Vascular Health and Risk Management

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ORIGINAL RESEARCH

Comparing the Association Between Depressive Symptoms and Cardiovascular Disease Among the Middle-Aged and Elderly Population: A National Survey of 9,049 Subjects Based on the Indonesian Family Life Survey-5

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Introduction: The association between depressive symptoms and cardiovascular disease (CVD) is widely acknowledged. However, there is a lack of relevant evidence among the middle-aged population in developing countries where depressive symptoms often go undetected and untreated. The objectives of this study were to assess the association between depressive symptoms and CVD in Indonesia and to compare the association between the middle-aged and elderly population.

Methods: This national cross-sectional population-based survey used secondary data from the publicly available Indonesian Family Life Survey (IFLS-5). Depressive symptoms were assessed using a modified Center for Epidemiologic Studies Depression (CESD-R-10) scale, and data on CVD and sociodemographic variables were self-reported. Binary logistic regression was performed to determine the association between depressive symptom and self-reported CVD after adjusting for confounding factors, with an adjusted odds ratio (AOR) and 95% confidence interval (CI) reported. Subgroup analysis was performed based on the age group.

Results: The study included 9049 respondents, predominantly the middle-aged (71.1%), female (52.6%), elementary school graduates (50.7%), non-smokers (59.0%), non-obese (77.3%), without depressive symptoms (82.2%), and without self-reported CVD (96.7%). Respondents with depressive symptoms were more likely to experience self-reported CVD (AOR = 1.56; 95% CI = 1.18–2.05; p-value = 0.002), after adjusting for potential confounders. A significant association was observed between depressive symptoms and self-reported CVD in elderly respondents (AOR = 1.89; 95% CI = 1.22–2.94; p-value = 0.005), whereas no significant association was observed in the middle-aged group (AOR = 1.39; 95% CI = 0.98–1.98; p-value = 0.063) after adjusting for confounders.

Conclusion: Respondents with depressive symptoms were associated with an increased risk of self-reported CVD, highlighting the urgent need for targeted prevention strategies, especially for those struggling with depressive symptoms.

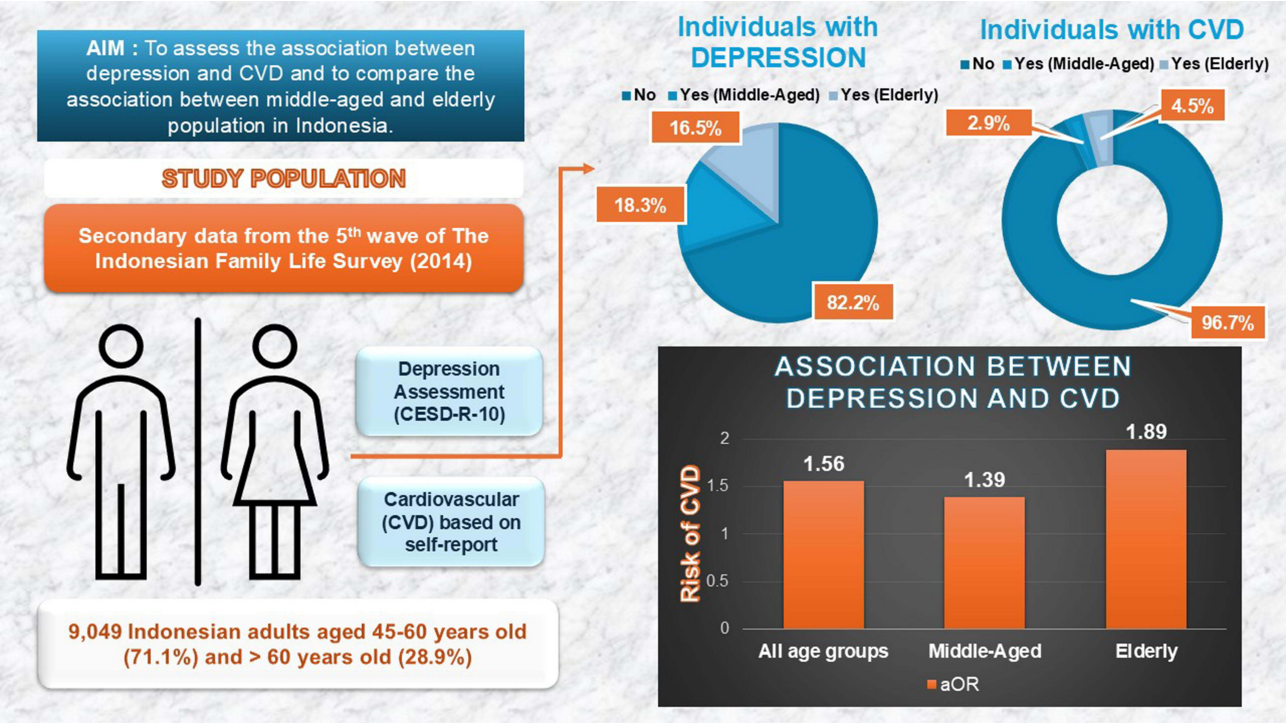
Keywords: depression, cardiovascular disease, middle-age, elderly, IFLS-5

Introduction

Depression is widely recognized as an invisible disease because many individuals may not recognize its symptoms until diagnosis.[1] Globally, approximately, 280 million individuals experience such mental health condition,[1] with 5% of cases occurring among the middle-aged population and 6% among the elderly.[2] In Indonesia, a high prevalence of depressive symptoms has been reported,[3] with the prevalence rates increasing with age.[4] However, despite documented increases, only 9% of affected individuals receive treatment.[5] This mental health condition has been associated with increased all-

Received: 17 August 2024
Accepted: 24 January 2025
Published: 25 February 2025

Graphical Abstract



cause mortality, the risk of multimorbidity,[6] the development of cardiovascular disease (CVD), and poorer outcomes in those with existing CVD.[1]

A recent meta-analysis of 26 studies comprising 1,957,621 individuals showed a significant impact of depression and depressive symptoms on the development of CVD.[7] This association may be bidirectional, as depressive symptoms consistently affect CVD, while CVD affects depressive symptoms in the short term.[8] A study reported that chronic depression lasting more than two years is significantly associated with an increased incidence of CVD compared to those without depression.[9] Depression is frequently linked to unhealthy lifestyles and poor treatment adherence, which can adversely affect CVD prognosis.[10] Continuous psychosocial stress experienced by depressive patients can lead to chronic inflammation in the body, promoting vascular injury and disrupting the hypothalamic–pituitary–adrenal (HPA) axis.[11] Prolonged inflammation and HPA axis activation can severely damage the cardiovascular system,[12,13] resulting in a higher risk of atherosclerosis and CVD events.[10] Therefore, the enhancement of understanding and awareness of psychological health risks is essential as part of a comprehensive strategy to alleviate the burden of CVD,[14] particularly in resource-poor settings where mental health remains neglected.

Several investigations on the association between depression and CVD have primarily focused on high-income countries,[7,15] leaving limited evidence available from low- and middle-income countries (LMICs), particularly Indonesia, where depression often goes undetected and untreated. This situation may present future challenges due to the high burden of late-life depression.[16] The association between depressive symptoms and CVD may also vary among age groups, with mood disease commonly arising during the middle-aged stage,[17] making them an understudied population in such a context. Furthermore, a higher frequency of depressive symptoms at baseline has been associated with an increased risk of CVD in the middle-aged population.[9,18] Since depression is considered a modifiable risk factor for CVD,[19–21] further investigations are necessary to ascertain its extent of contribution to the onset of disease. Limited reviews in LMICs have examined such association, often using smaller sample sizes,[22,23] and whether it differs across age groups remains unclear. Therefore, the primary objective of this study was to assess the association between

depressive symptoms and CVD in Indonesia. The secondary objective was to compare this association between the middle-aged and elderly population.

Materials and Methods

The study was conducted following the guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for cross-sectional analysis[24] (Table S1: STROBE Statement, Supplementary data).

Study Design and Data Source

This observational cross-sectional study used secondary data from the fifth wave of the Indonesian Family Life Survey (IFLS-5), a national longitudinal dataset. Data were collected from 2014 to 2015 and were publicly available on the RAND Corporation website after registration (https://www.rand.org/well-being/social-and-behavioral-policy/data/FLS/IFLS/access.html). IFLS was an ongoing health and socioeconomic survey conducted by the RAND Corporation since 1993, including over 30,000 individuals from 13 out of 33 provinces in Indonesia.[25] IFLS-5 adopted a multistage stratified sampling design representing 83% of the country's population across 13 provinces, comprising North Sumatra, West Sumatra, South Sumatra, Lampung, DKI Jakarta, West Java, Central Java, DI Yogyakarta, East Java, Bali, West Nusa Tenggara, South Kalimantan, and South Sulawesi.[25] The study was approved by the Health Research Ethics Committee of Universitas Padjadjaran, Indonesia on November 22, 2024 (No: 1205/UN6.KEP/EC/2024).

Study Population

The IFLS sampling scheme was stratified by province and urban/rural location, with random sampling conducted within these strata.[25] The selection of 13 provinces was aimed at maximizing population representation and capturing the cultural and socioeconomic diversity of Indonesia. Within each of the 13 provinces, 321 enumeration areas (EAs) were randomly selected from a nationally representative sampling frame used during the 1993 SUSENAS, a socioeconomic survey in Indonesia. In each selected EA, households were randomly chosen based on the 1993 SUSENAS listings obtained from the regional Badan Pusat Statistik (BPS) office. Finally, 20 households were selected from each urban EA, and 30 households were chosen from each rural EA.[25] In this study, data were obtained from respondents aged 45 years and above at the time of survey completion. Meanwhile, respondents lacking data on both depressive symptoms and CVD were excluded.

Depressive Symptoms Assessment

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale Revised (CESD-R-10), comprising 10 items describing the experiences related to depressive symptoms in the past week. The items included feeling bothered by little things, having trouble concentrating, feeling depressed, experiencing everything as an effort, feeling hopeful, feeling fearful, experiencing restless sleep, feeling happy, feeling lonely, and having difficulty getting going (Table S2: Depressive symptoms assessment questionnaire, Supplementary file). Respondents rated their feelings on a scale ranging from rarely or never (≤1 day, scored 1 point), some days (1–2 days, scored 2 points), occasionally (3–4 days, scored 3 points), to most often (5–7 days, scored 4 points). A total score of ≥10 showed the presence of depressive symptoms,[26,27] and the CESD-R-10 questionnaire was translated into Indonesian and re-translated into English by two professional translators. The validity and reliability of the CESD-R-10 have been established in previous studies involving the Indonesian population.[28–30]

CVD Assessment

CVD was assessed using a self-report questionnaire with the question, "Has a doctor/paramedic/nurse/midwife ever informed you that you had a CVD (heart attack/coronary heart disease/angina or other heart diseases)?" with response options included yes or no.[25]

Potential Confounders

Socio-demographic factors identified in previous studies as having significant effects on CVD[31–33] are considered to be potential confounders. These factors were assessed through a self-reported questionnaire, which gathered information on age (middle-aged or aged 45–59 years old/elderly or aged 60 years old or above),[8,34] gender (male/female), household location (urban/rural), level of education (no formal education, elementary school, middle school, high school, university, or higher institution), smoking habit (non-smoker, smoker), and obesity (non-obese/obese). Smoking habits were assessed using a question: "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars?" with response options of "Yes" or "No". Obesity data were obtained by calculating the Body Mass Index (BMI) based on self-reported weight and height.

Statistical Analysis

A descriptive method was used to analyze the characteristics of the respondents, and a chi-square test was performed to assess the bivariate association between depressive symptoms and self-reported CVD. The factors associated with the outcome at a significance level of $p < 0.25$ were included in the initial multivariate analysis,[32,35] which was subsequently adjusted for potential confounders. Subgroup analysis by age groups was conducted, and multivariate binary logistic regression was performed to determine the crude odds ratio (COR), adjusted odds ratio (AOR), and 95% confidence interval (95% CI). The significance level was set at $p < 0.05$, and all statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 27.0.

Results

Characteristics of Respondents

Among the surveyed 31,090 respondents aged 45 years and above, 22,041 (70.8%) were excluded because they lacked complete information on depressive symptoms and CVD, resulting in 9112 respondents. Furthermore, 63 respondents were excluded due to missing sociodemographic data. This resulted in a total of 9049 respondents included in the study.

The majority of included respondents were aged 45 to 59 years old (71.1%), female (52.6%), elementary school graduates (50.7%), urban dwellers (56.6%), non-smokers (59.0%), and non-obese (77.3%), as shown in Table 1. Furthermore, most respondents were not experiencing depressive symptoms (82.2%) and had no history of self-reported CVD (96.7%). Only a small proportion of respondents (0.8%) reported experiencing both depressive symptoms and self-reported CVD (Table 2).

Association Between Depressive Symptoms and Self-Reported CVD

Table 2 presented the bivariate analysis among respondents to ascertain the association between depressive symptoms and socio-demographic variables with self-reported CVD. In the multivariate analysis, respondents with depressive symptoms (AOR = 1.56; 95% CI = 1.18–2.05; p-value = 0.002) showed a significant association with CVD after adjusting for age, gender, residency, educational level, smoking habit, and obesity (Table 3).

Sub-Group Analysis Based on Age Groups

Sub-group analysis showed that elderly respondents with depressive symptoms (AOR = 1.89; 95% CI = 1.22–2.94; p-value = 0.005) had a significant association with CVD, adjusted by residency, educational level, and obesity. Meanwhile, the middle-aged groups did not show a significant association with CVD (AOR = 1.39; 95% CI = 0.98–1.98; p-value = 0.063), adjusted for gender, educational level, smoking habit, and obesity (Table 3).

Table 1 Sociodemographic Characteristics

No	Characteristics		N (%)		
			All Respondents (N=9049)	**Middle-Aged (45–59 years old) (N=6436)**	**Elderly (≥60 years old) (N=2613)**
1	Depressive Symptoms	No	7439 (82.2)	5256 (81.7)	2183 (83.5)
		Yes	1610 (17.8)	1180 (18.3)	430 (16.5)
2	CVD	No	8748 (96.7)	6252 (97.1)	2496 (95.5)
		Yes	301 (3.3)	184 (2.9)	117 (4.5)
3	Gender	Male	4290 (47.4)	3035 (47.2)	1255 (48.0)
		Female	4759 (52.6)	3401 (52.8)	1358 (52.0)
4	Residency	Rural	3923 (43.4)	2703 (42.0)	1220 (46.7)
		Urban	5126 (56.6)	3733 (58.0)	1393 (53.3)
5	Education level	University or higher	819 (9.1)	678 (10.5)	141 (5.4)
		High school	1498 (16.6)	1245 (19.3)	253 (9.7)
		Middle school	1093 (12.1)	847 (13.2)	246 (9.4)
		Elementary school	4589 (50.7)	3154 (49.0)	1435 (54.9)
		No education	1050 (11.6)	512 (8.0)	538 (20.6)
6	Smoking habit	Non-smoker	5336 (59.0)	3885 (60.4)	1451 (55.5)
		Smoker	3713 (41.0)	2551 (39.6)	1162 (44.5)
7	Obesity	No	6998 (77.3)	4744 (73.7)	2254 (86.3)
		Yes	2051 (22.7)	1692 (26.3)	359 (13.7)

Table 2 Bivariate Analysis of Association Between Depressive Symptoms and CVD

No	Factors	CVD; N (%)								
		All Age Groups (N = 9049)			**Middle-Aged (N = 6436)**			**Elderly (N = 2613)**		
		No	**Yes**	**p-value**	**No**	**Yes**	**p-value**	**No**	**Yes**	**p-value**
1	**Age**			<0.001*						
	Middle-aged	6252 (69.1)	184 (2.0)							
	Elderly	2496 (27.6)	117 (1.3)							
2	**Depressive Symptoms**			0.006*			0.090*			0.018*
	No	7210 (79.7)	229 (2.5)		5115 (79.5)	141 (2.2)		2095 (80.2)	88 (3.4)	
	Yes	1538 (17.0)	72 (0.8)		1137 (17.6)	43 (0.7)		401 (15.3)	29 (1.1)	
3	**Gender**			0.013*			0.001*			1.000
	Male	4169 (46.1)	121 (1.3)		2970 (46.1)	65 (1.0)		1199 (45.9)	56 (2.1)	
	Female	4579 (50.6)	180 (2.0)		3282 (51.0)	119 (1.9)		1297 (49.6)	61 (2.4)	

(*Continued*)

https://doi.org/10.2147/VHRM.S491961

Table 2 (Continued).

No	Factors	CVD; N (%)								
		All Age Groups (N = 9049)			Middle-Aged (N = 6436)			Elderly (N = 2613)		
		No	Yes	p-value	No	Yes	p-value	No	Yes	p-value
4	**Residency**			0.003*			0.304			<0.001*
	Rural	3818 (42.2)	105 (1.2)		2633 (41.0)	70 (1.0)		1185 (45.4)	35 (1.3)	
	Urban	4930 (54.5)	196 (2.2)		3619 (56.2)	114 (1.8)		1311 (50.2)	82 (3.1)	
5	**Educational level**			0.004*			0.107*			<0.001*
	University or higher	779 (8.6)	40 (0.4)		650 (10.1)	28 (0.4)		129 (4.9)	12 (0.5)	
	High school	1437 (15.9)	61 (0.7)		1204 (18.7)	41 (0.6)		233 (8.9)	20 (0.8)	
	Middle school	1051 (11.6)	42 (0.5)		821 (12.8)	26 (0.4)		230 (8.8)	16 (0.6)	
	Elementary school	4455 (49.2)	134 (1.5)		3080 (47.9)	74 (1.2)		1375 (52.6)	60 (2.3)	
	No education	1026 (11.3)	24 (0.3)		497 (7.7)	15 (0.2)		529 (20.2)	9 (0.4)	
6	**Smoking habit**			0.056*			0.057*			0.389
	Non-smoker	5142 (56.8)	194 (2.1)		3761 (58.4)	124 (2.0)		1381 (52.8)	70 (2.7)	
	Smoker	3606 (39.8)	107 (1.2)		2491 (38.7)	60 (0.9)		1115 (42.7)	47 (1.8)	
7	**Obesity**			0.002*			0.004*			0.021*
	No	6788 (75.0)	210 (2.3)		4626 (71.9)	118 (1.8)		2162 (82.7)	92 (3.5)	
	Yes	1960 (21.7)	91 (1.0)		1626 (25.3)	66 (1.0)		334 (12.8)	25 (1.0)	

Note: *significant factor ($p < 0.25$) to be subsequently included in the multivariate analysis.

Table 3 Multivariate Analysis of Association Between Depressive Symptoms and Self-Reported CVD

Factor	Self-Reported CVD			
Depressive Symptoms (compared with not having symptoms)	**All age groups**			
	Unadjusted OR (95% CI)	***p***	**Adjusted OR (95% CI)[a]**	***p***
	1.47 (1.12–1.93)	0.005*	1.56 (1.18–2.05)	0.002*
	Sub-group Analysis			
	Middle-aged group			
	Unadjusted OR (95% CI)	***p***	**Adjusted OR (95% CI)[b]**	***p***
	1.37 (0.97–1.94)	0.074	1.39 (0.98–1.98)	0.063
	Elderly group			
	Unadjusted OR (95% CI)	***p***	**Adjusted OR (95% CI)[c]**	***p***
	1.72 (1.12–2.65)	0.014*	1.89 (1.22–2.94)	0.005*

Notes: *significant factor ($p < 0.05$). [a]adjusted by age, gender, residency, educational level, smoking habit, and obesity. [b]adjusted by gender, educational level, smoking habit, and obesity. [c]adjusted by residency, educational level, and obesity.

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; p, p-value of significance (<0.05).

Discussion

The analysis results showed that nearly all the 9049 respondents reported no experience of depressive symptoms and self-reported CVD. After adjusting for confounding variables, respondents with depressive symptoms were associated with a higher likelihood of experiencing self-reported CVD.

Our study found that only 2.2% of the middle-aged population and 3.4% of the elderly population reported experiencing CVD alongside depressive symptoms. A previous similar study in Indonesia reported that 36 out of 38 CVD patients exhibited depressive symptoms.[36] Another study involving a larger sample across various countries, including those with low, lower-middle, upper-middle, and high-income countries, analyzed 15,983 patients with four or more depressive symptoms. This study reported outcomes of major CVD (10.3%), myocardial infarction (12.5%), heart failure (13.3%), and cardiovascular deaths (11.0%) after approximately 9.3 years of follow-up.[14] Due to the limited number of studies examining the association between depressive symptoms and CVD in Indonesia, our findings offer valuable insights and address a significant gap in the literature through the use of a large dataset.[25]

We observed a significant association between depressive symptoms and CVD across all age groups. However, in the subgroup analysis, the elderly were more likely to experience CVD compared to the middle-aged. This association remained significant after adjusting for several cardiovascular risk factors, including gender, educational level, smoking, and obesity. The results were in line with increasing evidence of the association between depression and a higher risk of experiencing CVD.[37–40] A meta-analysis of 26 studies reported that depression is associated with an elevated risk of all-cause mortality, including mortality due to CVD and congestive heart failure mortality.[7] Another study reported that individuals with moderate depressive symptoms had a 98% higher risk of CVD than those with no or minimal depressive symptoms, while those with moderately severe or severe depressive symptoms had a 141% higher risk of CVD.[41] One possible explanation for this association is the unhealthy lifestyle often adopted by individuals with depression, which typically includes sedentary behavior, poor dietary choices, and social isolation.[14,42] The underlying mechanisms of the association are multifactorial as reported in prior studies,[9,11–13] comprising autonomic nerve dysfunction, inflammation, endothelial dysfunction, platelet activation, and thrombosis.[43] Depression had been reported to be associated with high interleukin-6 (IL-6) activity, and elevated IL-6 levels impacted serotonin metabolism within the central nervous system[44] and stimulated higher activity of the hypothalamic–pituitary–adrenal (HPA) axis.[45] HPA-axis hyperactivity resulting from persistent depressive symptoms could increase cortisol hormone release.[46,47] Excessive cortisol hormone production might lead to dysregulation of blood glucose, increased blood tension, atherosclerosis, and impairment of endothelial cells of blood vessels, which were considered symptoms of cardiovascular impairment.[48] Moreover, the depressive state has been reported to influence thrombocyte activity and epinephrine hormone levels, resulting in vasoconstriction and blood clots as a feedback mechanism of the body against concurrent inflammation.[34,49] The result was in line with a study reporting that there were higher inflammation markers in individuals with depression compared to those without the condition.[44] Furthermore, the association between depression and a higher risk of experiencing CVD might be explained by altered behaviors, including changes in dietary patterns, sleep disturbance, medication non-adherence, smoking or alcohol addiction, and physical inactivity.[50]

Subgroup analysis showed a significant association between depressive symptoms and self-reported CVD in elderly respondents, while no significant association was observed in the middle-aged group after adjusting for confounders. The results were consistent with previous studies,[44,45,47] suggesting that the feeling of social or emotional isolation among the elderly may have contributed to their susceptibility to CVD.[47] Moreover, late-life depression was linked to a higher risk of both all-cause and cardiovascular mortality.[16] Late-life depression was often characterized by a higher prevalence of somatic symptoms[46] and vascular pathology,[48] showing poor physical health compared to the mental health condition in the middle-aged groups. However, other investigations showed a significant association between depression and CVD in the middle-aged population compared to elderly ones,[9,49] possibly due to differences in inflammation levels.[9] On the other hand, a previous cohort study showed that depressive symptoms might be associated with incident CVD among both the middle-aged and older Chinese adults.[34] The results suggested that the impact of age on the relationship between depression and CVD remained inconclusive. In addition to methodological differences, variations in sociocultural contexts across these studies might have partly explained the differing results.

This analysis results showed the importance of clinicians in recognizing the risk of CVD in patients with depressive symptoms, particularly among the elderly. Given the increased odds of CVD among patients with depressive symptoms, it was necessary to enhance screening and evaluate mental health as an additional monitoring tool. Moreover, mental health screening among those with established CVD might be crucial for optimizing secondary prevention. Tailored and targeted interventions using a multidisciplinary method and collaborative integrated care between healthcare professionals were also necessary to improve mental health and reduce CVD risk.

This study represented the first attempt to explore the association between depressive symptoms and self-reported CVD in both the middle-aged and elderly population using a population-based national survey in Indonesia. This study has the potential to address the gap in the investigation of the relationship between depressive symptoms and cardiovascular diseases in Indonesia, particularly with a large sample size. While no IFLS data has been collected since the fifth wave, the IFLS data remains a significant national survey that represents 83% of Indonesia's population and can serve as a baseline for conducting studies in recent years. The investigation had several limitations, as depressive symptoms and CVD were assessed through self-reporting rather than clinical diagnosis by healthcare professionals, which might have introduced recall and misclassification biases. Although the CES-D-10 tool used for depression assessment was validated for screening the condition symptoms, a more structured and objective diagnosis was warranted, preferably in conjunction with clinical evaluation. This study utilized large-scale database from self-reported healthcare professionals-diagnosed CVD. Another large-scale study showed good agreement (accuracy: 77.5%) between self-reported incident CVD and medical records.[51] A cross-sectional design cannot establish absolute causality or directional association. Lastly, other unmeasured factors not available in the database, such as the duration and severity of depressive symptoms and CVD,[9] physical activity,[52] pack years,[53,54] comorbidities,[55] medication nonadherence,[56] alcohol consumption,[52,57] inappropriate diet,[57,58] family history,[59] and the use of antidepressants and dietary supplements for depression treatment,[60] might have been associated with CVD.

Future longitudinal studies investigating the association between depressive symptoms and CVD should consider sampling weights and comprise larger and more diverse populations. Furthermore, there is a need for future investigations to develop tailored and targeted interventions aimed at improving mental health outcome.

Conclusion

Respondents with depressive symptoms were associated with an increased risk of self-reported CVD, highlighting the urgent need for targeted prevention strategies, especially those struggling with depressive symptoms.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the ethical review boards of the RAND's Human Subjects Protection Committee. The study was approved by the Health Research Ethics Committee of Universitas Padjadjaran, Indonesia, on November 22, 2024 (No: 1205/UN6.KEP/EC/2024).

Data Sharing Statement

This study used data from IFLS, which was accessible online through the RAND website at the following address: http://www.rand.org/labor/FLS/IFLS.html.

Informed Consent Statement

Written informed consent was obtained from all respondents before collecting the data.[25]

Acknowledgments

The authors thank M. Andhika Aji Pratama for his assistance in the data analysis process.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This investigation received support from a grant-in-aid from Universitas Padjadjaran, Indonesia. The funding body had no role in study design, writing the article, or the decision to submit it for publication.

Disclosure

The authors declared no potential conflicts of interest regarding the analysis, authorship, and/or publication of this article.

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