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REVIEW ARTICLE

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Depression and excess mortality in the elderly living in low- and middle-income countries: Systematic review and meta-analysis

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Objective: To investigate the association between depression and mortality in the elderly living in low- and middle-income countries.

Methods: A systematic review and meta-analysis was performed. We searched in five electronic databases for observational studies investigating the association between mortality and depression. Two reviewers worked independently to select articles, extract data, and assess study quality.

Results: A total of 10 studies including 13 828 participants (2402 depressed and 11 426 nondepressed) from six countries (Brazil, four articles; China, two articles; Botswana, India, South Africa, and South Korea, one article) were included. The overall unadjusted relative risk (RR) of mortality in depressed relative to nondepressed participants was 1.62 (95% CI, 1.39-1.88; $P < 0.001$), with high heterogeneity ($I^2 = 66\%$; 95% CI, 33-83; $P < 0.005$). After adjustment for publication bias, the overall RR decreased to 1.60 (95% CI, 1.37-1.86; $P < 0.001$). No significant differences were observed between subgroups except those defined by study quality. The high-quality studies had a pooled RR of 1.48 (95% CI, 1.32-1.67; $P < 0.001$), while the low-quality studies resulted had a pooled RR of 1.82 (95% CI, 1.25-2.65; $P < 0.005$).

Conclusions: Depression is associated with excess mortality in the elderly living in low- and middle-income countries. In addition, this excess mortality does not differ substantially from that found in high-income countries. This suggests environmental factors occurring in low- and middle-income countries might not have a direct association with the excess mortality in the depressed elderly.

KEYWORDS

depression, low- and middle-income countries, mortality

1 | INTRODUCTION

There is growing evidence that depression reduces survival in the elderly.[1,2] Recent meta-analyses estimated a relative risk (RR) of 1.59 (95% CI, 1.47-1.71)[3] for the association between depression and mortality for community dwelling elderly. The mechanisms by which depressive symptoms are associated with mortality may involve behavioral factors, exacerbation of comorbidities, and biological mechanisms related to aging.[4] For example, unhealthy behaviors in depressed people, such as smoking, sedentary lifestyle, and alcohol consumption, and poor adherence to treatments can contribute to unfavorable cardiovascular events.[5] In addition, the worse survival associated with depression may be related to psychophysiological mechanisms that include dysregulation of the hypothalamic–pituitary–adrenal axis, impaired immune function, and circadian variation in cortisol and melatonin.[6,7] It is also known that depression

is associated with poverty, low-educational status, and social exclusion.[8-10] In turn, social inequity directly affects health outcomes and decreases life expectancy.[11,12]

Currently, most of the available research on the association between depression and mortality among the elderly comes from high-income countries (HIC),[3,13] where demographic changes and population aging have occurred along the 20th century. Low- and middle-income countries (LMIC) are now experiencing a much faster demographic transition compared with HIC.[14,15] This accelerated population aging has changed the pattern of morbimortality towards a predominance of noncommunicable diseases (NCDs), including multiple consequences mainly related to depression, with increased economic burden, labor-health and social problems.[16,17] Mental health problems, among other NCDs, are often overlooked in public health policies in LMIC, and planning and current resources are not designed accordingly.[18-20]

Elderly populations in LMIC live in much more adverse social conditions, with difficulties with housing, food, and other needs.[15] They also have much more limited access to health care, including adequate treatment for chronic conditions, such as diabetes, cardiovascular diseases, and mental health problems, including depression.[18,21] Therefore, it is possible that the association between depression and mortality among the elderly living in LMIC can be even stronger than that estimated for HIC. Indeed, in a Chinese sample of community dwelling elderly people (rural and urban area), an RR of 2.07 (95% CI, 1.49-2.89) was found for the association between depression and mortality.[22]

Given the scarcity of data about the association between depression and excess mortality in the elderly in LMIC and the potential relevance of estimates adequate for LMIC, we conducted a systematic review and meta-analysis specifically aimed at estimating the association between mortality and depression in elderly populations living in LMIC.

Key points

- Depression is a common mental disorder in the elderly.
- Low- and middle-income countries had a rapid growth aging in their population, and it has been accompanied by an increase in diseases related to aging.
- Mortality is associated with depression in high-income countries. The reasons why depression leads to increased mortality are not well defined.
- The association between mortality and depression in low- and middle-income countries does not differ substantially from those found in systematic reviews with articles primarily from high-income countries.

2 | METHOD

We report this article following statement of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA).[23] Detailed protocol of this systematic review is found in Supporting Information Appendix 1.

2.1 | Search strategy and selection of studies

Search was conducted on June 30, 2017, in the following databases: Pubmed, Embase, Web of Science, Lilacs, and PsycInfo. Four groups of key descriptors were combined using Boolean operators "OR" and "AND" as follows: ("mortality" AND "depression" AND "Longitudinal studies" AND "low- and middle-income countries"). We combined terms indicating mortality (survival and death), depression (mood disorder, depressive, and depression), longitudinal studies (prospective, follow-up, and longitudinal), and LMIC (low income, developing countries, name of the countries, and among others). Detailed strategy of search strategy is in Supporting Information Appendix 2. On topic systematic reviews (Supporting Information Appendix 3) found by the search were analyzed, and their references were scanned for eligible articles.

Inclusion criteria for the articles were presenting results of longitudinal population-based studies (community dwelling, noninstitutionalized, and nationally representative samples); having been conducted in LMIC (according to the classification of the World Bank for at least one third of the series between 1987 and 2016)[24]; enrollment of population aged above 60 years; assessment of depression at baseline with a standardized tool or diagnostic interview by the research team; assessment of mortality during follow-up with death records or follow-up visits; publication in peer-reviewed journals; and English, Spanish, or Portuguese language.

Exclusion criteria for the articles were nonpopulation-based longitudinal studies (institutionalized and disease specific samples), absence of data to calculate mortality rates in the depressed and nondepressed; self-report of depression without the use of a standardized tool; identification by the use of antidepressants; any participants aged below 18 years or no participants aged above 60 years; no described separate data from those above 60 years; and intervention studies, letters, editorials, opinion articles, and conference abstracts.

Titles and abstracts were screened for inclusion, full text was assessed for eligibility, and two reviewers (DJB and LFF) extracted data independently. Disagreements were resolved by consensus and, when necessary, a third reviewer (SAS) was consulted.

2.2 | Data extraction and quality evaluation of articles

Data were extracted into a standard table with double entry that allowed the observation of errors between the extraction of data from the two reviewers and subsequent checking in the original articles. The following data were extracted: authors, names, year of publication, country, study population, age group, instrument used for diagnosis of depression, number of participants, prevalence of depression, follow-up time, deaths among the depressed, deaths among the nondepressed, effect measure, and adjustment variables.

Study quality was assessed by the completeness of the 22 items included in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[25] The STROBE evaluates

information that should be present in scientific articles of observational studies. The check list evaluates title and abstract (item 1), introduction (items 2 and 3), method (items 4-12), results (items 13-17), discussion (items 18-21), and source of funding (item 22). Check list items information is in the Supporting Information Appendix 4. A score was awarded for each assessed item (if the item did not apply to the article, it did not score). The score for each item could be from 0 to 1, where 0 = does not comply with the item in any way; 1 = complies with the item in full; and 0-1 = partially fulfills for each present item. Two reviewers (DJB and LFF) performed the assessment independently, and the final score was the average of their scores.

2.3 | Statistical analysis

Although the studies used a variety of measures of effect (hazard ratio, RR, odds ratio), for the present statistical analysis of the data, we used the RR as the measure of effect. We calculated the unadjusted RR for all articles. All analyses were conducted with only unadjusted RR. For the overall and subgroup analysis, we used a random effects model to estimate the pooled effect estimate and its 95% confidence interval. Random effects model is the appropriate analysis to account for heterogeneity between studies.[26]

In order to assess heterogeneity, we calculated the I^2 statistic with its 95% confidence interval.[27] An I^2 close to 0% indicates no heterogeneity between studies, close to 25% indicates low heterogeneity, close to 50% indicates moderate heterogeneity, and close to 75% indicates high heterogeneity.[27] To test whether heterogeneity is significant, we calculated the Q statistic. We analyzed subgroup analyses to identify heterogeneity between studies according to the following subgroups: country where studies were carried out, type of mortality data, follow-up period, depression prevalence, study quality assessment, and by adjusted covariables used.

To investigate publication bias, we used the funnel plot and the Duval & Tweedie's trim-and-fill procedure.[28] We used Egger's test to evaluate significance of the funnel plot.[29]

For statistical analysis, we used the Stata 13.0 software.[30] We used de metan, heterogi, metabias, and metatrim commands in Stata to perform the meta-analysis.

3 | RESULTS

3.1 | Identification and selection of articles

A total of 4517 abstracts were examined (3417 after duplicate abstracts were removed). We selected 58 articles for assessment of eligibility, which identified nine articles for inclusion in the meta-analysis (reasons for exclusion in Figure 1). One eligible article was identified among the references of other systematic reviews, resulting in a total of 10 articles included in the meta-analysis.

3.2 | Characteristics of articles

Among the 10 articles included, a total of 13 828 participants were followed, of whom 2402 (17.34%) presented depression at baseline as defined by the article, and 11 426 (82.66%) were nondepressed (Table 1).

The studies were conducted in the following LMIC: Brazil (four articles), China (two articles), Botswana (one article), India (one article), South Africa (one article), and South Korea (one article). There was great variability among the samples characteristic; in the selected studies, we had samples ranging from high-socioeconomic level population (one article) to low-socioeconomic level population (three articles). One study was a national representative sample while the other studies were a mix of local samples (city, district, or rural/urban samples). The follow-up period showed a high variability, ranging from 0.7 to 15 years. In four articles, information on vital status was acquired just from linkage with governmental information systems (local/national death index or security's database), in the other six articles was acquired with follow-up visits or with both visits and local/national systems (Table 1).

There was a great variability of instruments used to assess depression with GMS (two articles) and GDS-15 (two articles) being the most frequently used. There was also a great variability in the prevalence of depression, ranging between 4.3% and 38.5% (Table 1).

The STROBE-based quality scores ranged from 12.30 to 21.60, ie, from 58.57% to 98.18% of the maximum score of 22 points (Table 2). The least fulfilled items were potential sources of bias, decision on the sample size, and descriptive data. Ben-Arie et al, 1990[38] had a particularly low score; it had been published as a brief report in 1990, thus, prior to the standardization period of instrument for scientific writing.

3.3 | Meta-analysis

The unadjusted RR for the association of depression and mortality in the elderly in LMIC ranged among individual studies from 0.34 to

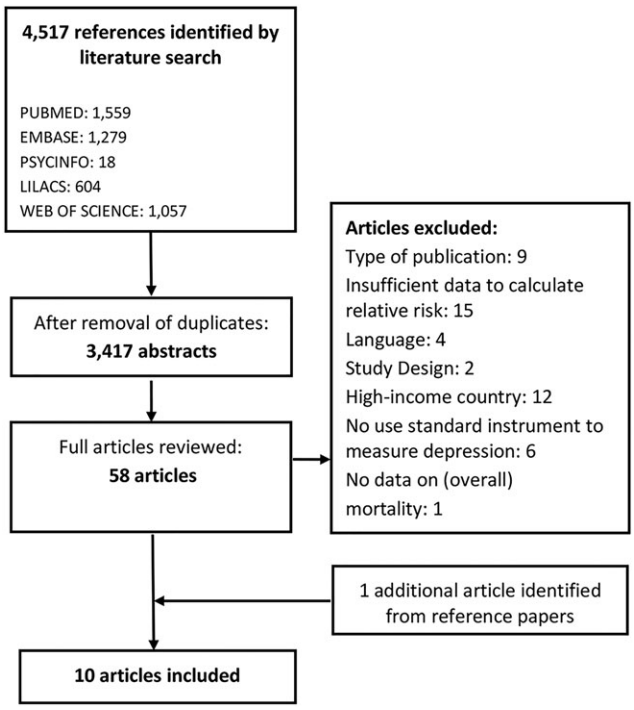

FIGURE 1 Flowchart of selection of studies

TABLE 1 Summarized articles included in this systematic review

Author and year	Country	Study population and sample characteristics	Mean age	Diagnosis of depression†	Follow-up	Sample (follow-up)	Death information	Depression (%)	Effect measure	Crude measure (IC 95%)	Adjustment variables
Maciel et al, 2008[31]	Brazil	>60 years low-socioeconomic level population	73.7 years	GDS-15	4.4 years	310 (279)	Follow-up visit and local registry	27.24%	Hazard ratio	No data	No data
Chen et al, 2014[22]	China	>60 years rural area population >65 urban area population	71.8 years	GMS	5.6 years	3336 (2978)	Follow-up visit local mortality system was consulted	4.30%	Hazard ratio	2.07 (1.49-2.89)	Age, sex, urban/rural area, educational level, occupation, family income, BMI, smoking, drinking, marital status, social network, hypertension, diabetes, heart disease, and cerebrovascular accident
Clausen et al, 2007[32]	Botswana	>60 years Country's population sample	73.5 years	MADRS	0.7 year	372 (265)	Follow-up visit.	6.79%	OR	3.6 (0.9-14.0)	Age
Diniz et al, 2014[33]	Brazil	>60 years low socioeconomic level population	69.6 years in depressed 68.6 years in non depressed	GHQ-12	10 years	1606 (1508)	Follow-up visit and National mortality system	38.53%	Hazard ratio	1.56 (1.3–1.88)	Sex, age, income, marital status, psychotropic drugs use, retirement, schooling, daily life activities, minimental, use of alcohol and tobacco, hypertension, diabetes, myocardial infarction, chagas' disease, physical activity, and BMI
Ferreira et al, 2015[34]	Brazil	>60 years Amparo/SP city's populational sample	75.2 years	GDS-15	7 years	2209 (2174)	National mortality system	34.18%	OR	2.39 (1.912-3.000)	No data
Jotheeswaran et al, 2010[35]	India	>65 years urban área population	71.4 years	GMS	4 years	1005 (748)	Follow-up visit	3.84%	Hazard ratio	2.2 (1.1–4.5)	Age and sex
Lima et al, 2009[36]	Brazil	>65 years High-socioeconomic level population	82.76 years in depressed 81.25 years in nondepressed	SPES	15 years	1667 (1639)	State's mortality system	21.10%	OR	1.41 (1.09-1.81)	No data

(Continues)

TABLE 1 (Continued)

Author and year	Country	Study population and sample characteristics	Mean age	Diagnosis of depression[†]	Follow-up	Sample (follow-up)	Death information	Depression (%)	Effect measure	Crude measure (IC 95%)	Adjustment variables
Yu et al, 1998[37]	China	>65 years Jing-Na District's population in Shanghai	No data	CES-D	5.4 years	3149 (3094)	Local mortality system	11.63%	RR	65–74 years 1.71 (1.25–2.34) >75 years 1.82 (1.37–2.41)	Level of education, social network, good health practices, smoking, drinking, hearing impairment, visual acuity, visits to the doctor, asthma, heart diseases, diabetes, kidney diseases, cancer, cerebrovascular accident, tuberculosis, hypertension, arterial and venous insufficiency, ulcers, B hepatites, liver diseases, anemia, and Parkinson's disease
Ben-Arie et al, 1990[38]	South Africa	>65 years Low socioeconomic level population	No data	CATEGO	3.5 years	150 (143)	Follow-up visit	15.33%	No data	No data	No data
Jeong et al, 2013[39]	South Korea	>65 years Seongnam City	76.34 years	Clinical interview DSM-IV	4.6 years	1000 (1000)	Ministry of Public Administration and Security's national database	10.3%	Hazard ratio	Minor depression 2.64 (1.61–4.32) Major depression 1.68 (0.95–2.98)	Age, education level, cognitive function, alcohol use, and smoking

[†]Abbreviations: CES-D, Center for Epidemiological Scale-Depression; CATEGO, Present State Examination—Catego System; GDS-15, Geriatric Depression Scale; GHQ-12, General Health Questionnaire-12; GMS, Geriatric Mental State; MADRS, Montgomery and Aasberg Depression Rating Scale SPES, Short Psychiatric Evaluation Schedule.

TABLE 2 Quality assessment of studies using the strength of reporting of observational studies in epidemiology checklist

Author and year	Strobe guide items†																					
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	TOTAL	%‡
Maciel et al, 2008[31]	0.75	1.00	1.00	1.00	1.00	1.00	0.75	1.00	0.75	1.00	1.00	0.70	0.90	0.75	1.00	0.65	NA	1.00	1.00	1.00	1.00	1.00	19.25	91.67
Chen et al, 2014[22]	0.75	1.00	1.00	1.00	1.00	1.00	0.80	0.90	0.85	0.00	1.00	0.80	1.00	0.75	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	19.85	90.23
Clausen et al, 2007[32]	0.75	1.00	1.00	1.00	1.00	1.00	0.75	1.00	0.85	0.30	1.00	0.60	1.00	0.70	1.00	0.83	NA	1.00	1.00	1.00	1.00	1.00	18.78	89.44
Diniz et al, 2014[33]	0.90	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.90	1.00	1.00	0.90	1.00	0.90	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	21.60	98.18
Ferreira et al, 2015[34]	0.75	1.00	1.00	1.00	0.75	1.00	0.60	0.60	0.00	0.75	1.00	0.80	0.42	0.50	1.00	0.90	NA	1.00	0.75	0.75	0.75	1.00	16.32	77.70
Jotheeswaran et al. 2010[35]	1.00	1.00	1.00	1.00	0.80	1.00	0.75	1.00	0.75	1.00	1.00	1.00	1.00	0.75	1.00	1.00	NA	1.00	1.00	1.00	0.50	1.00	19.55	93.10
Lima et al, 2009[36]	0.75	1.00	1.00	1.00	0.90	1.00	0.90	0.75	0.75	0.50	1.00	1.00	1.00	1.00	1.00	1.00	NA	1.00	1.00	1.00	1.00	1.00	19.55	93.10
Yu et al, 1998[37]	0.90	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.50	1.00	21.40	97.27
Ben-Arie et al, 1990[38]	1.00	0.50	0.75	1.00	1.00	0.75	0.75	0.60	0.00	0.50	0.60	0.00	0.58	0.10	1.00	0.17	NA	1.00	0.50	1.00	0.50	0.00	12.30	58.57
Jeong et al, 2013[39]	0.75	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.5	0.5	1.00	0.75	1.00	1.00	1.00	1.00	0.75	1.00	1.00	1.00	0	0.75	19.00	86.36

†0 = Does not comply with the item in any way; 1 = complies with the item in full; 0 to 1 = partially fulfills for each present item; NA = Does not apply. ‡Percentage of compliance of all of the total items excluding the ones does not apply (NA).

3.17, with a pooled estimate of 1.62 (95% CI, 1.39-1.88; *P*< 0.001) (Table 3; Figure 2). There was high heterogeneity among the studies with I^2 = 66% (95% CI, 33-83; *P* = 0.002). Ben-Arie et al, 1990[38] was an outlier not only in study quality but also in the estimated effect (RR = 0.34, 95% CI, 0.09-1.33). Excluding Ben-Arie et al, 1990[38] from the analysis had limited influence on the estimated effect (RR = 1.64, 1.42–1.89, 95% CI) or heterogeneity (I = 63%, 95% CI 24–82; p < 0.01)

After adjusting for publication bias by the Duvall and Tweedie's trim-and-fill procedure, the unadjusted RR was 1.60 (95% CI, 1.37-1.86; *P* < 0.001). Inspection of the funnel plot (Supporting Information Appendix 5) suggests an asymmetric distribution of the studies, but the Egger's test (*P* = 0.691) did not show significant evidence of publication bias.

Several subgroup analysis were performed among them by study quality. Studies complying with more than 90% of the STROBE items had a pooled RR of 1.48 (95% CI, 1.32-1.67; *P* < 0.001), while those complying less had a pooled RR of 1.82 (95% CI, 1.25-2.65; *P* = 0.002) (Table 3).

4 | DISCUSSION

To the best of our knowledge, this is the first systematic review focusing on the association between depression and mortality among elderly populations living in LMIC. We hypothesized that the estimate for such association might be larger than that found in recent meta-analyses with studies from HIC, mainly because elderly from LMIC live under very unfavorable socioeconomic adversities and have very limited access to care for their chronic conditions. We found 10 articles on the association between depression and mortality in LMIC; of these nine had not been included in previous published systematic reviews. Our pooled estimate was RR = 1.62 (95% CI, 1.39-1.88), similar to those found in previous meta-analysis with articles primarily from community dwelling in HIC, RR = 1.81 (95% CI, 1.58-2.07)[40] and RR = 1.59 (95% CI, 1.47-1.71).[3]

Our findings suggest that, in elderly populations living in LMIC, depression probably increases the risk of death in a magnitude similar to that observed in HIC. This may mean that the mechanisms behind the association between depressive symptoms and higher mortality in LMIC are probably similar to those involved in the association observed in studies from HIC. Nevertheless, to understand the association between depression and mortality, it is important to control for confounding factors related to increased general mortality in elderly populations, such as age, sex, social inequality, unhealthy behaviors, access to health services, social network, and disability.[4,41] Many of these confounding factors of general mortality differ substantially between LMIC and HIC.[42,43] Unfortunately, it was not possible to account for this confounding factors in this meta-analysis because of lack of individual participant data and because most of the included studies did not adjust their analyses by these variables.

Although the articles examined have been carried out in LMIC, which would allow to infer similarities between the surveys, there were great differences among them regarding sample size, research scenario, cohort design, follow-up period, and instrument for definition of depression diagnosis. It was observed a high heterogeneity

TABLE 3 Meta-analysis of unadjusted relative risk for mortality among depressed and nondepressed

				Heterogeneity		
	N	RR	IC 95%	I^2(%)	IC 95%	*p**
Unadjusted analysis						
All studies	10	1.62	1.39-1.88	66	33-83	0.002
Studies excluding outlier†	9	1.64	1.42-1.89	63	24-82	0.006
Subgroup analysis						
Country of study						
Brazil	4	1.60	1.25-2.06	84	56-94	<0.001
Other countries	6	1.65	1.37-2.00	31	0-72	0.205
Death data						
Follow up visits	6	1.58	1.26-1.99	41	0-77	0.134
Information systems	4	1.65	1.29-2.09	83	58-93	<0.001
Follow up						
Less than 5 years	4	1.57	0.83-2.98	61	0-87	0.054
Over 5 years	6	1.60	1.37-1.87	74	40-88	0.002
Depression prevalence						
Under 20%	6	1.65	1.37-2.00	31	0-72	0.205
Over 20%	4	1.60	1.25-2.06	84	59-94	<0.001
Study quality‡						
Under 90%	4	1.82	1.25-2.65	59	0-86	0.063
Over 90%	6	1.48	1.32-1.67	38	0-75	0.152
Adjusted variables						
Yes	4	1.58	1.42-1.76	0	0-75	0.437
No	6	1.47	1.04-2.09	86	66-94	<0.001

†Ben-Arie et al, 1990 ‡Compliance to STROBE *P value for the Q statistic.

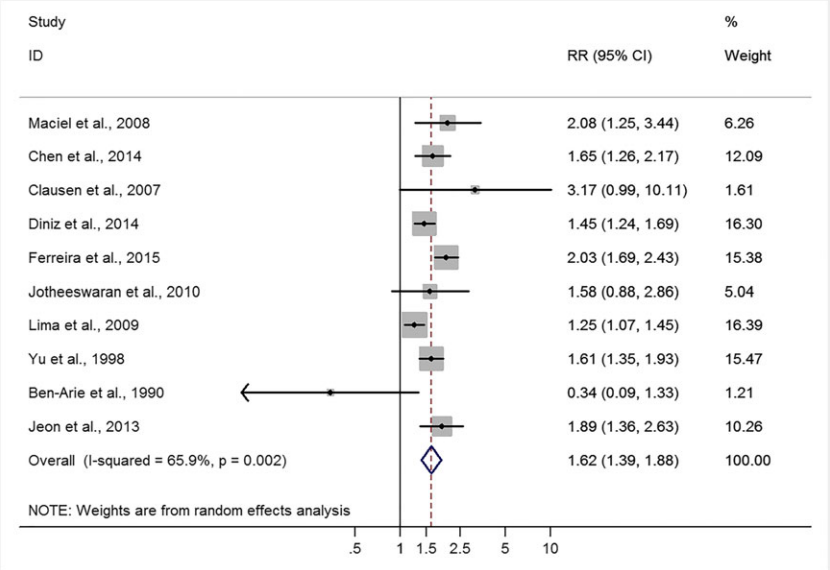

FIGURE 2 Forest plot of unadjusted relative risk of the included studies [Colour figure can be viewed at wileyonlinelibrary.com]

(I^2 = 66%) between studies. We found an important variability in the sample and research scenario, including populations with high-socioeconomic level. Lima et al, 2009,[36] high-economic sample, represented a weight of 16.39% in the meta-analysis. Excluding this study, the estimated effect was RR = 1.70 (95% CI, 1.47-1.96; *P* < 0.001). In addition, nine of the 10 articles that met the inclusion criteria for LMIC are currently considered as an upper-middle-income countries (Brazil, Botswana, China, and South Africa) or HIC (South Korea). Only one study was conducted in a country that maintains lower-middle-income country (India).[24] These facts might have contributed to a scenario with social determinants of health more similar to those of HIC.[44]

The results in the different subgroups did not differ substantially from the RR of the pooled sample, except for study quality, with the studies with better quality having a lower RR (1.48) than those with poorer quality (1.82). This suggests that studies of poorer quality may overestimate the association of depression and mortality. However, because of the small number of studies (n = 10) and the great overall heterogeneity (I^2 = 66%), these results should be interpreted with caution.

The identification of more articles from LMIC than in previous systematic reviews was probably due to the inclusion of the Lilacs regional database and the eligible languages (English, Portuguese, and Spanish). It is clear that to obtain systematic reviews aimed at incorporating studies carried out in LMIC, it is imperative to search into regional databases and languages other than English. In a publication that sought to identify methods for conducting systematic reviews in LMIC, 15% of the eligible articles were in Chinese, Spanish, French, Portuguese, and Russian.[45]

This systematic review highlights the need to carry out original research about depression and mortality in LMIC elderly population. Moreover, high-quality studies with regional or country representative population-based samples, using validated depression diagnostic instruments or clinical diagnoses including the assessment of the persistence or not over time of the depression diagnosis are needed. Another very relevant point in LIMC context is to understand how social determinants of health influence in the incidence of mental health problems in vulnerable elderly population and, therefore, can impact in outcomes such as premature mortality.

This study has strengths and limitations. The primary strength of this study was its focus on LMIC. Nevertheless, we identified at least five limitations in this study. First, we searched only one regional database (Lilacs) and restricted our search to three languages, thus, possibly missing relevant articles indexed in other national or regional databases and in other languages such as Chinese. Second, we identified only 10 studies, therefore, limiting the statistical power and, thus, the interpretation of the meta-analysis results. Third, we were only able to examine the RRs of mortality in depressed individuals without adjustment for variables such as comorbidities, lifestyle, gender, and age, which might explain the association between depressions with mortality as we have shown above. Fourth, although the articles examined have been carried out in LMIC, we found an important socioeconomic heterogeneity, including populations with high-socioeconomic level; this fact might have contributed to the results found in our study, which do not differ from those found in HIC. Fifth, there is always the possibility of publication bias; the pooled RR was essentially the same after the Duvall and Tweedie's trim-and-fill procedure, and Egger's test was not significant, suggesting the meta-analysis was not significantly affected by publication bias.

5 | CONCLUSION

Despite the limitations, this meta-analysis found an evident excess mortality in the depressed elderly living in LMIC. In addition, this excess mortality does not differ substantially from that found in systematic reviews with articles primarily from HIC. This suggests environmental factors occurring in LMIC might not have a direct association with the excess mortality in the depressed elderly. Furthermore, studies should be conducted in LMIC to identify factors involved in this association that may differ from HIC.

CONFLICTS OF INTEREST

None declared.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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