

RESEARCH ARTICLE

Prevalence of depression and its association with health-related quality of life in people with heart failure in low- and middle-income countries: A systematic review and meta-analysis

Henok Mulugeta ^{1,2*}, Peter M. Sinclair², Amanda Wilson²

1 Department of Nursing, College of Health Science, Debre Markos University, Debre Markos, Amhara Region, Ethiopia, **2** School of Nursing and Midwifery, Faculty of Health, University of Technology Sydney, Sydney, New South Wales, Australia

* mulugetahenok68@gmail.com OPEN ACCESS

Citation: Mulugeta H, Sinclair PM, Wilson A (2023) Prevalence of depression and its association with health-related quality of life in people with heart failure in low- and middle-income countries: A systematic review and meta-analysis. PLoS ONE 18(3): e0283146. <https://doi.org/10.1371/journal.pone.0283146>

Editor: Muktar Beshir Ahmed, University of Adelaide School of Medical Sciences: The University of Adelaide Adelaide Medical School, AUSTRALIA

Received: December 12, 2022

Accepted: March 2, 2023

Published: March 23, 2023

Copyright: © 2023 Mulugeta et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its [Supporting Information](#) files.

Funding: There was no funding for this systematic review. It is part of a PhD thesis by HM. HM is a higher degree research candidate at the University of Technology Sydney (UTS), funded by the International Research Training Program (IRTP).

Abstract

Introduction

Heart failure is a growing public health concern around the world. People with heart failure have a high symptom burden, such as depression, which affects health-related quality of life (HRQoL). The objective of this systematic review and meta-analysis was to estimate the pooled prevalence of depression and evaluate its association with HRQoL among people with heart failure in low- and middle-income countries (LMICs).

Methods

This systematic review was conducted in accordance with the JBI methodology. Electronic databases such as MEDLINE, PsycINFO, EMBASE, CINAHL, Web of Science, Scopus and JBI EBP were searched to identify relevant studies published from January 2012 to August 2022. The methodological quality of each article was assessed using relevant JBI critical appraisal instruments. A random-effects model was employed to estimate the pooled prevalence of depression. Heterogeneity across the studies was investigated using Cochrane's Q test and I^2 statistic. The Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines 2020 were followed for reporting the results. All statistical analyses were performed using STATA version 17 software.

Results

After screening, a total of 21 eligible articles with 5074 participants with heart failure were included in this review. The pooled prevalence of depression among people with heart failure in LMICs was 51.5% (95% CI = 39.7, 63.3%, $I^2 = 99.00\%$). Subgroup analysis revealed, the highest prevalence in studies whose participants were in-patients, and from the Middle

The IRTP is a commonwealth scholarship funded by the Australian government and the Department of Education and Training. The funder has no role in any aspect of the project. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

Abbreviations: CVD, Cardiovascular diseases; HF, Heart failure; HRQoL, Health-related quality of life; JBI, Joanna Briggs Institute; LMICs, Low and middle income countries; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

East and North Africa, and studies utilizing Becks Depression Inventory (BDI). Depression was positively associated with HRQoL.

Conclusion

This review revealed that almost half of all people with heart failure in low- and middle-income countries have comorbid depression. People with heart failure and depressive symptoms had poor HRQoL. Therefore, early screening of depression is critical for improving HRQoL in this population.

Systematic review registration: PROSPERO CRD42022361759.

Introduction

Cardiovascular diseases (CVD) are the leading cause of mortality globally with an estimated 17.9 million deaths in 2019, accounting for 32% of all deaths [1]. It is predicted that over 23 million people will die annually from CVDs worldwide by 2030 [2]. The burden of CVD is increasing in low- and middle-income countries (LMICs) where 75% of all deaths are related to CVD [3]. This burden can be attributed to a lack of primary health care services to support the early detection and management of cardiovascular risk factors [4].

Heart failure is a major CVD associated with high morbidity and mortality [5]. The global prevalence of heart failure (HF) is increasing due to ageing and population growth, with an estimated 64 million people affected [6, 7]. It is responsible for more than 300,000 global deaths annually [8, 9]. Although there are limited data from population-based studies, the available data from hospital-based studies show that heart failure is increasingly prevalent in low- and middle-income countries (LMICs) [10]. People with heart failure have many debilitating symptoms such as depression and poor health-related quality of life (HRQoL) compared to the general population due to the unpredictable nature of the disease [11, 12].

The psychological impact of HF, such as depression, is increasing significantly and leads to a poor prognosis [13]. People with HF who are depressed have an increased risk of poor HRQoL compared to those without depression [13, 14]. The findings from two recent systematic reviews found the prevalence of any severity of depression in people with heart failure was 42% [15], and the overall HRQoL in these populations was moderate [16]. However, these reviews only included a small number of studies from LMICs. This means there is considerable uncertainty about the prevalence of depression in this region. A systematic review and meta-analysis conducted in China found that 43% of people with heart failure have depressive symptoms [17]. However, this figure does not represent the burden of the problem in LMICs as all data were from China.

While there are many studies on depression and its association with HRQoL among HF patients in LMICs, the results are inconsistent and inconclusive, meaning the current burden of the problem remains unknown in these populations [18]. In this systematic review, we aimed to estimate the regional burden of depression and assess the association between depression and HRQoL in people with HF in LMICs. The findings of this review will provide contemporary evidence with the potential to assist healthcare policymakers and researchers in developing intervention programs and guidelines for improving the management and care of people with heart failure in LMICs.

Review questions

This review sought to answer the following two questions:

1. What is the prevalence of depression in people with heart failure in LMICs?
2. Is there an association between depression and HRQoL in people with heart failure in LMICs?

Inclusion and exclusion criteria

Participants (population)

This review included studies from LMICs whose participants who are 18 years or older and had a confirmed diagnosis of heart failure.

Condition

The prevalence of depression and/or association of depression with HRQoL in the participants. For the purpose of this review, heart failure is defined as the inability of the heart to effectively pump blood as evidenced by either signs and symptoms based on Framingham criteria or reduced ejection fraction (<40%) [19, 20]. Depression is defined as the persistent feeling of unhappiness and lack of interest in daily activities with symptoms for at least two weeks, based on DSM-5 diagnostic criteria [21]. Health-related quality of life was defined as self-reported physical, mental, emotional, and social health functioning [22].

Context

Low-and-middle income countries. For the purposes of this review, low to middle income countries were defined using the World Bank atlas method [23] based on the stratification of economies based on gross national income (GNI) per capita. Low-income countries are those with a GNI per capita of \$US1,045 or less; lower and upper middle-income economies are those with a GNI per capita between \$US1,046 and \$US4,095 and \$US4,096 and \$US12,695 and respectively.

Outcomes

The primary outcome of this review was the prevalence of depression. The secondary outcome was the association between depression and HRQoL scores measured using a psychometrically validated instrument.

Types of studies. Observational (cross-sectional, cohort, case-control) studies that reported the prevalence of depression and/or association of depression with HRQoL in people with heart failure.

For the secondary objective of this review, the following inclusion criteria were considered using the PEO (P = Population, E = exposure, O = outcome) model.

Population. Adults with a confirmed diagnosis of heart failure.

Exposure of interest. Depression.

Outcome. HRQoL.

Methods

Design

This systematic literature review has followed methodology guidelines outlined by the Joanna Briggs Institute (JBI) methodology for Systematic Reviews [24] and is reported in line with the PRISMA 2020 guidelines [25]. The protocol for this systematic review was registered in the PROSPERO online database (registration number CRD42022361759) and previously published [26].

Search strategy

The search strategy aimed to locate both published and unpublished studies. Information sources were electronic databases, conference proceedings, websites, dissertations, and direct contact with the author if required. A preliminary original search of MEDLINE (Ovid) and CINAHL (EBSCO) was undertaken in May 2022 and was updated in August 2022. The last search was done on August 20, 2022. The text words in the titles and abstracts of relevant articles and the index terms used to describe the articles were analysed and used to inform a full search strategy in collaboration with a faculty librarian. The search strategy was developed using the **CoCoPop** (**Co** = Condition, **Co** = Context, **Pop** = Population) model considering the **PEO** (P = Population, E = exposure, O = outcome) model for the second research question of this review. The databases searched includes MEDLINE (Ovid), PsycINFO (EBSCOhost), EMBASE (Ovid), CINAHL (EBSCOhost), Web of Science (Direct access), Scopus (Direct access) and JBI EBP database (Ovid). Index terms (subject headings) and keywords used for the search strategy were adapted for each database. The full search strategy for each database is attached in [S1 Table](#). The reference lists of all identified relevant studies and systematic reviews were screened to identify additional studies. A search for unpublished studies was conducted using Google scholar, Mednar, ProQuest and dissertation databases. Articles published in English language from January 2012 to August 2022 were included to establish the most recent estimate.

Study selection and outcome

Following the search, all identified citations were collated and uploaded into EndNote V20 (Clarivate Analytics, PA, USA). After removing duplicates, two researchers (HM and PS) screened all titles and abstracts from the original search against the predefined inclusion criteria. The full text of selected citations was assessed in detail against the inclusion criteria independently by the reviewers (HM and PS). The reasons for excluding papers were recorded and reported. Any disagreements between the reviewers were resolved through discussion. The search results and the study inclusion process were reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [25].

Quality appraisal

Two independent reviewers (HM and PS) critically appraised the eligible studies for methodological quality using a standardised JBI critical appraisal instrument for studies reporting prevalence data [27]. The tool is comprised of 9 items that focus on target population, sample size adequacy, study subject and setting (context), reliability of condition measurement, appropriateness of the statistical test used to analyse the data, and adequacy of the response rate with the option to answer 'No', 'Yes', or 'unclear'. Authors of papers were contacted to request missing or additional data for clarification, where required. Following the critical appraisal, the reviewers included or excluded studies based on the overall appraisal quality. A study was

excluded if it had more than three 'No' or 'unclear' quality categories. This threshold criterion is consistent with that used in a similar published systematic review [28]. The quality of eligible articles to assess the association between depression and HRQoL were also appraised using the JBI cross-sectional studies critical appraisal tool for studies reporting association (etiology/risk) [29]. Any disagreements were resolved through discussion. The results of the critical appraisal are reported in narrative and table form (Tables 1 and 5).

Data extraction

The JBI data extraction tool for prevalence data and association (etiology/risk) studies were used to extract the following information from each included study for each research question: authors, year of publication, country, region, design, population, sample size, sampling methods, outcome measuring tool, prevalence of depression, HRQoL mean score based on exposure (depression), measure of association, and quality appraisal score. When there was missing data, authors were contacted for relevant information. Two reviewers (HM and AW) independently conducted the primary data extraction and cross-checked for inconsistencies. Any disagreements and discrepancies between the reviewers were resolved by discussion.

Data analysis and synthesis

A narrative presentation of the outcomes including text, table, and figure, were used to discuss the characteristics of the included studies and synthesise the prevalence of depression and its association with HRQoL. A random-effects model with DerSimonian and Laird model was used to estimate the pooled effect size of depression, as recommended by Tufanaru et al. [30]. Subgroup analyses were conducted to investigate the variation between different study characteristics, such as region, type of outcome measuring instrument, and type of study population. Heterogeneity was assessed statistically using the standard chi-squared and I-squared tests. The sources of heterogeneity were analysed using subgroup analysis, and meta-regression. The presence of publication bias was assessed visually using a funnel plot, and statistical tests for funnel plot asymmetry was checked by Egger test statistics. A leave-one-out sensitivity analysis was also conducted for assessing the influence of each study on the overall effect size estimate. The pooled effect size was presented using a forest plot. All statistical analysis was performed using STATA Version 17 statistical software.

Results

Search results

The online electronic search process yielded 4222 articles (4156 from databases and 66 from other sources) of which 1303 were duplicates. After reviewing the title and abstract, we excluded 2844 irrelevant articles. From the remaining 75 articles, 49 were removed after full text assessment. A further five articles were excluded due to poor methodological quality leaving 21 relevant primary research articles eligible for this systematic review (Fig 1).

Assessment of methodological quality for prevalence studies

This review included 21 articles with moderate to high methodological quality. One study [31] scored 9 points, five studies [32–36] scored 8 points, and the remaining 15 studies [37–51] scored 7 points in the JBI critical appraisal checklist [27] for studies reporting prevalence data (Table 1).

Table 1. Methodological quality of included prevalence studies.

Included articles	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Quality score/9
Edmealem A, et al. [37]	Y	Y	U	Y	Y	U	Y	Y	Y	7
DeWolfe A, et al. [38]	Y	Y	Y	Y	Y	Y	Y	Y	U	7
Okviansanti F, et al. [39]	U	Y	Y	Y	Y	Y	N	Y	Y	7
Pushkarev GS, et al. [40]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Fan X, et al. [32]	Y	Y	Y	Y	Y	Y	U	Y	Y	8
Zahid I, et al. [41]	U	U	Y	Y	Y	Y	U	Y	Y	7
Yazew KG, et al. [33]	Y	Y	Y	Y	Y	Y	U	Y	Y	8
AbuRuz ME [34]	U	Y	Y	Y	Y	Y	Y	Y	Y	8
Pan S, et al. [42]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Husain MI, et al. [35]	Y	Y	Y	Y	Y	Y	U	Y	Y	8
Tran NN, et al. [36]	U	Y	Y	Y	Y	Y	Y	Y	Y	8
Tsabadze N, et al. [43]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Erceg P, et al. [44]	U	Y	Y	Y	Y	Y	N	Y	Y	7
Alemoush RA, et al. [31]	Y	Y	Y	Y	Y	Y	Y	Y	Y	9
Saima D, et al. [45]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Ghanbari A, et al. [46]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Zhang X, et al. [47]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Khan S, et al. [48]	U	Y	Y	Y	Y	Y	N	Y	Y	7
Molavynjad S, et al. [49]	U	Y	Y	Y	Y	Y	N	Y	Y	7
Son YJ, et al. [50]	U	Y	Y	Y	Y	Y	U	Y	Y	7
Son YJ, et al. [51]	U	Y	Y	Y	Y	Y	U	Y	Y	7

Y = yes; N = No; U = Unclear.

<https://doi.org/10.1371/journal.pone.0283146.t001>

Overall study characteristics

Of the 21 studies, seven were conducted in East Asia and Pacific region [32, 36, 39, 42, 47, 50, 51], four in the Middle East and North Africa [31, 34, 46, 49], three in Sub-Saharan Africa [33, 37, 43], three in Europe and Central Asia [38, 40, 44], and four in South Asia [35, 41, 45, 48]. Most studies used a descriptive cross-sectional design (n = 17, 81%) and the remaining (n = 4, 19%) were prospective cohort studies. Many (57%) of the studies were conducted in outpatient population, and most (33%) used consecutive sampling technique. The sample size of the included studies ranged from 43 [37] to 1009 [35]. Included studies assessed the prevalence of depression using nine different psychometrically validated instruments. Five studies [32, 35, 40, 45, 49] used Beck Depression Inventory (BDI), five [33, 38, 39, 41, 50] used Patient Health Questionnaire-9 (PHQ-9), four [31, 34, 47, 48] used Hospital Anxiety and Depression Score (HADS), two [44, 51] Geriatric Depression Scale (GDS), and the remaining five [36, 37, 42, 43, 46] each used Cardiac Depression Scale (CDS), Patient Health Questionnaire-2 (PHQ-2), Hamilton Rating Scale for Depression (24-items) (HAM-D₂₄), Geriatric Depression Scale (GDS), International Statistical Classification of Diseases and Related Health Problems V10 (ICD-10) (Table 2).

Prevalence of depression in people with heart failure in LMICs

In total, 21 studies reported the prevalence of depression in people with heart failure in LMICs. The lowest and the highest prevalence of depression were 11.1% [37] and 97.0% [49], respectively (Table 1). The pooled regional prevalence of depression among people with heart

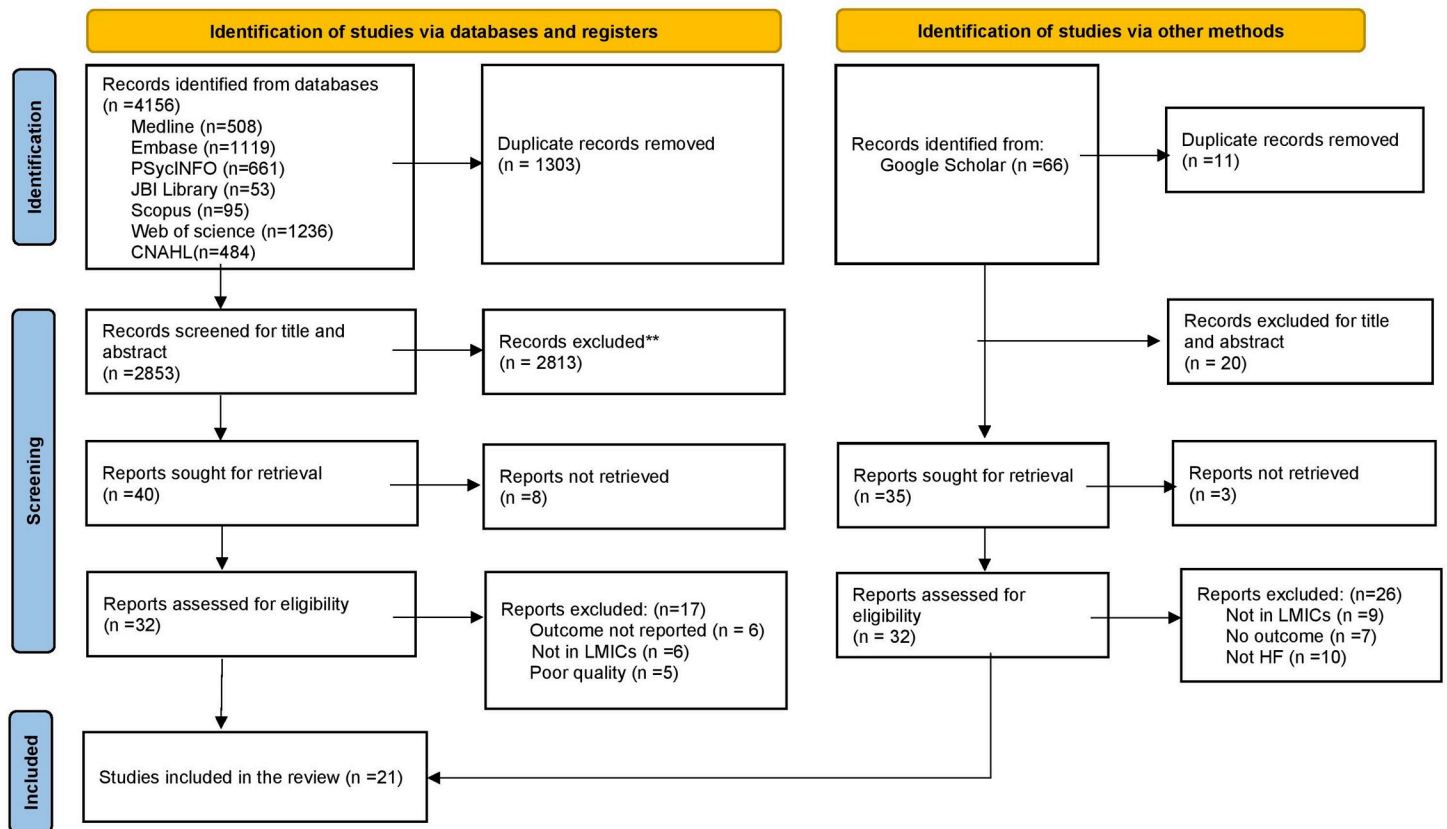


Fig 1. PRISMA flow diagram of literature identification, study selection and inclusion process.

<https://doi.org/10.1371/journal.pone.0283146.g001>

failure in LMICs was 52% (95% CI = 39.73, 63.3%, $I^2 = 99.00\%$). The overall pooled effect size of depression presented using forest plot (Fig 2).

Sub-group analysis

Subgroup analysis was done using region where the studies were conducted, study population and the outcome measuring instrument. The result showed that the highest prevalence was observed among studies conducted in Middle East and North Africa, among inpatients and studies that screened depression using BDI (Table 3).

Assessment of heterogeneity

The result of this meta-analysis using the random-effects model revealed a high heterogeneity across the included studies ($I^2 = 99\%$, $P = 0.001$). Heterogeneity is inevitable in meta-analysis due to difference in study quality, methodology, sample size and inclusion criteria for participants [52, 53]. Consequently, meta-regression was performed using publication year, sample size and quality score as covariates to find possible sources of heterogeneity among the included studies. The result of the meta-regression analysis showed that no significant linear relationship existed between the outcome (depression) and the covariates. Therefore, none of the three covariates were significantly associated with the presence of heterogeneity (Table 4). The high heterogeneity can be attributed to chance or other factors not included in this review.

Table 2. Characteristics of included studies for prevalence of depression among people with heart failure in LMICs.

ID	Author (reference)	Publication year	Country	Region	Study design	Population	Sample size	Sampling method	Outcome measuring tool	Prevalence	Quality score
1	Edmealem A, et al. [37]	2020	Ethiopia	Sub-Saharan Africa	Cross-Sectional	Outpatient	43	Stratified	PHQ-2	11.1	7
2	DeWolfe A, et al. [38]	2012	Georgia	Europe and Central Asia	Prospective cohort	Outpatient	314	Unreported	PHQ-9	13.0	8
3	Okviansanti F, et al. [39]	2020	Indonesia	East Asia and Pacific	Cross-Sectional	Outpatient	155	Consecutive	PHQ-9	85.2	7
4	Pushkarev GS, et al. [40]	2018	Russia	Europe and central Asia	Prospective cohort	Outpatient	260	Unreported	BDI	60.0	7
5	Fan X, et al. [32]	2015	China	East Asia and Pacific	Cross-Sectional	Inpatient	152	Consecutive	BDI	44.0	8
6	Zahid I, et al. [41]	2018	Pakistan	South Asia	Cross-Sectional	Outpatient	170	Consecutive	PHQ-9	60.0	7
7	Yazew KG, et al. [33]	2019	Ethiopia	Sub-Saharan Africa	Cross-Sectional	Outpatient	422	Systematic random	PHQ-9	51.1	8
8	AbuRuz ME [34]	2018	Jordan	Middle East and North Africa	Cross-Sectional	Outpatient	200	Convenient	HADS	65.0	8
9	Pan S, et al. [42]	2016	China	East Asia and Pacific	Cross-Sectional	Inpatient	366	Consecutive	HAM-D24	57.4	7
10	Husain MI, et al. [35]	2019	Pakistan	South Asia	Cross-Sectional	Outpatient	1009	Unreported	BDI	66.0	8
11	Tran NN, et al. [36]	2022	Vietnam	East Asia and Pacific	Cross-Sectional	Inpatient	128	Convenient	ICD-10	46.9	8
12	Tsabedze N, et al. [43]	2021	South Africa	Sub-Saharan Africa	Cross-Sectional	Outpatient	103	Consecutive	DASS-21	52.4	7
13	Erceg P, et al. [44]	2013	Serbia	Europe and Central Asia	Cross-Sectional	Inpatient	136	Consecutive	GDS	55.9	7
14	Alemoush RA, et al. [31]	2021	Jordan	Middle East and North Africa	Prospective follow up	Outpatient	127	Consecutive	HADS	47.3	9
15	Dastgeer S, et al. [45]	2016	Pakistan	South Asia	Prospective follow up	Inpatient	400	Unreported	BDI	64.7	7
16	Ghanbari A, et al. [46]	2015	Iran	Middle East and North Africa	Cross-Sectional	Inpatient	239	Gradual sampling	CDS	57.7	7
17	Zhang X, et al. [47]	2020	China	East Asia and Pacific	Cross-Sectional	Inpatient	254	Convenient	HADS	18.1	7
18	Khan S, et al. [48]	2012	Pakistan	South Asia	Cross-Sectional	Inpatient	121	Consecutive	HADS	30.0	7
19	Molavynejad S, et al. [49]	2019	Iran	Middle East and North Africa	Cross-Sectional	Inpatient	151	Convenient	BDI	97.0	7
20	Son YJ, et al. [50]	2018	South Korea	East Asia and Pacific	Cross-Sectional	Outpatient	190	Convenient	PHQ-9	30.0	7
21	Son YJ, et al. [51]	2012	South Korea	East Asia and Pacific	Cross-Sectional	Outpatient	134	Unreported	GDS	67.9	7

<https://doi.org/10.1371/journal.pone.0283146.t002>

Assessment of publication bias

Visual inspection of the funnel plot suggested asymmetry, as eight studies lay to the left and 13 to the right of the line (Fig 3). However, this was not statistically significant as evidenced by Egger's test ($P = 0.81$), which confirmed the results were not influenced by publication bias. It

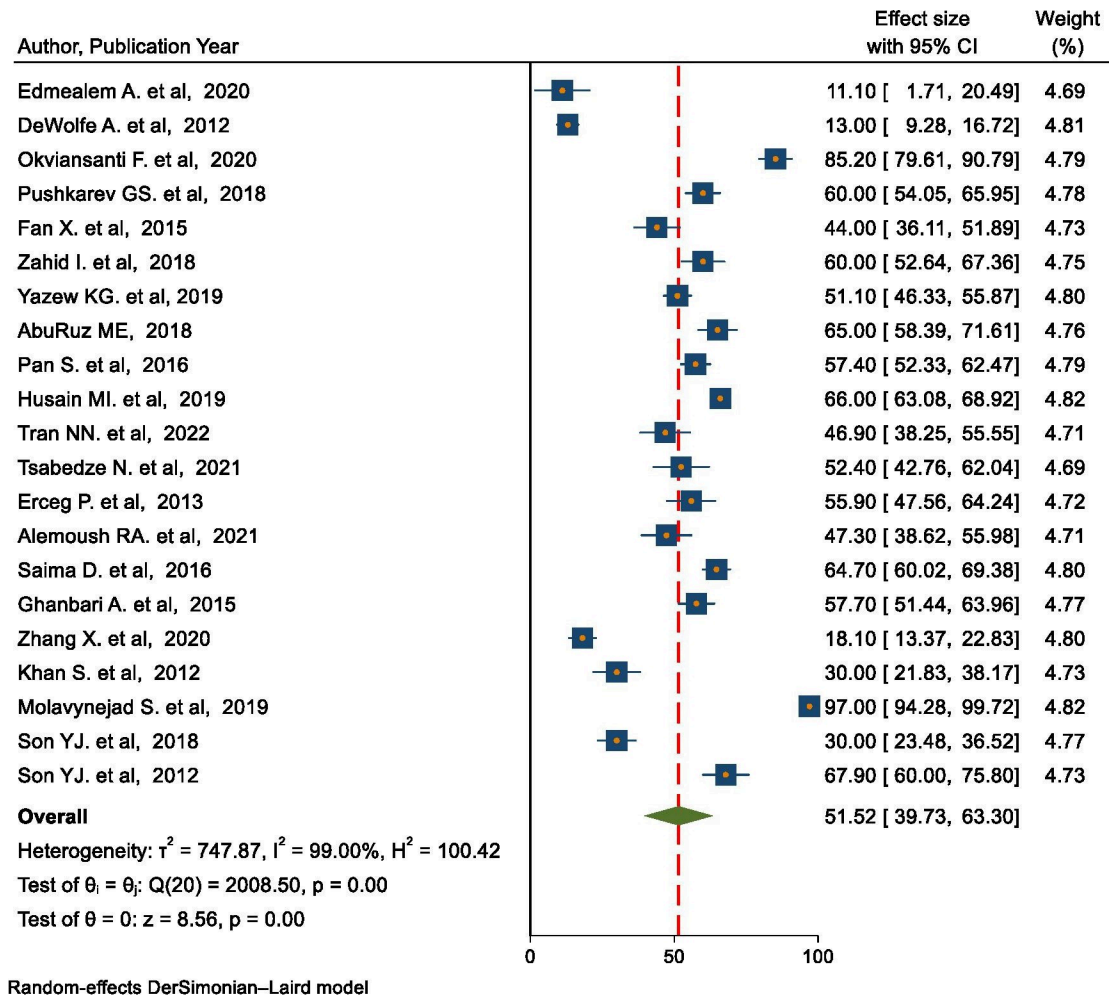


Fig 2. The pooled prevalence of depression in people with heart failure in LMICs.

<https://doi.org/10.1371/journal.pone.0283146.g002>

is worth noting that asymmetry in funnel plots is not always linked to publications bias [54], and that high heterogeneity may explain the visual asymmetry in the funnel plot.

Sensitivity analysis. The result of leave-one-out sensitivity analysis using a random effects model demonstrated that no single study unduly influenced the pooled estimate of depression. For each study, the displayed effect size corresponds with the overall effect size computed from meta-analysis excluding that study (Fig 4).

The association between depression and HRQoL

Of the 21 eligible studies, only six reported an association between depression and HRQoL using depression as exposure variable and HRQoL as outcome. There were variations in the ways that depression and HRQoL were measured among these studies. For instance, two studies [44, 51] used GDS, two studies [31, 34] used HADS, one study [43] used DASS-21 and one study [38] used PHQ-9 to measure depression. Likewise, four studies [38, 43, 44, 51] used MLHFQ and the other two studies [31, 34] used SF-36 to measure HRQoL. Regarding the critical appraisal, the JBI cross-sectional studies critical appraisal tool for studies reporting

Table 3. Subgroup analysis on the prevalence of depression among people with heart failure in LMICs.

Subgroup	Number of studies	Sample size	Pooled Prevalence	Heterogeneity	
				I ²	P-value
By region					
East Asia and pacific	7	1379	49.91	98.5	<0.001
South Asia	4	3708	55.62	95.6	<0.001
Middle East and North Africa	4	717	66.91	98.8	<0.001
Sub-Saharan Africa	3	568	38.35	96.6	<0.001
Europe and Central Asia	3	710	42.86	99.1	<0.001
Latin America and Caribbean	0
By Population					
Outpatient	12	3127	50.79	98.6	<0.001
Inpatient	9	1947	52.47	99.2	<0.001
By outcome measurement tool					
BDI	5	1972	66.51	99	<0.001
PHQ-9	5	1251	47.82	99.2	<0.001
HADS	4	702	40.04	97.8	<0.001
GDS	2	270	61.98	76.1	0.04
Others (CDS, HAM-D24, PHQ-2, ICD-10, DASS-21)	5	879	45.35	95	<0.001

<https://doi.org/10.1371/journal.pone.0283146.t003>

association (etiology/risk) was used to assess the quality of each study, and the result showed that all six studies had good methodological quality (Table 5).

Concerning the effect size, five studies [31, 34, 38, 44, 51] used beta(β) as effect size to report the association between depression and HRQoL, while one study [43] used Odds Ratio (OR) to indicate the strength of association, with all six studies reporting a statistically significant association between depression and HRQoL. All included studies evaluating the association between depression as the exposure variable and HRQoL as an outcome are profiled in Table 6.

Discussion

The burden of heart failure has increased over the past decade in LMICs with a significant economic impact and alteration in psychological, physical, and emotional well-being [55]. Evidence regarding the burden of depression and its impact on HRQoL in people with HF from LMICs is limited. This review was conducted to estimate the pooled regional prevalence of depression, and to investigate the association between depression and HRQoL among people with heart failure in LMICs. To our knowledge, this is the first review to estimate the current prevalence of depression in people with HF in LMICs. The result of this review revealed that the pooled regional prevalence of depression in people with heart failure in LMICs was 51.5% (95% CI = 39.73, 63.30%, I² = 99.00%). This reinforces the understanding that depression is a common comorbid condition in people with heart failure and is consistent with the findings of the previous systematic review [56]. Our estimate is higher than the global prevalence of

Table 4. Meta-regression analysis of factors associated with heterogeneity.

Heterogeneity source	Coefficients	Standard Error	P-value
Sample size	0.02	0.03	0.49
Publication Year	1.09	1.99	0.58
Quality score	-7.53	10.90	0.49

<https://doi.org/10.1371/journal.pone.0283146.t004>

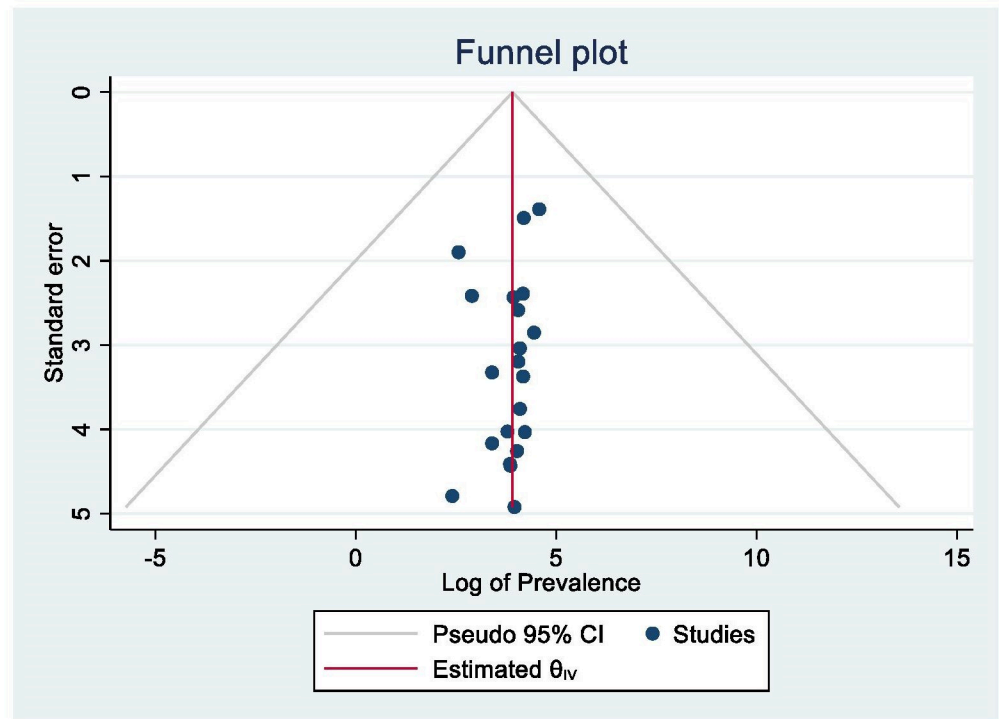


Fig 3. Funnel plot to test the publication bias of the 21 studies.

<https://doi.org/10.1371/journal.pone.0283146.g003>

depression in people with heart failure [15]. The higher prevalence in LMICs might be due to variation in the socio-demographic characteristics of the study participants, discrepancy of instruments, sample size, study setting, and level of economic status [35, 57].

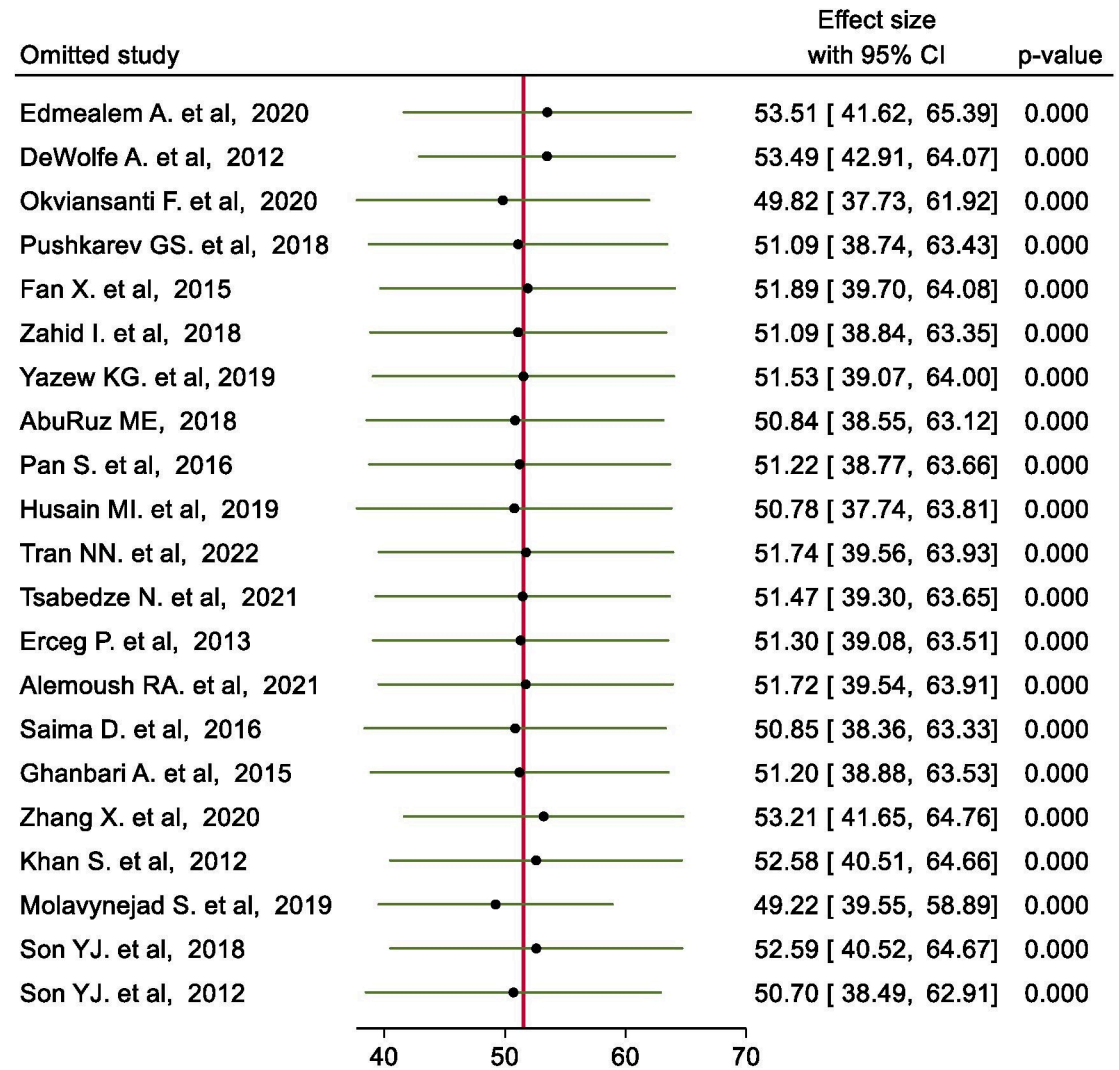
The subgroup analysis of this review showed significant variation in the prevalence of depression among different groups. For instance, the highest (66.9%) and the lowest (38.4%) pooled prevalence was observed in studies from the Middle East and North Africa regions and Europe and Central Asia, respectively. This variation might be due to socioeconomic, health care coverage, sample size and methodological differences among the included studies across the regions. In the present review, the prevalence of depression is higher among inpatients than outpatients. A similar finding was observed in the previous systematic review [58]. This might be due to the severity of the disease or the fact that hospitalized patients are more unwell and have more socioeconomic burdens than outpatients. Consistent with the previous systematic review conducted in China [17], the pooled prevalence of depression in the current review

Table 5. Methodological quality of included studies for association of depression and HRQoL.

Included articles	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Quality score/8
DeWolfe A, et al. [38]	Y	Y	Y	Y	Y	Y	Y	Y	8
AbuRuz ME [34]	Y	Y	Y	Y	Y	Y	Y	Y	8
Tsabedze N, et al. [43]	Y	Y	Y	Y	Y	Y	Y	Y	8
Erceg P, et al. [44]	Y	Y	Y	Y	Y	Y	Y	Y	8
Alemoush RA, et al. [31]	Y	Y	Y	Y	Y	Y	Y	Y	8
Son YJ, et al. [50]	Y	Y	Y	Y	Y	Y	Y	Y	8

Y = yes; N = No; U = Unclear.

<https://doi.org/10.1371/journal.pone.0283146.t005>



Random-effects DerSimonian–Laird model

Fig 4. Result of sensitivity analysis of the 21 studies.

<https://doi.org/10.1371/journal.pone.0283146.g004>

was highest (66.5%) when measured using Beck Depression Inventory (BDI). The lowest prevalence of depression (40.1%) was observed when measured using Hospital Anxiety and Depression Score (HADS). This difference could be due to differences in definitions of depression and cut-off points to diagnose depression across the various scales. However, further research would be helpful to investigate the factors that might lead to such differences across the depression measuring scales.

The association of depression with HRQoL has been reported in several recent studies. The results of this systematic review also demonstrated that six studies among the included studies showed a significant association between depression and HRQoL, although there were insufficient data to estimate the pooled effect size. This finding is similar to previous studies conducted in Europe [59–61]. These studies found that people with heart failure who have depressive symptoms had poor quality of life compared to those who did not have depressive symptoms, and this was also correlated with an increased burden of morbidity and mortality

Table 6. The association between depression and health-related quality of life in people with heart failure.

Author [year of publication]	Country	Sample size	Depression measuring tool	HRQoL measuring tool	Outcome (HRQoL score) based on exposure		Type of comparison	Outcome measure with result	Conclusion
					Depressed	Non-Depressed			
Erceg P, et al. [2013] [44]	Serbia	136	GDS	MLHFQ	57.9±17.6	40.9±17.1	Linear regression	$\beta = 0.41$, P = 0.001	1 unit increase in the depression score was associated with a 0.41 unit increase in MLHFQ QoL score
Tsabedze N, et al. [2021] [43]	South Africa	103	DASS-21	MLHFQ	28 (10–54)	5(0–17)	Logistic regression	OR = 1.04, P = 0.001	Depressed people are 1.04 times more likely to have poor HRQoL as compared to non-depressed one
Son YJ, et al. [2012] [51]	South Korea	134	GDS	MLHFQ	59.4±9.97	45.1±8.8	Linear regression	$\beta = 0.44$, P = 0.001	1 unit increase in the depression score was associated with a 0.44 unit increase in MLHFQ QoL score
DeWolfe A, et al. [2012] [38]	Georgia	314	PHQ-9	MLHFQ,	74.9±11.9	58.4±13.5	Linear regression	$\beta = 1.83$, P = 0.001	1 unit increase in the depression score was associated with a 1.83 unit increase in MLHFQ QoL score
Alemoush RA, et al. [2021] [31]	Jordan	127	HADS	SF-36	Linear regression	$\beta = -0.37$, P = 0.001	1 unit increase in the depression score was associated with a 0.37 unit decrease in SF-36 QoL score
AbuRuz ME [2018] [34]	Jordan	200	HADS	SF-36	Linear regression	$\beta = -0.32$, P = 0.001	1 unit increase in the depression score was associated with a 0.32 unit decrease in SF-36 QoL score

<https://doi.org/10.1371/journal.pone.0283146.t006>

due to HF [51]. The findings of this review highlight the need to understand the factors that contribute to the increased incidence of depression in people with heart failure living in LMICs, as well as the factors that contribute to a poorer quality of life. This will enable targeted interventions and support strategies to be designed and evaluated to improve outcomes for this population.

The findings of this meta-analysis have implications for clinical practice. We included articles published between 2012 and 2022. This cut-off date was decided arbitrarily by the authors to estimate the most recent prevalence rate which should have more relevance to current clinical practice. Determining the most recent prevalence of depression provides up-to-date evidence to develop comorbid depression prevention strategies in this group and ultimately improving HRQoL. Determining the effect of depression on HRQoL can help health-care providers prioritize during their routine clinical practice, which will reduce the overall burden of morbidity and mortality. However, some limitations should be considered for future research. First, the interpretation of the results must be taken cautiously as the meta-analysis had statistically significant heterogeneity across the included studies which was not fully explained by the variables examined. Second, the conclusion of positive association between depression and HRQoL, as reported in six studies, should be interpreted cautiously due to our inability to summarise the pooled effect size.

Conclusion

This systematic review and meta-analysis revealed that one in two people with heart failure in LMICs have comorbid depression. Depression was positively associated with HRQoL in

people with heart failure. Early detection and treatment of depression in people with heart failure is highly recommended to reduce its burden in LMICs. Future research should investigate the factors associated with depression and HRQoL in this population.

Supporting information

S1 Table. Search strategy of databases from January 2012 to August 2022.
(DOCX)

S1 Checklist. PRISMA 2020 checklist.
(DOCX)

Acknowledgments

We would like to thank UTS Faculty of Health librarian, and all authors of the included studies in this systematic review and meta-analysis.

Author Contributions

Conceptualization: Henok Mulugeta, Peter M. Sinclair, Amanda Wilson.

Data curation: Henok Mulugeta, Amanda Wilson.

Formal analysis: Henok Mulugeta.

Investigation: Amanda Wilson.

Methodology: Henok Mulugeta, Peter M. Sinclair, Amanda Wilson.

Software: Henok Mulugeta.

Supervision: Peter M. Sinclair, Amanda Wilson.

Validation: Amanda Wilson.

Writing – original draft: Henok Mulugeta, Peter M. Sinclair, Amanda Wilson.

Writing – review & editing: Henok Mulugeta, Peter M. Sinclair, Amanda Wilson.

References

1. Flora GD, Nayak MK. A brief review of cardiovascular diseases, associated risk factors and current treatment regimes. *Current pharmaceutical design*. 2019; 25(38):4063–84. <https://doi.org/10.2174/1381612825666190925163827> PMID: 31553287
2. Jayaraj JC, Davatyan K, Subramanian S, Priya J. Epidemiology of myocardial infarction. *Myocardial Infarction*. 2018:9–19.
3. Ruan Y, Guo Y, Zheng Y, Huang Z, Sun S, Kowal P, et al. Cardiovascular disease (CVD) and associated risk factors among older adults in six low-and middle-income countries: results from SAGE Wave 1. *BMC public health*. 2018; 18(1):1–13. <https://doi.org/10.1186/s12889-018-5653-9> PMID: 29925336
4. Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. *Journal of the American College of Cardiology*. 2020; 76(25):2982–3021. <https://doi.org/10.1016/j.jacc.2020.11.010> PMID: 33309175
5. Thida M, Asdornwiset U, Thosingha O, Dumavibhat C, Chansatitporn N. Symptom Experience, Symptom Management Strategies, and Health Related Quality of Life among People with Heart Failure. *Pacific Rim International Journal of Nursing Research*. 2021; 25(3):359–74.
6. Lippi G, Sanchis-Gomar F. Global epidemiology and future trends of heart failure. *AME Med J*. 2020; 5(15):1–6.
7. Groenewegen A, Rutten FH, Mosterd A, Hoes AW. Epidemiology of heart failure. *European journal of heart failure*. 2020; 22(8):1342–56. <https://doi.org/10.1002/ejhf.1858> PMID: 32483830

8. Bowen RE, Graetz TJ, Emmert DA, Avidan MS. Statistics of heart failure and mechanical circulatory support in 2020. *Annals of translational medicine*. 2020; 8(13). <https://doi.org/10.21037/atm-20-1127> PMID: 32793672
9. Chadda KR, Fazmin IT, Ahmad S, Valli H, Edling CE, Huang CL, et al. Arrhythmogenic mechanisms of obstructive sleep apnea in heart failure patients. *Sleep*. 2018; 41(9):zsy136. <https://doi.org/10.1093/sleep/zsy136> PMID: 30016501
10. Agbor VN, Ntusi NA, Noubiap JJ. An overview of heart failure in low-and middle-income countries. *Cardiovascular Diagnosis and Therapy*. 2020; 10(2):244. <https://doi.org/10.21037/cdt.2019.08.03> PMID: 32420107
11. Audi G, Korologou A, Koutelekos I, Vasilopoulos G, Karakostas K, Makrygianaki K, et al. Factors Affecting Health Related Quality of Life in Hospitalized Patients with Heart Failure. *Cardiol Res Pract*. 2017; 2017:4690458. <https://doi.org/10.1155/2017/4690458> PMID: 29201489
12. Reavell J, Hopkinson M, Clarkesmith D, Lane DA. Effectiveness of Cognitive Behavioral Therapy for Depression and Anxiety in Patients With Cardiovascular Disease: A Systematic Review and Meta-Analysis. *Psychosom Med*. 2018; 80(8):742–53. <https://doi.org/10.1097/PSY.0000000000000626> PMID: 30281027
13. Freedland KE, Rich MW, Carney RM. Improving quality of life in heart failure. *Current cardiology reports*. 2021; 23(11):1–7. <https://doi.org/10.1007/s11886-021-01588-y> PMID: 34599415
14. Senthilkumar A, Subitha L, Saravanan E, Giriappa DK, Satheesh S, Menon V. Depressive Symptoms and Health-Related Quality of Life in Patients with Cardiovascular Diseases Attending a Tertiary Care Hospital, Puducherry—A Cross-Sectional Study. *Journal of Neurosciences in Rural Practice*. 2021; 12(02):376–81. <https://doi.org/10.1055/s-0041-1724227> PMID: 33927527
15. Moradi M, Doostkami M, Behnamfar N, Rafiemanesh H, Behzadmehr R. Global prevalence of depression among heart failure patients: a systematic review and meta-analysis. *Current problems in cardiology*. 2021:100848. <https://doi.org/10.1016/j.cpcardiol.2021.100848> PMID: 34006389
16. Moradi M, Daneshi F, Behzadmehr R, Rafiemanesh H, Bouya S, Raeisi M. Quality of life of chronic heart failure patients: a systematic review and meta-analysis. *Heart failure reviews*. 2020; 25(6):993–1006. <https://doi.org/10.1007/s10741-019-09890-2> PMID: 31745839
17. Lin X-x, Gao B-B, Huang J-y. Prevalence of depressive symptoms in patients with Heart Failure in China: a meta-analysis of comparative studies and epidemiological surveys. *Journal of Affective Disorders*. 2020; 274:774–83. <https://doi.org/10.1016/j.jad.2020.05.099> PMID: 32664014
18. Allabadi H, Alkaiyat A, Alkhayyat A, Hammoudi A, Odeh H, Shtayeh J, et al. Depression and anxiety symptoms in cardiac patients: a cross-sectional hospital-based study in a Palestinian population. *BMC Public Health*. 2019; 19(1):1–14.
19. Löfström U, Hage C, Savarese G, Donal E, Daubert JC, Lund LH, et al. Prognostic impact of Framingham heart failure criteria in heart failure with preserved ejection fraction. *ESC Heart Failure*. 2019; 6(4):830–9. <https://doi.org/10.1002/ehf2.12458> PMID: 31207140
20. Hage C, Löfström U, Donal E, Oger E, Kaplon-Cieślicka A, Daubert J-C, et al. Do patients with acute heart failure and preserved ejection fraction have heart failure at follow-up: implications of the framingham criteria. *Journal of Cardiac Failure*. 2020; 26(8):673–84. <https://doi.org/10.1016/j.cardfail.2019.04.013> PMID: 31035008
21. Truschel J. Depression definition and DSM-5 diagnostic criteria. 2020.
22. Karimi M, Brazier J. Health, health-related quality of life, and quality of life: what is the difference? *Pharmacoeconomics*. 2016; 34(7):645–9. <https://doi.org/10.1007/s40273-016-0389-9> PMID: 26892973
23. The World Bank. World Development Indicators / The World by Income and Region 2022 [Available from: <https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html>].
24. Aromataris E, Munn Z. JBI manual for evidence synthesis. JBI: Adelaide, Australia. 2020.
25. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International Journal of Surgery*. 2021; 88:105906. <https://doi.org/10.1016/j.ijsu.2021.105906> PMID: 33789826
26. Mulugeta H, Sinclair PM, Wilson A. Prevalence of depression and its association with health-related quality of life in people with heart failure in low-and middle-income countries: a protocol for systematic review. *medRxiv*. 2023:2023.01.20.23284815.
27. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *International journal of evidence-based healthcare*. 2015; 13(3):147–53. <https://doi.org/10.1097/XEB.0000000000000054> PMID: 26317388

28. Nour M, Lutze SA, Grech A, Allman-Farinelli M. The Relationship between Vegetable Intake and Weight Outcomes: A Systematic Review of Cohort Studies. *Nutrients*. 2018; 10(11):1626. <https://doi.org/10.3390/nu10111626> PMID: 30400139
29. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al. Chapter 7: Systematic reviews of etiology and risk JBI; 2020. 2021.
30. Tufanaru C, Munn Z, Stephenson M, Aromataris E. Fixed or random effects meta-analysis? Common methodological issues in systematic reviews of effectiveness. *International journal of evidence-based healthcare*. 2015; 13(3):196–207. <https://doi.org/10.1097/XEB.000000000000065> PMID: 26355603
31. Alemoush RA, Al-Dweik G, AbuRuz ME. The effect of persistent anxiety and depressive symptoms on quality of life among patients with heart failure. *Applied Nursing Research*. 2021; 62:151503. <https://doi.org/10.1016/j.apnr.2021.151503> PMID: 34814999
32. Fan X, Meng Z. The mutual association between depressive symptoms and dyspnea in Chinese patients with chronic heart failure. *European Journal of Cardiovascular Nursing*. 2015; 14(4):310–6. <https://doi.org/10.1177/1474515114528071> PMID: 24634388
33. Yazew KG, Beshah DT, Salih MH, Zeleke TA. Factors Associated with Depression among Heart Failure Patients at Cardiac Follow-Up Clinics in Northwest Ethiopia, 2017: A Cross-Sectional Study. *Psychiatry Journal Print*. 2019; 2019:6892623. <https://doi.org/10.1155/2019/6892623> PMID: 31428624
34. Aburuz ME. Anxiety and depression predicted quality of life among patients with heart failure. *Journal of Multidisciplinary Healthcare*. 2018; 11:367–73. <https://doi.org/10.2147/JMDH.S170327> PMID: 30104881
35. Husain MI, Chaudhry IB, Husain MO, Abrol E, Junejo S, Saghir T, et al. Depression and congestive heart failure: A large prospective cohort study from Pakistan. *Journal of psychosomatic research*. 2019; 120:46–52. <https://doi.org/10.1016/j.jpsychores.2019.03.008> PMID: 30929707
36. Tran NN, Bui VS, Nguyen VH, Hoang TPN, Vo HL, Nguyen HT, et al. Prevalence of depression among heart failure inpatients and its associated socio-demographic factors: Implications for personal-and family-based treatment management in health facilities in Vietnam. *European Review for Medical and Pharmacological Sciences*. 2022; 26(3):879–87. https://doi.org/10.26355/eurrev_202202_27996 PMID: 35179753
37. Edmealem A, Olis CS. Factors Associated with Anxiety and Depression among Diabetes, Hypertension, and Heart Failure Patients at Dessie Referral Hospital, Northeast Ethiopia. *BEHAVIOURAL NEUROLOGY*. 2020; 2020. <https://doi.org/10.1155/2020/3609873> PMID: 32509038
38. DeWolfe A, Gogichaishvili I, Nozadze N, Tamariz L, Quevedo HC, Julian E, et al. Depression and quality of life among heart failure patients in Georgia, Eastern Europe. *Congestive Heart Failure*. 2012; 18(2):107–11. <https://doi.org/10.1111/j.1751-7133.2011.00226.x> PMID: 22432557
39. Okviasanti F, Yusuf A, Kurniawati ND. Anxiety, Depression, and Coping Mechanism Among Outpatients With Heart Failure. *PROCEEDINGS OF THE 4TH INTERNATIONAL CONFERENCE ON SUSTAINABLE INNOVATION 2020—HEALTH SCIENCE AND NURSING (ICOSIHSN 2020)2021*. p. 387–96.
40. Pushkarev GS, Kuznetsov VA, Fisher YA, Soldatova AM, Enina TN. Depression and all-cause mortality in patients with congestive heart failure and an implanted cardiac device. *Turk Kardiyoloji Dernegi Arsivi*. 2018; 46(6):479–87. <https://doi.org/10.5543/tkda.2018.04134> PMID: 30204139
41. Zahid I, Baig MA, Ahmed Gilani J, Waseem N, Ather S, Farooq AS, et al. Frequency and predictors of depression in congestive heart failure. *Indian Heart Journal*. 2018; 70 Suppl 3:S199-S203. <https://doi.org/10.1016/j.ihj.2018.10.410> PMID: 30595257
42. Pan S, Liu Z-W, Lv Y, Song W-Q, Ma X, Guan G-C, et al. Association between neutrophilic granulocyte percentage and depression in hospitalized patients with heart failure. *BMC psychiatry*. 2016; 16(1):1–9. <https://doi.org/10.1186/s12888-016-1161-6> PMID: 27955661
43. Tsabedze N, Kinsey J-LH, Mpanya D, Mogashoa V, Klug E, Manga P. The prevalence of depression, stress and anxiety symptoms in patients with chronic heart failure. *International Journal of Mental Health Systems*. 2021;15.
44. Erceg P, Despotovic N, Milosevic DP, Soldatovic I, Zdravkovic S, Tomic S, et al. Health-related quality of life in elderly patients hospitalized with chronic heart failure. *Clinical Interventions In Aging*. 2013; 8:1539–46. <https://doi.org/10.2147/CIA.S53305> PMID: 24255598
45. Dastgeer S, Babar HAK, Saad AA. Level of Depression in Patients Admitted with Chronic Heart Failure. *Medical Forum Monthly*. 2016; 27(10):61–4.
46. Ghanbari A, Moaddab F, Salari A, Nezhad Leyli EK. Depression status and related factors in patients with heart failure. *Iranian Heart Journal*. 2015; 16(3):22–7.

47. Zhang X, Zou H, Hou D, He D, Fan X. Functional status mediates the association of nutritional status with depressive symptoms in patients with heart failure. *Journal of Advanced Nursing*. 2020; 76(12):3363–71. <https://doi.org/10.1111/jan.14522> PMID: 32932558
48. Khan S, Khan A, Ghaffar R, Awan ZA. Frequency of depression in patients with chronic heart failure. *Journal of Ayub Medical College, Abbottabad: JAMC*. 2012; 24(2):26–9. PMID: 24397045
49. Molayynejad S, Babazadeh M, Zarea K, Ataeeara S. Anxiety, Depression and Quality of Life among Patients with Heart Failure. *JOURNAL OF RESEARCH IN MEDICAL AND DENTAL SCIENCE*. 2019; 7(3):69–77.
50. Son YJ, Seo EJ. Depressive Symptoms and Physical Frailty in Older Adults With Chronic Heart Failure: A Cross-Sectional Study. *Research in Gerontological Nursing*. 2018; 11(3):160–8. <https://doi.org/10.3928/19404921-20180207-01> PMID: 29451933
51. Son Y-J, Song Y, Nam S, Shin W-Y, Lee S-J, Jin D-K. Factors associated with health-related quality of life in elderly Korean patients with heart failure. *Journal of Cardiovascular Nursing*. 2012; 27(6):528–38. <https://doi.org/10.1097/JCN.0b013e31823fa38a> PMID: 22343211
52. Melsen W, Bootsma M, Rovers M, Bonten M. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clinical Microbiology and Infection*. 2014; 20(2):123–9. <https://doi.org/10.1111/1469-0691.12494> PMID: 24320992
53. Higgins JPT. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. *International Journal of Epidemiology*. 2008; 37(5):1158–60. <https://doi.org/10.1093/ije/dyn204> PMID: 18832388
54. Tang J-L, Liu JL. Misleading funnel plot for detection of bias in meta-analysis. *Journal of clinical epidemiology*. 2000; 53(5):477–84. [https://doi.org/10.1016/s0895-4356\(99\)00204-8](https://doi.org/10.1016/s0895-4356(99)00204-8) PMID: 10812319
55. Polikandrioti M, Panoutsopoulos G, Tsami A, Gerogianni G, Saroglou S, Thomai E, et al. Assessment of quality of life and anxiety in heart failure outpatients. *Archives of Medical Science-Atherosclerotic Diseases*. 2019; 4(1):38–46. <https://doi.org/10.5114/amsad.2019.84444> PMID: 31211269
56. Ishak WW, Edwards G, Herrera N, Lin T, Hren K, Peterson M, et al. Depression in heart failure: a systematic review. *Innovations in clinical neuroscience*. 2020; 17(4–6):27. PMID: 32802590
57. Ahmed B, Enam SF, Iqbal Z, Murtaza G, Bashir S. Depression and anxiety: a snapshot of the situation in Pakistan. *International Journal of Neuroscience and Behavioral Science*. 2016; 4(2):32.
58. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure: a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. *Journal of the American college of Cardiology*. 2006; 48(8):1527–37. <https://doi.org/10.1016/j.jacc.2006.06.055> PMID: 17045884
59. Müller-Tasch T, Peters-Klimm F, Schellberg D, Holzapfel N, Barth A, Jünger J, et al. Depression is a major determinant of quality of life in patients with chronic systolic heart failure in general practice. *Journal of cardiac failure*. 2007; 13(10):818–24. <https://doi.org/10.1016/j.cardfail.2007.07.008> PMID: 18068614
60. Aggelopoulou Z, Fotos NV, Chatziefstratiou AA, Giakoumidakis K, Elefsiniotis I, Brokalaki H. The level of anxiety, depression and quality of life among patients with heart failure in Greece. *Applied Nursing Research*. 2017; 34:52–6. <https://doi.org/10.1016/j.apnr.2017.01.003> PMID: 28342624
61. Serafini G, Pompili M, Innamorati M, Iacorossi G, Cuomo I, Della Vista M, et al. The impact of anxiety, depression, and suicidality on quality of life and functional status of patients with congestive heart failure and hypertension: an observational cross-sectional study. *The Primary Care Companion for CNS Disorders*. 2010; 12(6):27352. <https://doi.org/10.4088/PCC.09m00916gry> PMID: 21494352