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Association between depression and subjective cognitive complaints in 47 low- and middle-income countries

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ABSTRACT

People with depression and subjective cognitive complaints (SCC) may be at particularly high risk for developing dementia. However, to date, studies on depression and SCC are limited mainly to single high-income countries. Thus, the aim of the present study was to investigate the association between depression and SCC in adults from low- and middle-income countries (LMICs). Cross-sectional, community-based data were analyzed from the World Health Survey. 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). ICD-10 Diagnostic Criteria for Research was used for the diagnosis of subsyndromal depression, brief depressive episode, and depressive episode. Multivariable linear regression was conducted to explore the associations. Data on 237,952 individuals aged ≥18 years [mean (SD) age 38.4 (16.0) years; females 50.8%] were analyzed. After adjustment for potential confounders (age, sex, education, anxiety), compared to no depressive disorder, subsyndromal depression (b-coefficient 7.91; 95%CI = 5.63–10.18), brief depressive episode (b-coefficient 10.37; 95%CI = 8.95–11.78), and depressive episode (b-coefficient 13.57; 95%CI = 12.33–14.81) were significantly associated with higher mean SCC scores. The association was similar in all age groups (i.e., 18–44, 45–64, and ≥65 years), and both males and females. All depression types assessed were associated with worse SCC among adults in 47 LMICs. Future longitudinal studies are needed to investigate whether older people with depression and SCC are at higher risk for dementia onset in LMICs.

1. Introduction

Dementia is a syndrome which constitutes deterioration in memory, thinking, behavior and the ability to conduct activities of daily living (World Health Organization, 2021). The prevalence of dementia increases with age, with 5–8% of the global population aged ≥60 years reported to have dementia (World Health Organization, 2021), and almost 60% of those with dementia live in low- and middle-income countries (LMICs) (World Health Organization, 2021). Subjective cognitive complaints (SCC) refer to everyday concerns cited by people both with and without objective evidence of memory impairment (Mitchell, Alex J., 2008), and have been found to be a predictor of the

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future development of dementia (Mendonça et al., 2016). For example, previous systematic reviews have found that SCC (compared to no SCC) are associated with a significantly higher risk of progression to dementia (Mendonça et al., 2016), even in the presence of normal baseline objective cognition (Mitchell, A. J. et al., 2014). Moreover, biological changes associated with an increased risk of dementia, such as increases in white matter lesions, temporal atrophy, and altered cerebrospinal fluid biomarkers have also been observed in individuals with SCC (Mosconi et al., 2008; Van Norden et al., 2008; Striepens et al., 2010).

Currently, there is much interest in the relationship between SCC, depression, and altered risk of developing dementia. Depression has been independently reported to increase the risk of dementia (Kessing and Andersen, 2004), with a number of potential mechanisms proposed, including vascular disease; alterations in glucocorticoid steroids and hippocampal atrophy; increased deposition of β-amyloid plaques; inflammatory changes; and deficits of nerve growth factors or neurotrophins (Byers and Yaffe, 2011). Previous studies, mainly from high-income countries, have shown that SCC is common among individuals with depression (Hill et al., 2016). Indeed, changes in attention, concentration and decisiveness are listed in one of the supplementary criteria for depression in ICD10, whilst the DSM V criteria includes slowing down of thought, and diminished ability to think, concentrate or indecisiveness. Given the high degree of correlation between SCC and depression, there has been debate over whether SCC is an independent risk factor for dementia from depression, and whether this may be due to a common neurobiology. In one recent longitudinal study carried out on 1307 US participants, depression (HR 1.4; 95%CI 1.1–1.7) and SCC (HR = 2.0; 95%CI = 1.8–2.2) demonstrated independent risks for mild cognitive impairment (MCI) or/dementia in a cohort aged over 50 years. However, the risk was highest when depression and SCC co-occur (HR 2.8; 95%CI = 2.4–3.4), with half of the participants in this group developing MCI/dementia within 7.2 years of follow-up (compared to 12.2 years in participants without depression or SCC) (Liew, 2019). This suggests that screening for SCC in people with depression may lead to the identification of those who are at particularly high risk for dementia.

However, to date, there are almost no data on studies on the association between depression and SCC from LMICs. This is an important research gap as the number of people with dementia is highest in such settings (World Health Organization, 2021), and health services may be less well resourced (Bitton et al., 2019). Furthermore, the effect of age on strength of any association between SCC and depression has not been examined in this population. Given this background, the aim of the present study was to investigate the cross-sectional association between depression and SCC in 237,952 individuals aged ≥18 years from 47 LMICs.

2. Methods

The World Health Survey (WHS) was a cross-sectional survey carried out in 2002–2004. Survey details are available elsewhere (Üstün et al., 2003). 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.

2.1. Subjective cognitive complaints (SCC)

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 (Koyanagi et al., 2017, 2020). 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 to 100 to create a SCC scale with higher values representing worse subjective cognitive function.

2.2. Depression

The severity of depressive symptoms was established based on the individual questions of the World Mental Health Survey version of the Composite International Diagnostic Interview (CIDI), which assessed the duration and persistence of depressive symptoms in the past 12 months (Kessler and Üstün, 2004). Following the algorithms used in a previous WHS publication (Ayuso-Mateos et al., 2010), four mutually exclusive groups were established based on the ICD-10 Diagnostic Criteria for Research (ICD-10-DCR) (World Health Organization, 1993) where criterion B referred to symptoms of depressed mood, loss of interest, and fatigability. The algorithms used to define the four mutually exclusive groups were the following:

Depressive episode: At least two criterion B symptoms with a total of at least four depressive symptoms lasting two weeks most of the day or all of the day.

Brief depressive episode: Same criteria as depressive episode but did not meet the two-week duration criterion.

Subsyndromal depression: At least one criterion B symptom with the total number of symptoms being three or less. The criteria of duration of at least two weeks and presence of symptoms during most of the day had to be met.

No depressive disorder: None of the above.

In some analyses, we also dichotomized this variable as the absence or presence of any depression (i.e., depressive episode, brief depressive episode, subsyndromal depression).

2.3. Control variables

The control variables were selected based on previous literature (Begum et al., 2014) and included age, sex, highest level of education achieved (no formal, primary, secondary, tertiary), and anxiety. Anxiety was assessed by the question 'Overall in the past 30 days, how much of a problem did you have with worry or anxiety' with answer options being none, mild, moderate, severe, and extreme. In accordance with previous WHS publications, those who answered severe and extreme were considered to have anxiety (Koyanagi and Stickley, 2015; Wong et al., 2013).

2.4. Statistical analysis

The statistical analysis was done with Stata 14.2 (Stata Corp LP, College station, Texas). Data were publicly available for 69 countries. Of these, 10 countries were excluded due to a lack of sampling information. Furthermore, 10 high-income countries were excluded in order to focus on LMICs. Moreover, Turkey was deleted due to lack of data on education, while Morocco was deleted due to lack of data on anxiety. Thus, the

Table 1
Sample size, prevalence of any depression, and mean subjective cognitive complaints score by country.

Country	N	Any depression[a]		SCC score[b]	
		%	[95%CI]	Mean	[95%CI]
Bangladesh	5942	18.1	[16.3,20.0]	25.1	[23.9,26.3]
Bosnia & Herzegovina	1031	8.3	[5.8,11.9]	15.9	[13.7,18.0]
Brazil	5000	22.6	[21.0,24.3]	22.2	[21.3,23.2]
Burkina Faso	4948	17.1	[14.4,20.3]	14.8	[13.0,16.6]
Chad	4870	18.7	[16.2,21.5]	25.1	[23.5,26.7]
China	3994	2.0	[1.4,2.9]	17.4	[15.4,19.5]
Comoros	1836	8.3	[6.8,10.1]	36.7	[35.1,38.3]
Croatia	993	13.6	[11.4,16.2]	19.2	[17.2,21.2]
Czech Republic	949	12.6	[10.2,15.5]	17.4	[14.7,20.0]
Dominican Republic	5027	16.1	[14.6,17.8]	15.5	[14.5,16.5]
Ecuador	5675	8.0	[6.6,9.8]	18.7	[17.4,20.0]
Estonia	1020	14.6	[12.8,16.6]	15.5	[13.9,17.1]
Ethiopia	5089	12.2	[11.0,13.6]	20.4	[19.0,21.8]
Georgia	2950	10.7	[8.6,13.3]	16.0	[14.2,17.8]
Ghana	4165	8.4	[7.2,9.9]	16.4	[15.3,17.6]
Hungary	1419	11.4	[9.5,13.5]	13.0	[11.6,14.3]
India	10,687	13.9	[12.3,15.7]	25.8	[24.2,27.4]
Ivory Coast	3251	12.2	[10.5,14.1]	17.9	[16.4,19.5]
Kazakhstan	4499	6.8	[5.0,9.3]	19.6	[17.1,22.2]
Kenya	4640	13.3	[11.3,15.6]	14.1	[12.9,15.4]
Laos	4988	2.7	[2.2,3.2]	22.7	[21.6,23.8]
Latvia	929	13.1	[10.6,16.0]	24.6	[22.2,27.1]
Malawi	5551	10.1	[8.9,11.4]	14.7	[13.7,15.6]
Malaysia	6145	2.9	[2.4,3.7]	15.1	[14.3,15.9]
Mali	4886	9.6	[8.4,11.0]	14.7	[13.6,15.7]
Mauritania	3902	6.6	[5.2,8.4]	26.5	[24.7,28.2]
Mauritius	3968	10.7	[9.2,12.3]	17.3	[16.0,18.6]
Mexico	38,746	10.8	[10.2,11.4]	11.9	[11.5,12.4]
Myanmar	6045	0.9	[0.6,1.5]	18.0	[16.0,20.0]
Namibia	4379	7.2	[6.1,8.4]	18.7	[17.4,20.1]
Nepal	8820	16.8	[15.8,17.9]	20.3	[19.6,21.0]
Pakistan	6501	10.1	[9.1,11.2]	15.8	[15.0,16.6]
Paraguay	5288	10.6	[9.6,11.7]	14.4	[13.7,15.2]
Philippines	10,083	4.8	[4.2,5.5]	29.9	[28.4,31.3]
Republic of Congo	3075	12.3	[9.3,16.1]	24.0	[20.8,27.2]
Russia	4427	11.6	[9.9,13.5]	29.1	[26.8,31.4]
Senegal	3461	15.5	[13.6,17.5]	16.0	[14.8,17.2]
Slovakia	2535	10.3	[6.5,16.0]	16.3	[12.6,20.1]
South Africa	2629	7.2	[5.8,9.0]	20.7	[18.9,22.5]
Sri Lanka	6805	2.9	[2.4,3.6]	13.6	[12.6,14.6]
Swaziland	3117	10.9	[8.9,13.2]	22.8	[20.8,24.9]
Tunisia	5202	11.0	[9.5,12.6]	15.3	[14.1,16.5]
Ukraine	2860	13.0	[10.8,15.4]	17.5	[15.7,19.2]
Uruguay	2996	9.1	[8.1,10.2]	9.4	[8.5,10.3]
Vietnam	4174	0.6	[0.4,0.9]	9.3	[7.6,10.9]
Zambia	4165	8.0	[7.0,9.2]	14.0	[13.0,15.0]
Zimbabwe	4290	5.6	[4.7,6.7]	15.1	[14.0,16.3]

Abbreviation: SCC Subjective cognitive complaints.
[a] Any depression referred to depressive episode, brief depressive episode, or subsyndromal depression.
[b] The cognitive complaints score (outcome) ranged from 0 to 100 with higher scores representing worse cognition.

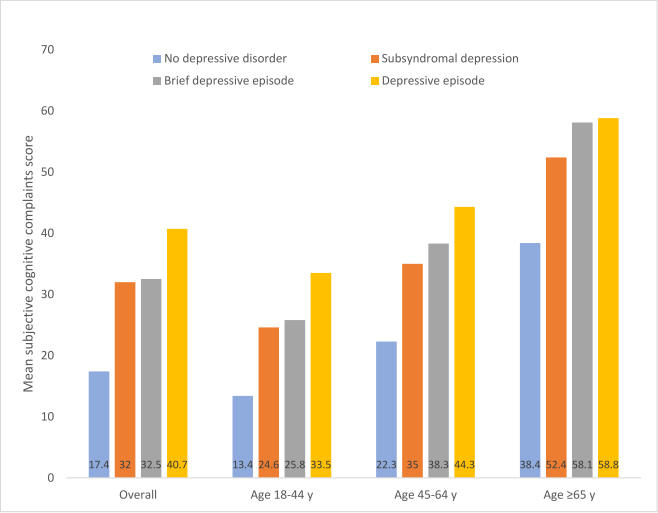

Fig. 1. Mean subjective cognitive complaints score by type of depression (overall and by age groups)
The cognitive complaints score ranged from 0 to 100 with higher scores representing worse cognition.

final sample consisted of 47 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 association of depression types (exposure variable) and subjective cognitive complaints (outcome) was estimated by multivariable linear regression. This analysis was also stratified by age groups (18–44, 45–64, ≥65 years) and sex. Next, in order to assess whether there is between-country heterogeneity in the association between any depression and subjective cognitive complaints, we conducted country-wise analysis. The Higgins's I^2 statistic was calculated, which 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 (Higgins et al., 2003). A pooled estimate (overall and by country-income level) was obtained by combining the estimates for each country into a random effect meta-analysis.

The regression analyses were adjusted for age, sex, education, anxiety, and country except for 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 (Koyanagi et al., 2017; Koyanagi and Stickley, 2015). 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-coefficient with 95% confidence intervals (CIs). The level of statistical significance was set at $P < 0.05$.

Table 2
Sample characteristics (overall and by depression type).

Characteristic		Overall	Depression type			
			No depressive disorder	Subsyndromal depression	Brief depressive episode	Depressive episode
Age	Mean (SD)	38.4 (16.0)	39.8 (16.1)	45.4 (17.6)	40.7 (16.8)	46.0 (17.6)
Sex	Female	50.8	48.8	60.6	65.3	64.6
	Male	49.2	51.2	39.4	34.7	35.4
Education	No formal	26.1	25.0	44.5	28.4	37.8
	Primary	31.0	30.7	27.1	30.3	32.5
	Secondary	33.7	34.7	22.2	32.7	23.4
	Tertiary	9.2	9.6	6.2	8.6	6.3
Anxiety	No	88.5	91.9	79.9	74.1	59.5
	Yes	11.5	8.1	20.1	25.9	40.5

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

Table 3
Association between depression types (or covariates) and subjective cognitive complaints (outcome) estimated by multivariable linear regression.

Characteristics		Overall	Age (years)			Sex	
			18–44	45–64	≥65	Male	Female
Depression type	No depressive disorder	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Subsyndromal depression	7.91* [5.63,10.18]	7.24* [5.11,9.37]	8.00* [4.75,11.26]	9.73 [-1.43,20.89]	7.29* [4.40,10.18]	8.08* [4.50,11.66]
	Brief depressive episode	10.37* [8.95,11.78]	9.25* [7.55,10.94]	11.26* [8.46,14.05]	13.52* [9.38,17.66]	10.76* [8.33,13.19]	10.04* [8.31,11.77]
	Depressive episode	13.57* [12.33,14.81]	13.87* [12.44,15.29]	13.08* [10.53,15.63]	12.63* [9.55,15.72]	15.12* [13.33,16.90]	12.45* [10.90,13.99]
Age (years)		0.42* [0.40,0.44]	0.20* [0.16,0.23]	0.62* [0.53,0.71]	0.77* [0.63,0.91]	0.34* [0.32,0.36]	0.50* [0.47,0.53]
Sex	Female	Ref.	Ref.	Ref.	Ref.		
	Male	−4.44* [-4.88,-4.00]	−3.20* [-3.67,-2.73]	−6.76* [-7.74,-5.79]	−6.41* [-8.52,-4.30]		
Education	No formal	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Primary	−2.68* [-3.42,-1.95]	−2.22* [-3.19,-1.26]	−3.67* [-5.19,-2.16]	−6.26* [-8.72,-3.79]	−2.38* [-3.36,-1.40]	−2.19* [-3.16,-1.22]
	Secondary	−5.74* [-6.59,-4.89]	−5.09* [-6.20,-3.98]	−8.52* [-10.19,-6.85]	−11.75* [-14.87,-8.64]	−4.61* [-5.74,-3.48]	−6.13* [-7.17,-5.10]
	Tertiary	−9.45* [-10.45,-8.46]	−7.00* [-8.17,-5.83]	−12.39* [-14.25,-10.53]	−16.22* [-20.40,-12.04]	−7.93* [-9.17,-6.69]	−9.87* [-11.21,-8.53]
Anxiety	No	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
	Yes	15.55* [14.60,16.49]	15.10* [13.92,16.28]	16.63* [14.80,18.45]	13.64* [11.03,16.24]	16.55* [15.10,18.00]	14.63* [13.48,15.78]

Abbreviation: Ref. Reference category.
Data are b-coefficients [95% confidence interval].
Models are adjusted for all variables in the respective columns and country.
The cognitive complaints score (outcome) ranged from 0 to 100 with higher scores representing worse cognition.
*P < 0.001.

3. Results

The final sample consisted of 237,952 individuals aged ≥18 years [mean (SD) age 38.4 (16.0) years; female 50.8%]. The number of people in each age group was: age 18–44 years n = 148,537; age 45–64 years n = 56,256; age ≥65 years n = 24,086. Overall, the prevalence (95%CI) and mean (95%CI) of any depression and SCC score were 11.8% (11.4%–12.2%) to 19.8 (19.5–20.1), respectively. The sample size, prevalence of any depression, and mean SCC score of each country included in the study are shown in Table 1. The prevalence of any depression ranged from 0.6% (Vietnam) to 22.6% (Brazil), while the mean SCC score ranged from 9.3 (Vietnam) to 36.7 (Comoros). The sample characteristics are provided in Table 2. All depression types were more common among females, while the prevalence of anxiety was very high (40.5%) among those with depressive episode. All types of depression had much higher mean SCC score compared to those without any depressive disorder (Fig. 1). For example, in the overall sample, the mean SCC score was 17.4 among those with no depressive disorder but this increased to 40.7 among those with depressive disorder. Similar trends were found for all age groups in terms of increasing SCC with increased levels of depression. After adjustment for age, sex, education, and anxiety, compared to no depressive disorder, subsyndromal depression, brief depressive episode, and depressive episode had 7.91 (95%CI = 5.63–10.18), 10.37 (95%CI = 8.95–11.78), and 13.57 (95% CI = 12.33–14.81) higher mean SCC scores, respectively (Table 3). Similar results were found for all age groups and both males and females. Country-wise analysis showed that any depression was significantly associated with higher SCC scores in all countries, with the exception of Comoros (Fig. 2). The overall estimate based on a meta-analysis was b-coefficient 10.56 (95%CI = 9.51–11.60) with a high level of heterogeneity (I^2 = 73.1%). The pooled estimated for low-income countries (b-coefficient 9.94; 95%CI = 8.23–11.64; I^2 = 78.7%) and middle-income countries (b-coefficient 11.09; 95%CI = 9.84–12.34; I^2 = 62.9%) were similar.

4. Discussion

4.1. Main findings

In this large predominantly nationally representative sample of adults from 47 LMICs, it was observed that compared to no depressive disorder, subsyndromal depression, brief depressive episode, and depressive episode had 7.91, 10.37, and 13.57 higher mean SCC scores, even after adjustment for factors such as education and anxiety, with the severest form of depression (depressive episode) having the highest score. The trend to increased SCC scores with increased levels of depression was seen in all age groups (i.e., 18–44, 45–64, ≥65 years). Depression was significantly associated with higher mean SCC scores in all countries included in the study, except for Comoros, and a high level of between-country heterogeneity was observed.

4.2. Interpretation of findings

Findings from the present study concur with previous literature that has predominantly focused on single high-income countries (HICs) (Schweizer et al., 2018; Burmester et al., 2016; Reid and MacLullich, 2006). Our study adds to previous literature by showing for the first time that depression (including depression subtypes) is strongly associated with SCC in a large sample from 47 LMICs. There are several plausible biological pathways that may explain the depression/SCC relationship. First, depression is associated with an increase in inflammation (Berk et al., 2013), and inflammation has been implicated in memory complaints. For example, in a study of 12,336 participants, it was found that people with a midlife inflammation composite score in the top quartile had a 7.8% steeper cognitive decline, compared to participants in the lowest quartile. In cognitive domain-specific analyses, elevated midlife inflammatory markers were most consistently associated with declines in memory (Walker et al., 2019). Second, depression is associated with oxidative and nitrosative stress, which contribute to neuroprogression, and can thus potentially increase risk of SCC (Berk et al., 2013). Third, it may be hypothesized that SCC *per se* may increase risk of depression.

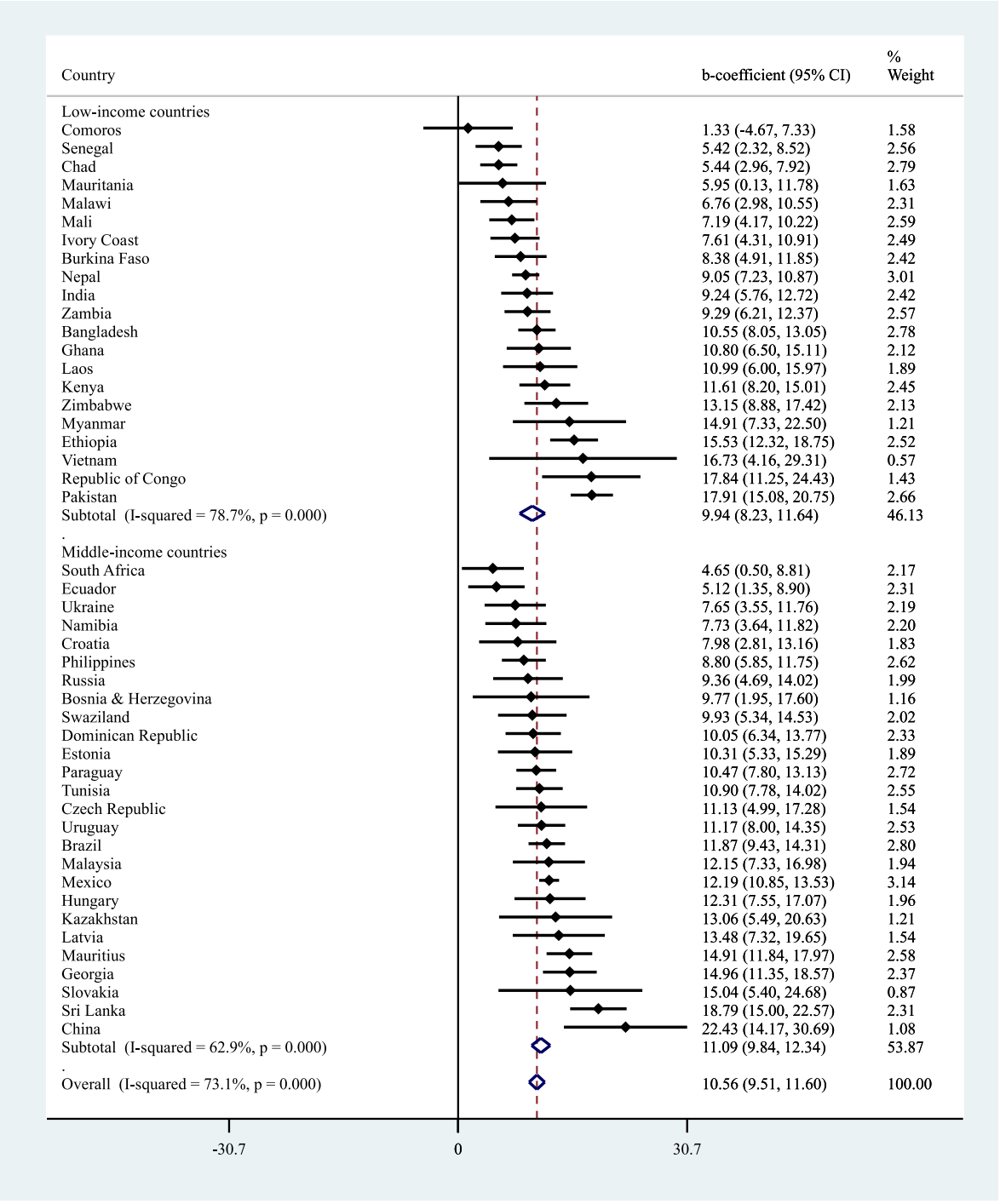

Fig. 2. Country-wise association between any depression and subjective cognitive complaints (outcome) estimated by multivariable linear regression Abbreviation: CI Confidence interval
Models are adjusted for age, sex, education, and anxiety.
Any depression referred to depressive episode, brief depressive episode, or subsyndromal depression.
The cognitive complaints score (outcome) ranged from 0 to 100 with higher scores representing worse cognition.
Overall estimate was obtained by meta-analysis with random effects.

Specifically, depression could occur as a "reactive" response to the underlying SCC, and symptoms could worsen with increasing severity with SCC. For example, experiencing forgetfulness and a fear of developing dementia may trigger depression onset. Moreover, greater depression symptom severity has been found to worsen SCC in Australian youth attending mental health services (Allott et al., 2020), suggesting that the association between depression and SCC may be bidirectional. Finally, negatively biased self-evaluation is a core feature of depression that may play a role in the more severely depressed patients' tendency to underestimate their own cognitive abilities (Serra-Blasco et al., 2019). This may partly explain the reason why depressive episode was more strongly associated with SCC than milder forms (i.e., subsyndromal depression and brief depressive episode).

4.3. Implications of the study findings and areas for future research

In our study, we found that depressive episode was most strongly associated with SCC but that even milder forms such as subsyndromal depression and brief depressive episode are also associated with a relatively large decline in SCC. The present findings are important as previous literature has shown that older people with depression and SCC are at highest risk of developing MCI/dementia, compared to those with either condition alone (Liew, 2019). This study describes this association in LMICs and thus highlights the possibility of identifying older adults with SSC and depression in these countries as a group at high risk of developing dementia whom interventions could be targeted towards (Liew, 2019). The findings of our study suggest that screening for SCC in all types of depression (i.e., even milder forms) in older adults in LMICs may help in the identification of those who are at particularly high risk of dementia. This may be a particularly useful tool in the context of many LMICs, as SCC can be self-reported and does not require burdensome neuropsychological testing and specially trained staff. In the context of HICs, it may be possible to test for biomarkers of neurocognitive disorders (e.g., amyloid protein, tau protein) to assess whether a patient may be at very early stages of neurocognitive disorders. Specific interventions may be possible and small trials are beginning to emerge suggesting improved cognitive outcome with some drug treatments in patients with depression and SCC (Lavretsky et al., 2020). In resource-limited settings, a more cost-effective strategy is often necessary. In LMICs, interventions often focus on behavioral changes, and in the context of depression and SCC, physical activity promotion may be beneficial as some studies have suggested a positive impact on depression (Craft and Perna, 2004), and possible reduced risk for dementia onset (Ahlskog et al., 2011). Future studies should assess the health benefits of physical activity promotion in people who are identified to have both depression and SCC, especially in LMICs.

Interestingly in our study, while depression was associated with significantly higher SCC scores in all countries except one, there was a high level of between-country heterogeneity in the association. Specifically, this may be owing to age barriers in relation to depression diagnosis differing between countries, or differing depression treatment or its availability between settings. In addition, there may also be differing levels of stigma between countries in relation to seeking depression diagnosis and treatment. Whether this between-country implies that the risk for dementia in those with depression and SCC differ by context is an important future research question. Furthermore, despite baseline SCC scores being much higher among older populations, the increase in mean SCC score associated with depression was similar in all age groups (i.e., 18–44, 45–64, ≥65 years). Although intervening in midlife and older age is known to be important in the prevention of dementia, the significance of our findings in terms of future dementia prevention among the younger population is unclear. Future studies of prospective design with long follow-up periods are necessary to clarify this issue.

4.4. Strengths and limitations

The use of large predominantly nationally representative datasets, and the focus on multiple LMICs, where no data on SCC and depression previously existed, are clear strength of the study. However, findings must be interpreted in light of the study's limitations. First, variables were self-reported and thus, reporting bias (e.g., recall and social desirability bias) may exist. Second, we used two questions to assess SCC, and these do not capture all dimensions of SCCs. Furthermore, there is no consensus on the measure to capture SCC (Molinuevo et al., 2017) and the measures used in previous studies range from a single question to a complex assessment involving multiple questions. Thus, the results could have differed if a different measure of SCC was used. Relatedly, due to the wording of the survey question, it was not possible to assess memory complaints and concentration problems separately in our study. Indeed, attentional/concentration difficulties may be partially influenced by, for example, ruminative tendencies that are a characteristic of depressive disorders (Kovács et al., 2020). Future research should assess memory complaints and concentration problems separately as this will provide domain-specific information on the potential associations between these components and depression severity. Next, the diagnosis of subsyndromal depression, brief depressive episode, and depressive episode was not assessed by a clinical interview. Thus, it is possible that there is some level of misclassification but clinical interviews are usually not logistically feasible in large epidemiological studies of this scale. Finally, the study was cross-sectional in nature and thus, the direction of the association cannot be determined.

5. Conclusion

Subsyndromal depression, brief depressive episode, and depressive episode were all associated with SCC among adults in 47 LMICs. Future longitudinal studies are needed to investigate whether older people with depression and SCC are at higher risk for dementia onset in LMICs.

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Author statement

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Data availability statement

Data used in this study are publicly available via the WHO website (https://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/whs/about), subject to approval.

Declaration of competing interest

None.

References

Ahlskog, J.E., Geda, Y.E., Graff-Radford, N.R., Petersen, R.C., 2011. Physical Exercise as a Preventive or Disease-Modifying Treatment of Dementia and Brain Aging, vol. 86, pp. 876–884.

Allott, K., Gao, C., Hetrick, S.E., Filia, K.M., Menssink, J.M., Fisher, C., Hickie, I.B., Herrman, H.E., Rickwood, D.J., Parker, A.G., 2020. Subjective cognitive functioning in relation to changes in levels of depression and anxiety in youth over 3 months of treatment. BJPsych open 6.

Ayuso-Mateos, J.L., Nuevo, R., Verdes, E., Naidoo, N., Chatterji, S., 2010. From depressive symptoms to depressive disorders: the relevance of thresholds. Br. J. Psychiatr. 196, 365–371.

Begum, A., Dewey, M., Hassiotis, A., Prince, M., Wessely, S., Stewart, R., 2014. Subjective cognitive complaints across the adult life span: a 14-year analysis of trends and associations using the 1993, 2000 and 2007 English Psychiatric Morbidity Surveys. Psychol. Med. 44, 1977–1987.

Berk, M., Williams, L.J., Jacka, F.N., O'Neil, A., Pasco, J.A., Moylan, S., Allen, N.B., Stuart, A.L., Hayley, A.C., Byrne, M.L., 2013. So depression is an inflammatory disease, but where does the inflammation come from? BMC Med. 11, 1–16.

Bitton, A., Fifield, J., Ratcliffe, H., Karlage, A., Wang, H., Veillard, J.H., Schwarz, D., Hirschhorn, L.R., 2019. Primary healthcare system performance in low-income and middle-income countries: a scoping review of the evidence from 2010 to 2017. BMJ global health 4, e001551.

Burmester, B., Leathem, J., Merrick, P., 2016. Subjective cognitive complaints and objective cognitive function in aging: a systematic review and meta-analysis of recent cross-sectional findings. Neuropsychol. Rev. 26, 376–393.

Byers, A.L., Yaffe, K., 2011. Depression and risk of developing dementia. Nat. Rev. Neurol. 7, 323–331.

Craft, L.L., Perna, F.M., 2004. The benefits of exercise for the clinically depressed. Prim. Care Companion J. Clin. Psychiatry 6, 104.

Higgins, J.P., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ 327, 557–560.
Hill, N.L., Mogle, J., Wion, R., Munoz, E., DePasquale, N., Yevchak, A.M., Parisi, J.M., 2016. Subjective cognitive impairment and affective symptoms: a systematic review. Gerontol. 56, e109–e127.
Kessing, L.V., Andersen, P.K., 2004. Does the risk of developing dementia increase with the number of episodes in patients with depressive disorder and in patients with bipolar disorder? J. Neurol. Neurosurg. Psychiatr. 75, 1662–1666.
Kessler, R.C., Üstün, T.B., 2004. The world mental health (WMH) survey initiative version of the world health organization (WHO) composite international diagnostic interview (CIDI). Int. J. Methods Psychiatr. Res. 13, 93–121.
Kovács, L.N., Takacs, Z.K., Tóth, Z., Simon, E., Schmelowszky, Á., Kökönyei, G., 2020. Rumination in major depressive and bipolar disorder–a meta-analysis. J. Affect. Disord. 276, 1131–1141.
Koyanagi, A., Stickley, A., 2015. The association between sleep problems and psychotic symptoms in the general population: a global perspective. Sleep 38, 1875–1885.
Koyanagi, A., Stubbs, B., Lara, E., Veronese, N., Vancampfort, D., Smith, L., Haro, J.M., Oh, H., DeVylder, J.E., 2020. Psychotic experiences and subjective cognitive complaints among 224 842 people in 48 low-and middle-income countries. Epidemiol. Psychiatr. Sci. 29.
Koyanagi, A., Vancampfort, D., Carvalho, A.F., DeVylder, J.E., Haro, J.M., Pizzol, D., Veronese, N., Stubbs, B., 2017. Depression comorbid with tuberculosis and its impact on health status: cross-sectional analysis of community-based data from 48 low-and middle-income countries. BMC Med. 15, 209.
Lavretsky, H., Laird, K.T., Krause-Sorio, B., Heimberg, B.F., Yeargin, J., Grzenda, A., Wu, P., Thana-Udom, K., Ercoli, L.M., Siddarth, P., 2020. A randomized double-blind placebo-controlled trial of combined escitalopram and memantine for older adults with major depression and subjective memory complaints. Am. J. Geriatr. Psychiatr. 28, 178–190.
Liew, T.M., 2019. Depression, subjective cognitive decline, and the risk of neurocognitive disorders. Alzheimer's Res. Ther. 11, 1–8.
Mendonça, M.D., Alves, L., Bugalho, P., 2016. From subjective cognitive complaints to dementia: who is at risk?: a systematic review. Am. J. Alzheimer's Dis. Other Dementias 31, 105–114.
Mitchell, A.J., Beaumont, H., Ferguson, D., Yadegarfar, M., Stubbs, B., 2014. Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: meta-analysis. Acta Psychiatr. Scand. 130, 439–451.
Mitchell, A.J., 2008. Is it time to separate subjective cognitive complaints from the diagnosis of mild cognitive impairment? Age Ageing 37, 497–499.
Molinuevo, J.L., Rabin, L.A., Amariglio, R., Buckley, R., Dubois, B., Ellis, K.A., Ewers, M., Hampel, H., Klöppel, S., Rami, L., 2017. Implementation of subjective cognitive decline criteria in research studies. Alzheimer's Dementia 13, 296–311.
Mosconi, L., De Santi, S., Brys, M., Tsui, W.H., Pirraglia, E., Glodzik-Sobanska, L., Rich, K.E., Switalski, R., Mehta, P.D., Pratico, D., 2008. Hypometabolism and altered cerebrospinal fluid markers in normal apolipoprotein E E4 carriers with subjective memory complaints. Biol. Psychiatr. 63, 609–618.
Reid, L.M., MacLullich, A.M., 2006. Subjective memory complaints and cognitive impairment in older people. Dement. Geriatr. Cognit. Disord. 22, 471–485.
Schweizer, S., Kievit, R.A., Emery, T., Henson, R.N., 2018. Symptoms of depression in a large healthy population cohort are related to subjective memory complaints and memory performance in negative contexts. Psychol. Med. 48, 104–114.
Serra-Blasco, M., Torres, I.J., Vicent-Gil, M., Goldberg, X., Navarra-Ventura, G., Aguilar, E., Via, E., Portella, M.J., Figuereo, I., Palao, D., 2019. Discrepancy between objective and subjective cognition in major depressive disorder. Eur. Neuropsychopharmacol 29, 46–56.
Striepens, N., Scheef, L., Wind, A., Popp, J., Spottke, A., Cooper-Mahkorn, D., Suliman, H., Wagner, M., Schild, H.H., Jessen, F., 2010. Volume loss of the medial temporal lobe structures in subjective memory impairment. Dement. Geriatr. Cognit. Disord. 29, 75–81.
Üstün, T.B., Chatterji, S., Mechbal, A., Murray, C.J., WHS Collaborating Groups, 2003. The world health surveys [chapter 58]. In: Murray, C., Evans, D.B. (Eds.), Health Systems Performance Assessment: Debates, Methods and Empiricism. World Health Organization, Geneva, Switzerland, pp. 115–126.
Van Norden, A., Fick, W.F., De Laat, K.F., Van Uden, I., Van Oudheusden, L., Tendolkar, I., Zwiers, M.P., De Leeuw, F.E., 2008. Subjective cognitive failures and hippocampal volume in elderly with white matter lesions. Neurology 71, 1152–1159.
Walker, K.A., Gottesman, R.F., Wu, A., Knopman, D.S., Gross, A.L., Mosley, T.H., Selvin, E., Windham, B.G., 2019. Systemic inflammation during midlife and cognitive change over 20 years: the ARIC Study. Neurology 92, e1256–e1267.
Wong, K.O., Hunter Rowe, B., Douwes, J., Senthilselvan, A., 2013. Asthma and wheezing are associated with depression and anxiety in adults: an analysis from 54 countries. Pulmonary medicine 2013.
World Health Organization, 2021. Dementia, p. 2020.
World Health Organization, 1993. The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research. World Health Organization.