27]. Given that a previous meta-analysis showed that older people with subjective memory complaints without evidence of objective cognitive impairment were twice more likely to develop dementia compared to people without subjective memory complaints [2], our study reinforces the notion that prevention of multimorbidity may lead to reduced risk of dementia by showing a positive association between multimorbidity and SCC in a large number of LMICs spanning multiple continents. In particular, given that SCC is based on self-report and does not require burdensome neuropsychological testing and specially trained staff, this could serve as a particularly useful tool in the context of LMICs to identify individuals with multimorbidity who are at particularly high risk for future cognitive decline. Our study also found that the association between multimorbidity and SCC may be mediated partially by psychological factors suggesting that screening for psychological problems among people with multimorbidity and addressing them may also lead to a reduction in cognitive decline. However, future longitudinal studies in this setting are necessary to provide more evidence regarding causality and temporal associations before any concrete recommendation can be made.

Finally, most previous studies on SCC have focused on their link with future onset of dementia among older people, and there is very limited information on their clinical significance or whether SCC can lead to any adverse outcomes among the younger population. Indeed, although there is growing consensus that intervening in mid-life is important for the prevention of dementia [27] since for example, cognitive dysfunction can appear up to 10 years before the actual dementia diagnosis [47], how SCC in younger adults relate to future cognitive decline is largely unknown and is an area for future research. Furthermore, in the context of multimorbidity, it would be of interest to know whether SCC among young adults can negatively affect multimorbidity, for example, by reducing response capacities for treatment, which can lead to an exacerbation of chronic conditions or multimorbidity.

Strengths and limitations

The strengths of the study include the large sample size, the use of predominantly nationally representative datasets, and data from a large number of LMICs. However, the results should be interpreted in the light of several limitations. First, all data used in our analysis was based on self-report. Thus, there is the possibility of reporting bias (e.g., social desirability bias, recall bias). In particular, it is possible for SCC to have affected the reporting of some variables due to memory problems (e.g., diagnosis of disorders, sleep problems). Second, although a total of 10 chronic conditions were included in the analysis, there may be other conditions such as malnutrition [48], stroke [49], and HIV infection [50], which were not included in the analysis but may be important conditions in relation to cognition. Third, it is also possible that there was misclassification for chronic conditions based on self-reported diagnosis especially in resource-limited settings as under-diagnosis may be common. Fourth, we used two questions on SCC to capture the level of SCC but there is currently no

consensus on SCC measures, and what has been used in previous studies range from a single question to a complex assessment involving multiple questions. Therefore, the results may have differed if a different measure of SCC was used. Fifth, the data were collected in 2002-2004, and thus, it is possible that the results do not reflect the current situation as multimorbidity, demographic, and cognitive profiles of the populations studied could have changed. However, we are not aware of any other population-based data with such a large number of LMICs that can be used to investigate the Multimorbidity-SCC relationship. Next, to assess perceived stress, we used an abridged version of the perceived stress scale, which can potentially differ in validity and reliability compared to the original scale. Furthermore, the diagnosis on depression was based solely on algorithms and was not based on a clinical diagnosis made by a clinician. Finally, given the cross-sectional nature of our study, causality or temporal associations cannot be established. Relatedly, mediation and confounding are identical statistically and can only be distinguished on conceptual grounds [51]. Thus, our mediated percentage is likely to be an overestimation given the various ways in which multimorbidity, SCC, and mental health problems can be intertwined.

Conclusions

Increasing numbers of chronic conditions were associated with a substantial worsening in SCC among adults in LMICs, regardless of sex and age. Future studies should investigate whether addressing psychological factors can improve cognition in people with multimorbidity, and whether screening for SCC in individuals with multimorbidity can be a useful tool to identify individuals who may be at particularly high risk for future cognitive decline.

CONFLICT OF INTEREST/DISCLOSURE STATEMENT

The authors have no conflict of interest to report.

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Tables and Figures

Table 1 Sample characteristics

Characteristic		Unweighted n/N	Overall (n=224842)	Age (years)					
				Unweighted n/N	18-44 (n=145969)	Unweighted n/N	45-64 (n=55124)	Unweighted n/N	≥65 (n=23503)
Age (years)	Mean (SD)		38.3 (16.0)		29.1 (7.5)		52.8 (5.8)		72.2 (7.0)
Sex	Male	100066/224743	49.3	64486/145929	50.3	24988/55097	48.2	10501/23496	44.0
Education	No formal	49060/224607	25.8	26018/145834	21.2	14661/55062	34.0	8244/23484	39.9
	Primary	73354/224607	30.9	46850/145834	31.3	18148/55062	30.1	8307/23484	30.7
	Secondary	84793/224607	34.0	61242/145834	37.9	17751/55062	26.5	5767/23484	23.1
	Tertiary	17400/224607	9.3	11724/145834	9.6	4502/55062	9.4	1166/23484	6.3
Angina	Yes	29856/224230	14.4	14221/145650	10.1	9528/54955	20.4	6072/23383	32.4
Arthritis	Yes	27769/222996	12.8	10622/145014	7.3	10311/54618	21.3	6784/23120	33.2
Asthma	Yes	10028/223560	5.0	5465/145170	4.1	2816/54809	6.2	1739/23340	9.3
Chronic back pain	Yes	11160/207061	6.6	4569/134512	4.2	3809/50796	9.9	2767/21520	16.7
Depression	Yes	13025/221226	6.6	6736/143802	5.3	3953/54200	8.8	2323/22983	11.6
Diabetes	Yes	6293/208048	3.0	1506/135021	1.1	2906/51096	6.2	1878/21693	9.0
Edentulism	Yes	13428/201104	5.9	3373/129780	1.9	4192/40509	9.1	5850/21607	29.0
Hearing problems	Yes	7162/223092	3.3	1388/144812	1.1	1791/54688	3.7	4024/23352	19.5
Tuberculosis	Yes	3147/195534	1.6	1759/125860	1.3	921/48452	2.1	465/20983	2.6
Visual impairment	Yes	10470/213866	4.8	2504/138140	1.7	3554/52815	7.6	4384/22724	20.8

Abbreviation: SD Standard deviation

Data are weighted % unless otherwise stated.

Table 2 Association between number of chronic conditions and subjective cognitive complaints (outcome) estimated by multivariable linear regression

No. of chronic		Sex		Age (years)		
conditions	Overall	Male	Female	18-44	45-64	≥65
0	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
1	7.13*	7.33*	6.82*	7.32*	6.11*	8.76*
	[6.57,7.69]	[6.48,8.17]	[6.04,7.60]	[6.64,7.99]	[4.99,7.23]	[6.49,11.03]
2	14.84*	14.65*	14.52*	15.30*	13.78*	14.05*
	[13.91,15.77]	[13.17,16.13]	[13.29,15.75]	[14.00,16.60]	[12.12,15.44]	[11.37,16.73]
3	21.10*	23.06*	19.19*	19.79*	19.66*	20.17*
	[19.49,22.70]	[19.99,26.13]	[17.47,20.90]	[17.52,22.06]	[17.41,21.92]	[16.21,24.14]
4	27.48*	29.43*	25.37*	26.63*	25.04*	25.49*
	[25.20,29.76]	[26.30,32.57]	[22.45,28.29]	[22.17,31.08]	[20.89,29.20]	[22.16,28.82]
≥5	33.99*	36.39*	31.53*	31.41*	32.68*	29.75*
	[31.45,36.53]	[32.25,40.54]	[28.20,34.87]	[24.16,38.66]	[28.33,37.02]	[25.82,33.68]

Abbreviation: Ref. Reference category

Estimates are b-coefficient [95% confidence interval].

The subjective cognitive complaints score ranged from 0 to 100 with higher scores representing worse subjective cognitive function.

Models are adjusted for age, sex, education, wealth, and country with the exception of the sex-stratified analysis which was not adjusted for sex.

* P<0.001

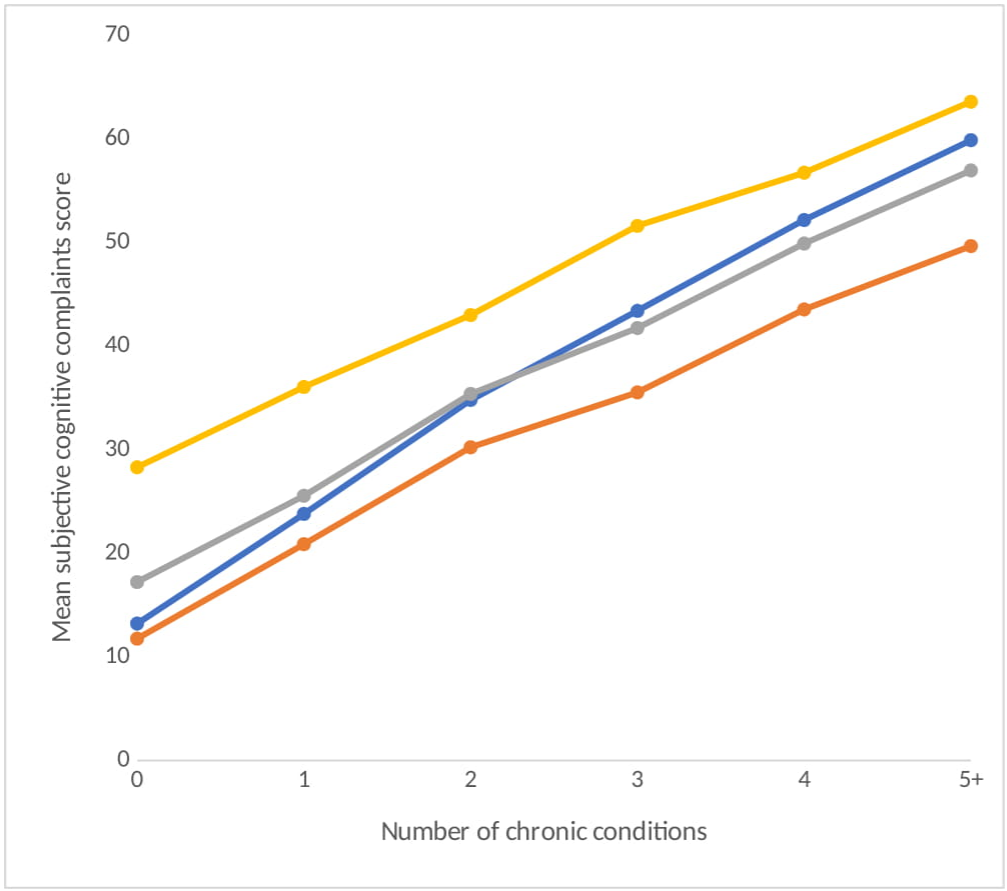

Figure 1 Mean subjective cognitive complaints score by number of chronic conditions (overall and by age groups)

The subjective cognitive complaints score ranged from 0 to 100 with higher scores representing worse subjective cognitive function.

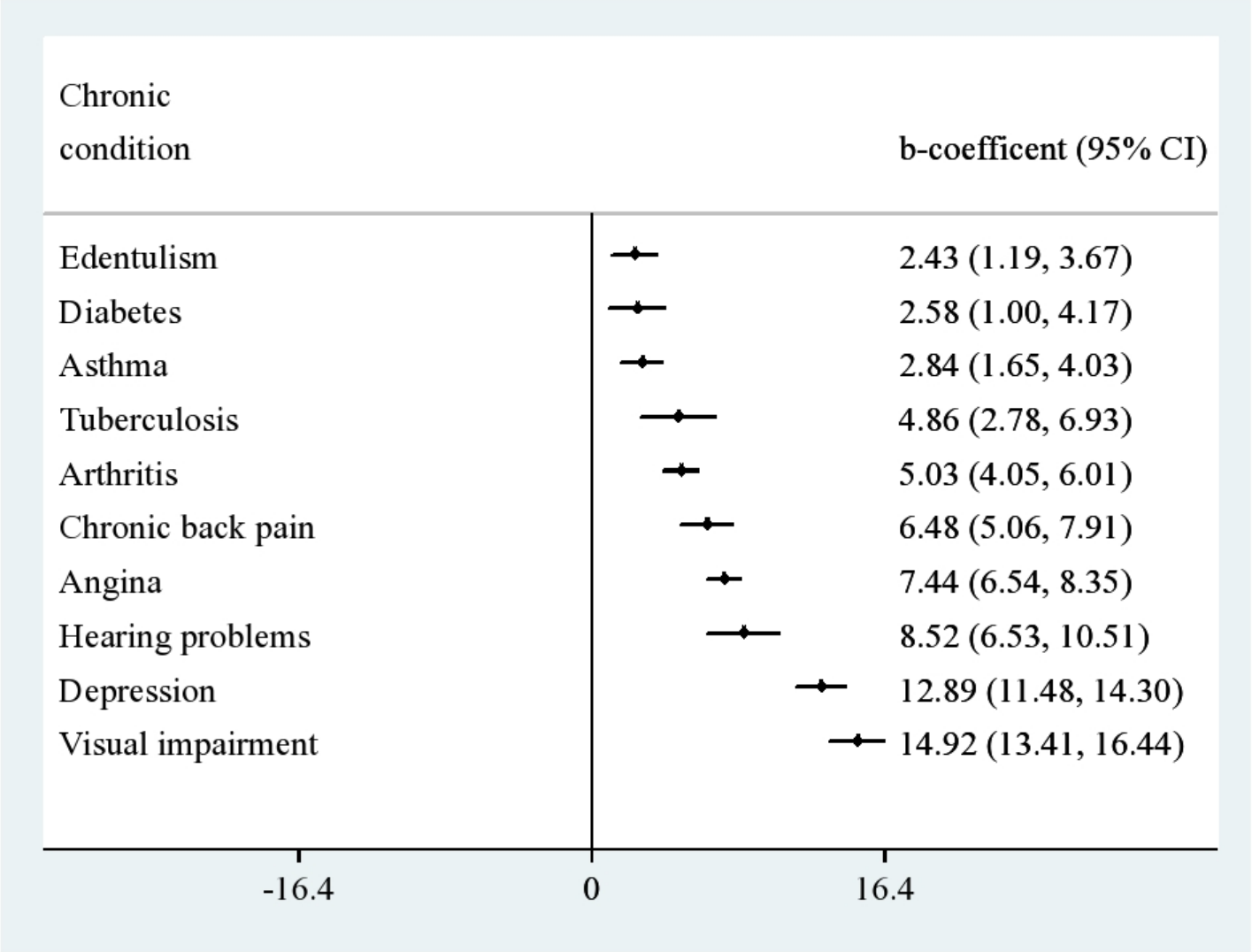

Figure 2 Association between individual chronic conditions and subjective cognitive complaints (outcome) estimated by multivariable linear regression

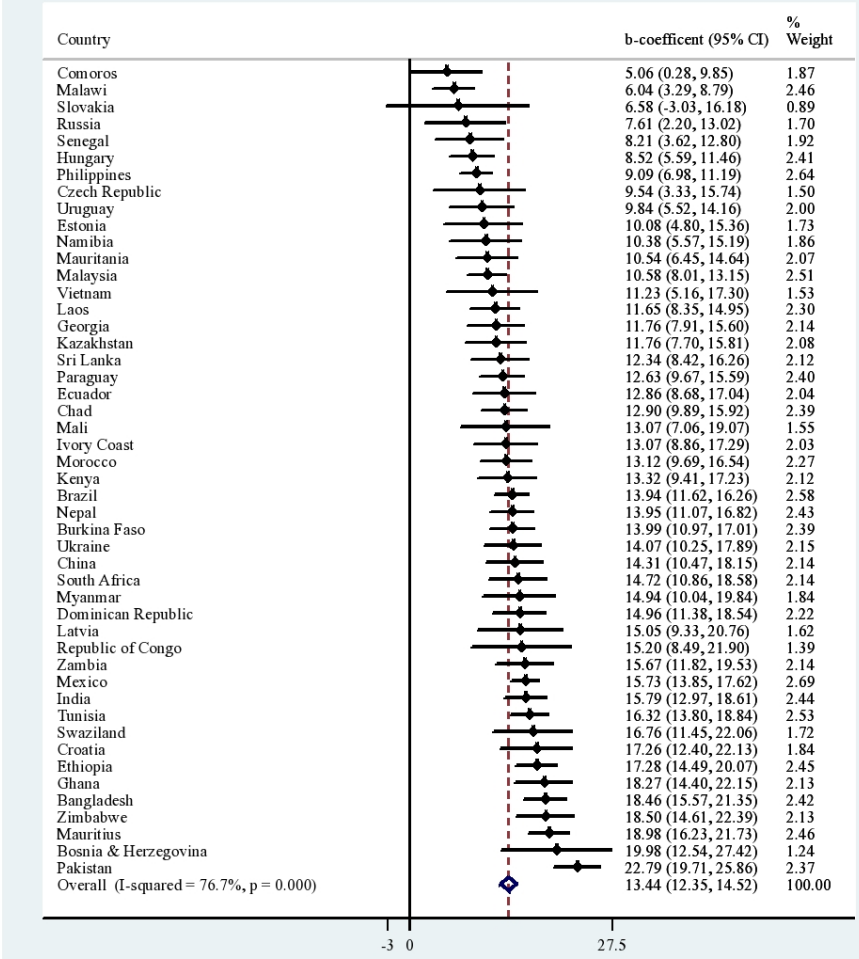

Figure 3 Country-wise association between multimorbidity and subjective cognitive complaints (outcome) estimated by multivariable linear regression

Abbreviation: CI Confidence interval

Multimorbidity referred to ≥2 chronic conditions.

The subjective cognitive complaints score ranged from 0 to 100 with higher scores representing worse subjective cognitive function.

Models are adjusted for age, sex, education, and wealth.

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