Anxiety symptoms and mild cognitive impairment among community-dwelling older adults from low- and middle-income countries

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ABSTRACT

Aim: Anxiety may be a risk factor for mild cognitive impairment (MCI) but there is a scarcity of data on this association especially from low- and middle-income countries (LMICs). Thus, we investigated the association between anxiety and MCI among older adults residing in six LMICs (China, Ghana, India, Mexico, Russia, South Africa), and the mediational effect of sleep problems in this association.

Methods: Cross-sectional, community-based, nationally representative data from the WHO Study on global AGEing and adult health (SAGE) were analyzed. The definition of MCI was based on the National Institute on Ageing-Alzheimer's Association criteria. Multivariable logistic regression analysis, meta-analysis, and mediation analysis were conducted to assess associations.

Results: The final sample included 32,715 individuals aged ≥50 years with preservation in functional abilities [mean (standard deviation) age 62.1 (15.6) years; 48.3% males]. Country-wise analysis showed a positive association between anxiety and MCI in all countries (OR 1.35-14.33). The pooled estimate based on meta-analysis with random effects was OR=2.27 (95%CI=1.35-3.83). Sleep problems explained 41.1% of this association.

Conclusions: Older adults with anxiety had higher odds for MCI in LMICs. Future studies should examine whether preventing anxiety or addressing anxiety among individuals with MCI can lead to lower risk for dementia onset in LMICs, while the role of sleep problems in this association should be investigated in detail.

Key words: anxiety, mild cognitive impairment, low- and middle-income countries, sleep problems, epidemiology.

INTRODUCTION

Dementia is a syndrome characterized by deterioration in cognitive function beyond what might be expected from normal ageing (World Health Organization, 2020). Dementia most commonly affects older adults and the global increase in the number of adults living into older age is increasing the global prevalence of dementia. Indeed, an estimated 47.5 million people worldwide had dementia in 2020, and this figure is expected to rise to 75.6 million in 2030 and 135.5 million in 2050 (World Health Organization, 2015). Dementia is one of the main causes of disability and dependency in older adults and has profound detrimental psychological, social, physiological, and economic impact on people living with the disease, their families, other care providers, and society as a whole (Veronese, et al, 2020). However, there is currently no cure for dementia and thus preventive efforts are essential to tackle its increasing prevalence.

Mild cognitive impairment (MCI) is a preclinical state to dementia (Morris, 2005), which is increasingly being considered an important "target" for the prevention of dementia. MCI has been defined as cognitive decline greater than what would be expected for an individual's age and education level, but not interfering notably with activities of daily life (Gauthier, et al, 2006). Several correlates of MCI have been identified including, for example, hypertension, diabetes mellitus, and cerebrovascular disease (Li, Xin, et al, 2013), as well as race (African American), low educational level, and depression (Lopez, et al, 2003). However, one understudied potential risk factor to date is anxiety. Anxiety may increase risk for cognitive decline via reductions in intellectually stimulating activities, sleep problems, or use of benzodiazepines. Indeed, literature has shown that anxiety is highly prevalent among those with MCI (Rozzini, et al, 2009). Importantly, previous studies have also shown that the co-occurrence of MCI and anxiety increases the likelihood of conversion to dementia

(specifically, Alzheimer's disease) (Gallagher, et al, 2011; Palmer, et al, 2007). Moreover, studies using a more proxy measure of anxiety, Neuropsychiatric Inventory-Questionnaire (NPI-Q), have demonstrated that high NPI-Q severity scores are associated with a higher conversion from MCI to dementia (Mallo, Patten, et al, 2020; Mallo, Valladares-Rodriguez, et al, 2020). However, to date, there is a scarcity of literature on the association between anxiety and MCI particularly from LMICs.

In addition, the role of sleep problems in the association between anxiety and MCI has been little investigated to date. Previous epidemiological studies have shown that psychopathology including anxiety is a very strong risk factor for insomnia onset (Soldatos, 1994). In turn, sleep problems have been identified as a risk factor for all cause cognitive decline and dementia with one recent meta-analyses identifying ten types of sleep conditions or parameters as being linked to higher risk of all-cause cognitive disorders (Xu, et al, 2020). For example, a study by Diem, et al. found that lower sleep efficiency and longer sleep latencies in older women were associated with 1.5 and 1.4 greater odds of developing MCI or dementia within five years (Diem, et al, 2016). Thus, it is possible that sleep problems are an important mediator in the association between anxiety and MCI.

Considering the above literature, the aim of the present study was to investigate the association between anxiety and MCI among older adults residing in six low- and middle-income countries (LMICs) (China, Ghana, India, Mexico, Russia, South Africa), and the mediational effect of sleep problems in this association. Studies from LMICs are highly relevant as almost 60% of people with dementia live in this setting (World Health Organization, 2020), and preventive strategies in these resource-limited settings are thus of vital importance.

METHODS

The survey

Data from the Study on Global Ageing and Adult Health (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). Briefly, 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. 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.

Anxiety symptoms

Anxiety symptoms were assessed by the question ‘Overall in the past 30 days, how much of a problem did you have with worry or anxiety’ with response alternatives: ‘none’, ‘mild’,

'moderate', 'severe', and 'extreme'. In accordance with previous publications using a dataset with the identical question, those who answered severe and extreme were considered to have anxiety (Stubbs, et al, 2017; Vancampfort, et al, 2017).

Mild cognitive impairment

MCI was ascertained based on the recommendations of the National Institute on Aging-Alzheimer's Association (Albert, et al, 2011). We applied the identical algorithms used in previous SAGE publications to identify MCI (Koyanagi, et al, 2018; Koyanagi, et al, 2019). Briefly, individuals fulfilling all of the following conditions were considered to have MCI:

(a) Concern about a change in cognition: Individuals who replied 'bad' or 'very bad' to the question "How would you best describe your memory at present?" and/or those who answered 'worse' to the question "Compared to 12 months ago, would you say your memory is now better, the same or worse than it was then?" were considered to have this condition.

(b) Objective evidence of impairment in one or more cognitive domains: was based on a <-1 SD cut-off after adjustment for level of education, age, and country. Cognitive function was assessed through the following performance tests: word list immediate and delayed verbal recall from the Consortium to Establish a Registry for Alzheimer's Disease (Morris, et al, 1989), which assessed learning and episodic memory; digit span forward and backwards from the Weschler Adult Intelligence Scale (Tulsky and Ledbetter, 2000), that evaluated attention and working memory; and the animal naming task (Morris, et al, 1989), which assessed verbal fluency.

(c) Preservation of independence in functional abilities: was assessed by questions on self-reported difficulties with basic activities of daily living (ADL) in the past 30 days (Katz, et al, 1963). Specific questions were: "How much difficulty did you have in getting dressed?" and "How much difficulty did you have with eating (including cutting up your food)?" The

answer options were none, mild, moderate, severe, and extreme (cannot do). Those who answered either none, mild, or moderate to both of these questions were considered to have preservation of independence in functional activities. All other individuals were deleted from the analysis (935 individuals aged ≥50 years).

(d) No dementia: Individuals with a level of cognitive impairment severe enough to preclude the possibility to undertake the survey were not included in the current study.

Sleep problems

Sleep problems were assessed 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?" with answer options 'none', 'mild', 'moderate', 'severe', and 'extreme'. This measure has been used in multiple previous publications (Koyanagi, et al, 2014; Selvamani, et al, 2018; Stickley, et al, 2019; Vancampfort, et al, 2018).

Control variables

The control variables were selected based on past literature (Lara, et al, 2016) and included age, sex, wealth quintiles based on income, years of education received, physical activity, alcohol use in the past 30 days, smoking (never, current, former), depression, diabetes, hypertension, stroke, and obesity [body mass index (BMI) ≥30 kg/m^2 based on measured weight and height]. Levels of physical activity were assessed with the Global Physical Activity Questionnaire and were classified as low, moderate, and high based on conventional cut-offs (Bull, et al, 2009). Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview (Kessler and Üstün, 2004) were used for the endorsement of past 12-month DSM-IV depression (American Psychiatric Association,

2013). Stroke and diabetes were based solely on self-reported lifetime diagnosis. Hypertension was defined as having at least one of: systolic blood pressure ≥140 mmHg; diastolic blood pressure ≥90 mmHg; or self-reported diagnosis.

Statistical analysis

The statistical analysis was performed with Stata 14.1 (Stata Corp LP, College station, Texas). The analysis was restricted to those aged ≥50 years as MCI is an age-related condition. The difference in sample characteristics by the presence or absence of anxiety 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 anxiety (exposure) and MCI (outcome). First, using the pooled sample including all countries, we constructed three models with different blocks of control variables to assess their influence in the anxiety-MCI association: Model 1 - adjusted for sociodemographic factors (age, sex, wealth, education, country): Model 2 - adjusted for factors in Model 1 and behavioral factors (physical activity, alcohol consumption, smoking); Model 3 (fully-adjusted model) - adjusted for factors in Model 2 and health conditions (depression, diabetes, hypertension, stroke, obesity). Second, based on the fully adjusted model, we conducted interaction analysis to assess whether the association between anxiety and MCI differs by age groups (50-64 and ≥65 years) and sex by including an interaction term (age groups X anxiety or sex X anxiety) in the model. Third, in order to assess the mediating effect of sleep problems in the association between anxiety and MCI, we conducted mediation analysis (Breen, et al, 2013). Specifically, we used the *khb* (Karlson Holm Breen) command in Stata for this purpose. This method can be applied in logistic regression models and decomposes the total effect [i.e., unadjusted for the mediator (i.e., sleep problems)] of a variable into direct (i.e., the effect of anxiety on MCI adjusted for the

mediator) 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). The mediation analysis adjusted for all factors in Model 3 (fully-adjusted model) mentioned above. Finally, we conducted country-wise analysis for the association between anxiety and MCI, and calculated the Higgins's I^2 based on estimates from each country order to assess between-country heterogeneity. The Higgins's I^2 represents the degree of heterogeneity that is not explained by sampling error with a value of <40% often considered as negligible and 40-60% as moderate heterogeneity (Higgins & Thompson, 2002). A pooled estimate was obtained by random-effects meta-analysis. The country-wise analysis was also adjusted for all factors in Model 3 (fully-adjusted model) with the exception of country.

In the regression analyses using the overall sample and the mediation analysis, adjustment for country was done by including dummy variables for each country in the model as in previous SAGE publications (Koyanagi, et al, 2014; Koyanagi, et al, 2018). The sample weighting and the complex study design were taken into account in the analyses. Results from the regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CIs). The level of statistical significance was set at $P<0.05$.

RESULTS

The final sample included 32,715 individuals (China n=12815; Ghana n=4201; India n=6191; Mexico n=2070; Russia n=3766; South Africa n=3672) aged ≥50 years with preservation in functional abilities [mean (standard deviation) age 62.1 (15.6) years; 48.3% males]. The sample characteristics overall are shown in **Table 1** and those by country are shown in **Table S1** of the Appendix. The overall prevalence of anxiety and MCI were 7.0% and 15.3%, respectively, although there was a wide range between countries with the range for anxiety

being 0.6% (China) to 16.0% (India) and that for MCI being 7.4% (Ghana) to 24.3% (China). The prevalence of MCI was higher among those with anxiety than in those without anxiety in all countries (**Figure 1**), especially in Russia (46.5% vs. 8.5%). The prevalence of anxiety among those with and without MCI is shown in **Figure 2**. The association between anxiety and MCI estimated by multivariable logistic regression using the overall sample is shown in **Table 2**. Anxiety was associated with a 1.91 (1.37-2.66) times higher odds for MCI in the fully-adjusted model (Model 3), and behavioral factors and health status had very little influence in this association as evidenced by the minimal attenuation in the ORs compared to Model 1 and 2. Interaction analysis showed that sex and age are not significant effect modifiers in this association. Next, the mediation analysis showed that 41.1% of the association between anxiety and MCI was mediated by sleep problems: total effect (OR=1.90; 95%CI=1.35-2.69; p<0.001); direct effect (OR=1.46; 95%CI=1.03-2.06; p=0.031); indirect effect (OR=1.30; 95%CI=1.22-1.39; p<0.001) (data only shown in text).

Finally, the country-wise association between anxiety and MCI is shown in **Figure 3**. Anxiety was associated with higher odds for MCI (OR>1) in all countries with the association being particularly strong in Russia. Based on a meta-analysis with random effects, the overall OR (95%CI) was 2.27 (1.35-3.83) with a high level of heterogeneity (I^2=81.0%). When Russia was omitted from the analysis, the I^2 was reduced to 40.1%.

DISCUSSION

Main findings

The results of our study show that older people from LMICs with anxiety symptoms are at an approximately 2 times higher odds for MCI. Age and sex were not significant effect modifiers in this association. Furthermore, behavior factors and health status had very little influence in this association. Based on the mediation analysis, 41% of the association

between anxiety and MCI was explained by sleep problems. Country-wise analysis showed that there is high level of between-country heterogeneity but this was mainly explained by the particularly strong association observed in Russia. To the best of our knowledge, this is the largest study on this topic to date, and one of the few from LMICs.

Interpretation of the findings

Findings from the present study support and add to previous literature on this topic which have found a higher prevalence of anxiety among those with MCI (Chen, et al, 2018). To date, we are aware of five studies which were conducted in LMICs (Baiyewu, et al, 2012; Muangpaisan, et al, 2008; Paddick, et al, 2015; Tatsch, et al, 2006; Zhang, et al, 2012), although all of them were of very small sample size. For example, one previous study found a high prevalence of anxiety among those with MCI compared to those without in one LMIC (Nigeria) (Baiyewu, et al, 2012), identifying a prevalence of almost 19% in the MCI group compared to 10% in the normal cognition group. Recently, two longitudinal studies on the relationship between anxiety and MCI have been conducted and these identified no significant associations (Kassem, et al, 2018; Paddick, et al, 2015). However, these studies have important limitations, they were both carried out in single high-income countries, consisted of very small sample sizes, and one study focused on females only (Kassem, et al, 2018). Further studies of a longitudinal design investigating the association between anxiety and MCI are required in multi-country studies, studies in LMICs, and consisting of representative samples.

There are several plausible mechanisms that may explain the positive association between anxiety and MCI found in our study. First, the presence of anxiety has been shown to be significantly associated with reduced functional status in performing activities of daily living

in older adults (Schultz, et al, 2004). A reduction in activities of daily living may be associated with an increase in risk of MCI owing to reduced brain stimulation. Second, studies have reported that use of benzodiazepines, a class of anxiolytic medications, is associated with elevated risk of cognitive decline or impairment (Kassem, et al, 2018). Finally, sleep problems may be an important mediator in the anxiety-MCI association. Indeed, the present study found that 41% of the association between anxiety and MCI was explained by sleep problems. Anxiety can increase the risk of sleep problems via rumination when attempting to sleep and it has been shown that a state of mental hyperarousal, frequently marked by worry, is a key risk factor for insomnia (Kalmbach, et al, 2018). Sleep problems in turn may increase the risk of MCI because the consolidation of memories is made when one sleeps (da Silva, Renata Alves Pachota Chaves, 2015). Indeed, literature has demonstrated a strong correlation between sleep disturbance and neuropsychological impairments in memory, processing speed and executive functioning (Naismith, et al, 2009; Naismith, et al, 2011).

Finally, we also found a high level of between-country heterogeneity in terms of the association between anxiety and MCI, which was mainly explained by the particularly strong association found in Russia. Although the reason for the particularly strong association in Russia is not known, this country had a particularly high level of education, high percentage of females, as well as high rates of alcohol consumption, and stroke, compared to other countries included in our study (see **Table S1** of the Appendix), and it is possible that these factors are playing a role (Curran, et al, 2020; Koch, et al, 2019; Vadikolias, et al, 2012). Future studies are necessary to understand why anxiety is more strongly associated with MCI in some settings.

Clinical implications

The observed associations in this study and others highlights the importance in addressing anxiety and sleep problems in order to aid in the prevention of MCI and ultimately dementia. There are several existing strategies that could be utilized to address these risk factors in older adults but lifestyle interventions may be most appropriate, especially in the context of LMICs. For example, physical activity can aid in the prevention of anxiety and result in better sleeping behaviors in older adults (Anderson and Shivakumar, 2013; Kline, 2014). In addition to physical activity, a healthy diet is also associated with lower levels of anxiety and better sleep (Nguyen, et al, 2017; Noorwali, et al, 2018). Finally, cessation of tobacco smoking has been found to be associated with a reduction in anxiety and improved sleep (McDermott, et al, 2013; Peters, et al, 2011). Since levels of physical activity are low, and the prevalence of malnutrition and smoking high in LMICs (Action on Smoking and Health, 2019; Perez-Escamilla, et al, 2018; World Health Organization, 2018), intervening to improve these parameters may reduce levels of MCI and ultimately dementia in this population.

Strengths and limitations

The strengths of the study include the large sample size and use of nationally representative data from six LMICs which together comprise nearly half of the worldwide population (Kowal, et al, 2012). However, the study results should be interpreted in the light of several limitations. First, anxiety symptoms were assessed with a single question and this question has not been validated. However, the use of extreme categories to define anxiety symptoms is likely to have improved specificity. Moreover, it should be noted that the present measures of MCI and sleep problems were not validated and thus, a certain degree of bias may have been introduced into the present findings. Second, given that there were no data on clinical

diagnoses of dementia available in the study, we cannot preclude the possibility that some people with mild dementia were included in our analytical sample. However, the prevalence of MCI in our study was within previously reported figures (Petersen, 2016). Finally, given the cross-sectional nature of the study, causality or temporal associations cannot be established. As mentioned above, the association between anxiety and MCI is likely to be bidirectional.

Conclusion

We found an approximately two-fold increased odds for MCI among older people in LMICs with anxiety. Future longitudinal studies are warranted to determine direction of associations and whether anxiety is a risk factor for MCI, especially in LMICs. Although the direction of the association could not be determined due to the cross-sectional nature of our study, it is important to note that previous studies have shown that anxiety-MCI comorbidity is associated with a particularly high risk for conversion to dementia (Li, Xiao-Xue and Li, 2018). The higher prevalence of anxiety among people with MCI compared to those without MCI in all countries included in our study is thus a concern. Future interventional studies are needed to assess the impact of preventing or addressing anxiety in people with MCI in terms of risk for conversion to dementia, especially in LMICs. Finally, the role of sleep problems in the association between anxiety and MCI should be investigated in detail.

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TABLES AND FIGURES

Table 1 Sample characteristics (overall and by anxiety)

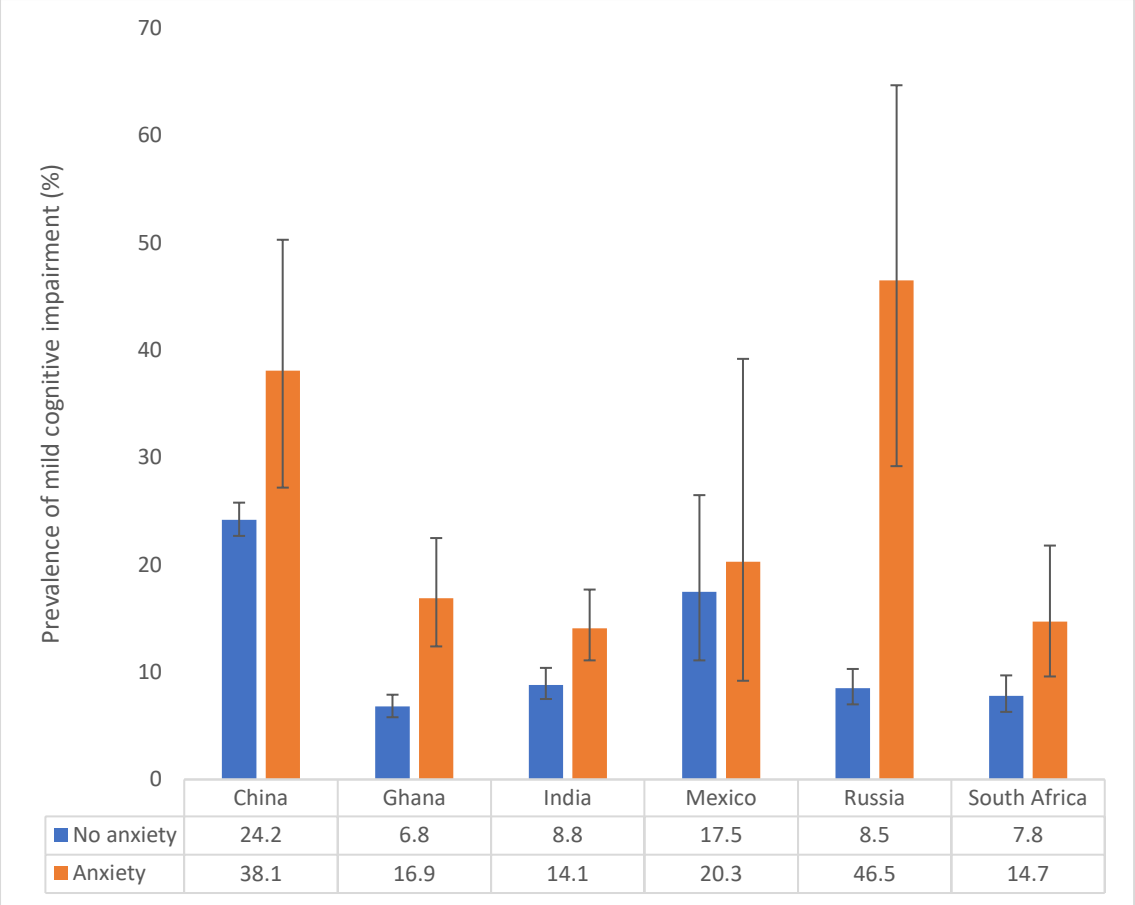
Characteristic		Overall	Anxiety		P-value[a]
			No	Yes	
Age (years)	Mean (SD)	62.1 (15.6)	62.1 (15.7)	62.7 (13.7)	0.084
Sex	Male	48.3	49.0	38.5	<0.001
	Female	51.7	51.0	61.5	
Education (years)	Mean (SD)	6.1 (8.9)	6.3 (8.9)	3.3 (6.7)	<0.001
Physical activity	High	50.0	50.1	48.4	0.805
	Moderate	23.0	22.9	23.8	
	Low	27.1	27.0	27.7	
Alcohol consumption	No	80.9	80.1	90.6	<0.001
	Yes	19.1	19.9	9.4	
Smoking	Never	58.7	59.5	47.1	<0.001
	Current	34.9	34.2	44.9	
	Former	6.4	6.3	8.0	
Depression	No	94.5	96.4	69.1	<0.001
	Yes	5.5	3.6	30.9	
Diabetes	No	93.2	93.5	90.0	0.002
	Yes	6.8	6.5	10.0	
Hypertension	No	45.1	44.3	55.6	<0.001
	Yes	54.9	55.7	44.4	
Stroke	No	97.2	97.3	96.6	0.315
	Yes	2.8	2.7	3.4	
Obesity	No	88.5	88.2	92.1	0.015
	Yes	11.5	11.8	7.9	

Abbreviation: SD Standard deviation
Data are % unless otherwise stated
[a] P-value was calculated by Chi-squared tests and Student's *t*-tests for categorical and continuous variables, respectively.

Table 2 Association between anxiety or covariates and mild cognitive impairment (outcome) estimated by multivariable logistic regression

		Model 1		Model 2		Model 3	
Characteristic		OR	95%CI	OR	95%CI	OR	95%CI
Anxiety	Yes vs. No	1.95***	[1.45,2.61]	1.92***	[1.44,2.58]	1.91***	[1.37,2.66]
Age (years)		1.03***	[1.02,1.03]	1.03***	[1.02,1.03]	1.02***	[1.02,1.03]
Sex	Female vs. Male	1.07	[0.96,1.20]	1.21*	[1.03,1.43]	1.20*	[1.01,1.43]
Wealth	Poorest	1.00		1.00		1.00	
	Poorer	0.95	[0.80,1.13]	0.95	[0.80,1.13]	0.95	[0.80,1.12]
	Middle	1.01	[0.83,1.23]	1.03	[0.85,1.25]	1.03	[0.85,1.26]
	Richer	0.68***	[0.56,0.82]	0.69***	[0.57,0.83]	0.68***	[0.57,0.82]
	Richest	0.42***	[0.34,0.52]	0.43***	[0.35,0.53]	0.42***	[0.34,0.51]
Education (years)		0.97**	[0.96,0.99]	0.97**	[0.96,0.99]	0.97**	[0.96,0.99]
Physical activity	High			1.00		1.00	
	Moderate			0.74***	[0.65,0.84]	0.74***	[0.65,0.84]
	Low			1.15*	[1.00,1.32]	1.14	[0.98,1.31]
Alcohol consumption	Yes vs. No			1.02	[0.87,1.21]	1.05	[0.89,1.24]
Smoking	Never			1.00		1.00	
	Current			1.19*	[1.01,1.40]	1.19*	[1.01,1.41]
	Former			1.22	[0.99,1.50]	1.19	[0.96,1.48]
Depression	Yes vs. No					0.85	[0.62,1.15]
Diabetes	Yes vs. No					1.08	[0.86,1.35]
Hypertension	Yes vs. No					1.07	[0.97,1.19]
Stroke	Yes vs. No					1.99***	[1.53,2.58]
Obesity	Yes vs. No					1.36**	[1.09,1.70]

Abbreviation: OR Odds ratio; CI Confidence interval
Models are adjusted for all variables in the respective columns and country.
* p<0.05, ** p<0.01, *** p<0.001



	China	Ghana	India	Mexico	Russia	South Africa
No anxiety	24.2	6.8	8.8	17.5	8.5	7.8
Anxiety	38.1	16.9	14.1	20.3	46.5	14.7

Figure 1 Prevalence of mild cognitive impairment by anxiety status
Bars denote 95% confidence intervals.

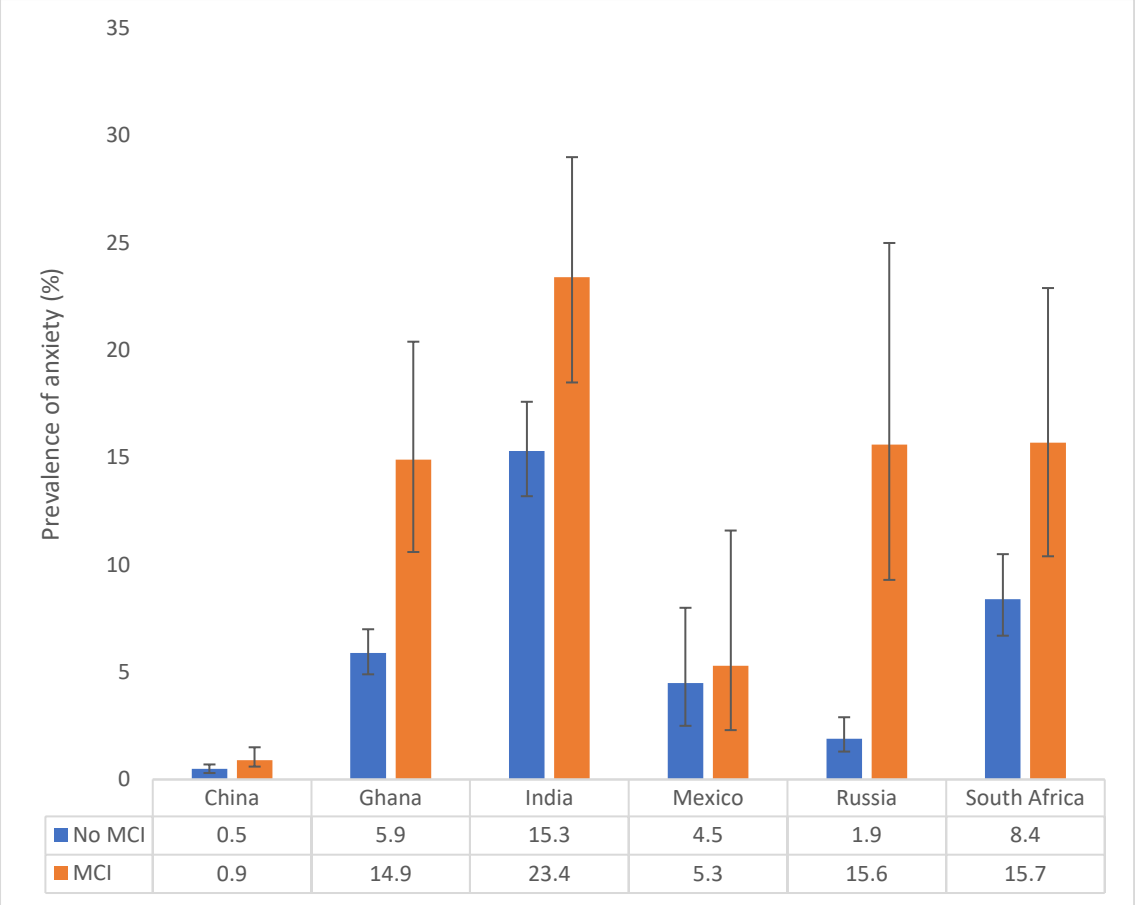


Figure 2 Prevalence of anxiety by mild cognitive impairment status
Abbreviation: MCI Mild cognitive impairment
Bars denote 95% confidence intervals.

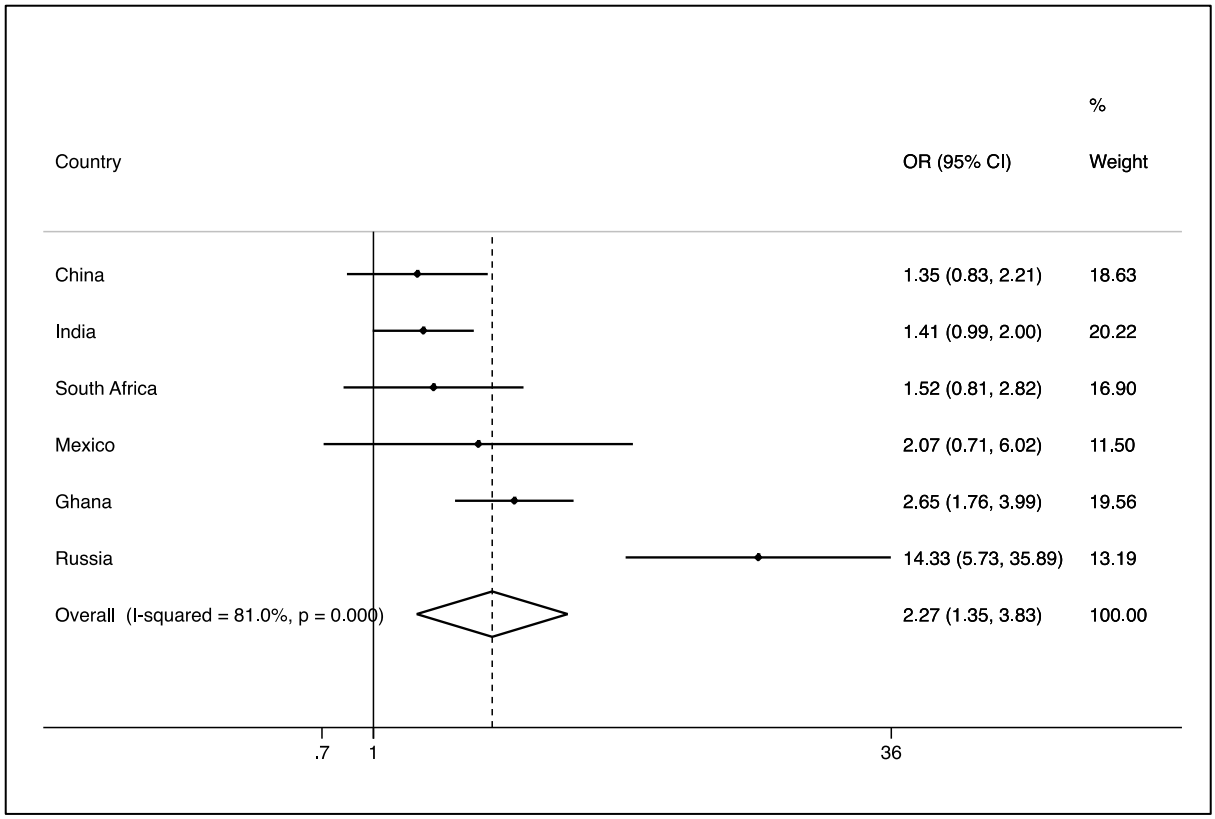


Figure 3 Country-wise association between anxiety and mild cognitive impairment (outcome) estimated by multivariable logistic regression

Abbreviation: OR Odds ratio; CI Confidence interval

Models are adjusted for age, sex, wealth, education, physical activity, alcohol use, smoking, depression, diabetes, hypertension, stroke, and obesity.

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

APPENDIX

Table S1 Sample characteristics by country

Characteristic		China	Ghana	India	Mexico	Russia	South Africa
MCI	Yes	24.3	7.4	9.7	17.6	9.6	8.5
Anxiety	Yes	0.6	6.5	16.0	4.6	3.3	9.3
Age (years)	Mean (SD)	62.4 (16.4)	64.2 (19.7)	61.1 (13.2)	62.3 (17.4)	63.4 (14.8)	61.4 (18.3)
Sex	Female	50.2	47.4	48.2	52.8	60.6	56.0
Education (years)	Mean (SD)	5.6 (8.1)	4.2 (9.9)	3.8 (7.4)	5.1 (7.9)	11.2 (5.1)	6.1 (10.1)
Physical activity	High	43.8	62.4	53.5	41.4	59.0	28.5
	Moderate	27.7	12.5	23.1	22.3	15.9	12.7
	Low	28.5	25.2	23.4	36.3	25.1	58.7
Alcohol consumption	Yes	23.0	30.9	7.0	25.8	33.6	14.0
Smoking	Never	64.2	75.3	45.2	60.3	69.3	66.6
	Current	29.3	10.7	50.4	20.5	21.8	23.8
	Former	6.5	14.0	4.3	19.3	8.9	9.7
Depression	Yes	1.0	7.0	11.9	10.2	3.2	2.9
Diabetes	Yes	6.5	3.6	6.8	17.1	6.8	9.1
Hypertension	Yes	60.5	59.3	36.7	61.5	71.7	78.6
Stroke	Yes	2.9	2.2	1.7	3.7	4.4	3.4
Obesity	Yes	5.9	9.9	2.5	28.5	34.5	46.6

Data are % unless otherwise stated.
Abbreviation: MCI Mild cognitive impairment; SD Standard deviation