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Systematic Review

Association of depression, anxiety and quality of life in patients with diabetes mellitus: a systematic review

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ABSTRACT

Diabetes mellitus (DM) is frequently associated with psychological comorbidities such as depression and anxiety, both of which may adversely affect quality of life (QoL). This systematic review aimed to evaluate the association between depression, anxiety, and QoL among patients with DM. A systematic literature search was conducted in PubMed/MEDLINE, Google Scholar, DOAJ, and the Cochrane Library according to PRISMA 2020 guidelines. Only studies that used validated instruments to measure depression, anxiety, and QoL in adult patients with type 1 or type 2 DM were included. Data extraction and risk-of-bias assessment were performed independently by two reviewers using ROBINS-I and RoB 2 tools. A total of 17 studies with 45 to 5,259 participants were included. The rate of depression varied from 8% to 57.8% and the rate of anxiety varied from 9% to 57.9%. QoL scores were consistently reported as being significantly negatively related to depression and anxiety across studies. Included data demonstrated strong negative correlations between wellbeing scores and depression ($p=-0.579$) and anxiety ($p=-0.632$). Significant inverse correlations between depression and QoL ($r=-0.690$, $p<0.001$) and anxiety and QoL ($r=-0.646$, $p<0.001$) were also observed. Many studies indicated that the combination of depression and anxiety was linked to physical, psychological, and social impairments. A reduction in depressive and anxiety symptoms was associated with improvement in the dimensions of QoL in intervention studies. There is a strong correlation between depression and anxiety with patient QoL in individuals with diabetes, highlighting the need to incorporate psychological assessment and mental health management into general diabetes care.

Keywords: Anxiety, Depression, Diabetes mellitus, Quality of life, Type 1 diabetes, Type 2 diabetes, Psychological distress, Systematic review, Comorbidity

INTRODUCTION

Diabetes mellitus (DM) is among the fastest growing chronic diseases of the modern age. As of 2024, the 11th edition of the International Diabetes Federation (IDF) Diabetes Atlas reported that approximately 10% of all adults in the world suffer from diabetes and that the number of people with diabetes is reaching almost 900 million by 2050.[1] It is estimated that in 2024, it caused 3.4 million deaths, killing one person every nine seconds or more than USD 1.015 trillion in global health expenditure, which is a 338% increase over the past 17 years.[2] The psychological impact of diabetes on the affected individuals is enormous and is very seldom recognized beyond the physical and economic costs. The routine management of daily tasks, such as measuring and adjusting blood glucose, dietary adjustments, monitoring for complications, and managing medications, can put the patient at a significantly higher risk of developing mental health-related issues, especially depression and anxiety. The psychological aspects are now recognized as being vital to the effective management of diabetes.

DM has been associated with a wide range of clinical comorbidities, of which depression is one of the most

common and important. A recent systematic review and meta-analysis of 39 studies with a total of 17,486 diabetic patients found a pooled prevalence of 35% (95% CI 30%-41%) of depression, with risk factors being female sex, unemployment, physical inactivity, non-compliance with medication and the presence of diabetes-related complications (e. g. neuropathy, nephropathy).[3] There is evidence that the burden of depression is disproportionately high among people with diabetes compared to the general population with prevalence rates approximately 2-3 times higher.[4] Two separate meta-analyses have confirmed that diabetes is associated with a 15-24% greater risk of depression than in nondiabetic patients.[5] This increased risk is biologically plausible because both diseases have common pathophysiological mechanisms such as hypothalamic-pituitary-adrenal (HPA) axis dysfunction, chronic systemic inflammation and impaired glucose metabolism. This co-occurrence of depression and diabetes therefore establishes a vicious cycle which is self-reinforcing and exacerbates glycemic control and psychological state.

Psychological comorbidities are also important but less well studied in diabetes, and one of these is anxiety disorders. A systematic review examining the prevalence of clinically significant anxiety among adults with diabetes showed that GAD was present in around 14% and a higher number of anxiety symptoms was found in up to 40% of people involved in clinical studies.[6] A bidirectional meta-analysis also showed that diabetic patients are at 41% increased risk for anxiety disorders and patients with pre-existing anxiety disorders are at 19% increased risk for diabetes.[7] Anxiety about diabetes specifically is problematic because it disrupts the ability of patients to engage in the self-care behaviors required for effective diabetes management, such as taking medication, exercising and following a diet.[8]

The psychological burden of depression and anxiety is not just a subjective burden but rather has measurable and clinically meaningful impacts on QoL and glycemic outcomes in diabetic patients. A systematic review of 20 studies conducted by the European Depression in Diabetes (EDID) Research Consortium found that all included studies reported a negative association between depressive symptoms and at least one aspect of QoL in people with diabetes, with those experiencing depressive symptoms showing severely lower diabetes-specific QoL and mild-to-moderate reductions in generic and domain-specific QoL.[9] From a clinical perspective, depression and diabetes distress have been significantly associated with poorer glycemic control ($r=0.23$, 95% CI 0.15 to 0.31, $p<0.001$) and reduced self-care behaviours ($r=-0.19$, 95% CI -0.28 to -0.10, $p<0.001$) in a meta-analysis of 61 studies involving 19,537 participants.[10] Longitudinal evidence further confirms that anxiety and depression in diabetes are bidirectionally and prospectively associated with health-related QoL, with changes in psychological status over time reflecting corresponding changes in QoL outcomes.[11] Together, these results support the idea that the psychological health of the patient is not a separate issue or hindrance in the treatment of diabetes, but is part of the treatment process and plays a central role in optimal diabetes outcomes.

Despite the growing recognition of this triple burden of depression, anxiety, and impaired QoL in people with diabetes, the existing literature remains fragmented, with studies varying considerably in their populations, measurement instruments, study designs, and reported outcomes. While prior reviews have examined depression or anxiety in diabetes in isolation, no comprehensive systematic review has jointly synthesized the evidence on the simultaneous association of both depression and anxiety with QoL across diverse diabetic populations and study designs.

The present systematic review therefore aims to address this gap by systematically reviewing and synthesizing the available evidence on the associations between depression, anxiety, and QoL in adult patients with T1DM and type 2 DM T2DM.

METHODS

Study design

This study was conducted as a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol was registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO) (Registration No. CRD420261375087).

Search strategy

A comprehensive and systematic literature search was conducted across four major electronic databases: PubMed/MEDLINE, Google Scholar, DOAJ (Directory of Open Access Journals), and the Cochrane Library. The search was performed without restrictions on publication date in order to capture the full breadth of available evidence. The search strategy was constructed using a combination of Medical Subject Headings (MeSH) terms and free-text keywords, organized around three conceptual domains: (1) the population: DM, T1DM, T2DM; (2) the exposures: depression, depressive symptoms, depressive disorder, anxiety, anxiety disorder, psychological distress, PHQ-9, BDI, HADS, GAD-7; and (3) the outcome: QoL, health-related QoL, HRQoL, SF-36, EQ-5D, WHOQOL, DQOL. Boolean operators (AND, OR) were used to combine terms within and across domains (Table 1).

In addition to database searching, reference lists of all included studies and relevant systematic reviews identified during the search were manually screened to identify any additional eligible studies not captured by the electronic search.

Table 1: Search strategy and database records.

Database/search engine	Search String (MeSH terms and keywords)	Total records found
PubMed/MEDLINE	(("Type 2 Diabetes Mellitus"(Mesh) OR T2DM(Title/Abstract)) AND (depression (Title/Abstract) OR anxiety (Title/Abstract)) AND ("Quality of Life"(Mesh) OR HRQoL (Title/Abstract) OR "quality of life"(Title/Abstract)))	247
Google Scholar	allintitle: diabetes depression anxiety "quality of life" OR HRQoL	82
DOAJ (Directory of Open Access Journals)	diabetes AND depression AND quality of life AND anxiety	549
Cochrane Library	diabetes mellitus AND depression AND quality of life AND anxiety	448

Eligibility criteria

Studies were included in this review if they met the following pre-specified criteria, defined using the PICOS framework. With respect to population, studies were required to include adult participants aged 18 years or older with a confirmed diagnosis of T1DM or T2DM. Studies focusing on gestational diabetes, prediabetes, or populations with other endocrine disorders were excluded. Regarding the exposure, eligible studies were required to have assessed depression and/or anxiety using validated, standardized psychometric tools such as the Patient Health Questionnaire-9 (PHQ-9), Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale (HADS), Center for Epidemiological Studies Depression Scale (CES-D), Generalized Anxiety Disorder-7 (GAD-7), or Beck Anxiety Inventory (BAI) and to have measured QoL using a validated scale such as the SF-36, EQ-5D, Diabetes QoL (DQOL), or the World Health Organization QoL Brief Version (WHOQOL-BREF). Studies using non-validated instruments were excluded. Regarding study design, randomized controlled trials (RCTs), cohort studies, case-control studies, and cross-sectional studies were all considered eligible. Reviews, meta-analyses, case reports, editorials, and conference abstracts were excluded. Only studies published in the English language were included.

Study selection

All records retrieved from the database searches were imported into EndNote (version 21.0) software and duplicates were removed. The study selection process was conducted in two sequential stages by two independent reviewers working in parallel. In the first stage, titles and abstracts of all retrieved records were screened against the eligibility criteria to exclude clearly irrelevant studies. In the second stage, full texts of all eligible studies were retrieved and assessed in detail for final inclusion or exclusion. Disagreements between the two reviewers were settled by discussion and consensus. The entire study selection process was documented and summarized in the PRISMA 2020 flow diagram (Figure 1). Following the completion of the selection process, a total of 17 studies met all eligibility criteria and were included in the final synthesis.

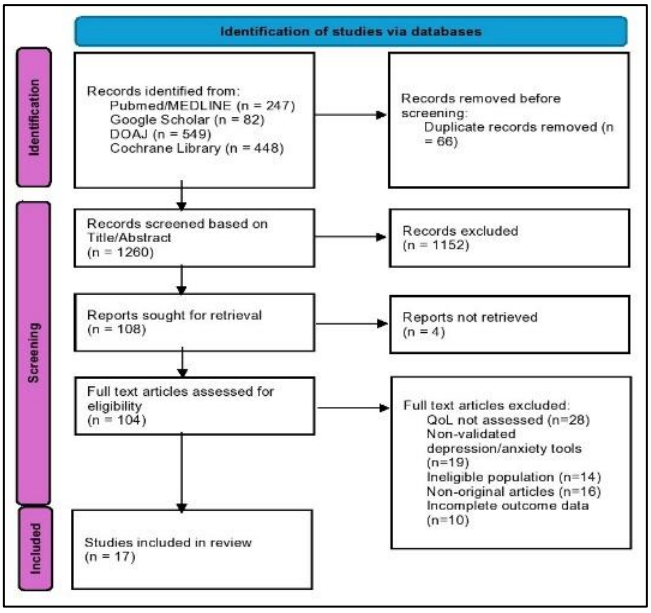

Figure 1: PRISMA chart showing selection and inclusion of studies.

Data extraction

Data from all 17 included studies were extracted independently by two reviewers using a pre-designed, standardized data extraction form. The extraction form was organized across seven domains, capturing 25 pre-specified variables. Study identification variables included the first author and year of publication, country, study design, and setting. Participant demographic variables included total sample size, mean age, sex distribution, type of diabetes, and duration of diabetes since diagnosis. Clinical characteristics recorded included HbA1c level and the presence or absence of diabetes-related complications.

For the assessment of depression, reviewers extracted the name of the validated tool used, the prevalence of depression among participants, and the mean severity score or categorized severity distribution. The same set of variables was extracted for anxiety assessment. QoL data included the instrument used, the overall QoL composite score, and the specific domains assessed.

The primary outcomes of interest were the statistical associations between depression and QoL, and between anxiety and QoL. Where both depression and anxiety were included in the same multivariate model, the combined effect on QoL was also recorded. Any discrepancies between the two reviewers during data extraction were resolved through discussion.

Risk of bias (Quality assessment)

The Cochrane Risk of Bias 2 (RoB 2) tool was used to assess RCTs, while the ROBINS-I tool was applied to non-randomized studies.

Non-randomized studies (ROBINS-I)

The overall risk of bias for most non-randomized studies was low to moderate, and the main concerns were related to confounding, participant selection, and outcome measurement (Figures 2 and 3). Studies including those by Lloyd et al, Mosaku et al, Khuwaja et al, Papelbaum et al, Maia et al, Ramkisson et al, Martino et al, Ranjan et al, Woon et al, Sharma et al, Shen et al, Alwhaibi, Herhaus et al, and Bubulac et al showed moderate risk of bias mainly because of insufficient adjustment for potential confounding variables such as socioeconomic status, comorbidities, duration of diabetes, medication adherence, lifestyle factors, and baseline psychological conditions.[12-25]

Selection bias was generally low since most studies were based on specific outpatient clinic, tertiary hospital, or community-based diabetic populations. But some concerns were found in those studies that were based on convenience sampling, single-center recruitment or relatively small sample sizes, such as Martino et al, Lloyd et al, and Ranjan et al which could hamper the generalizability of results.[12,18,19]

Bias related to classification of exposure and deviations from intended exposure was rated as low in most studies, because depression, anxiety, and QoL were consistently assessed using validated psychometric instruments, such as HADS, PHQ-9, BDI, GAD-7, SDS, SAS, WHOQOL-BREF, EQ-5D, and SF-36.

Missing data bias was generally low; with a few exceptions including poor follow-up reporting in some cross-sectional studies and attrition issues in longitudinal studies, including Liu et al.[11]

The overall risk of outcome measurement bias was judged to be low as the majority of studies employed standardized and validated instruments, both for psychological symptoms and for evaluation of QoL. There is social desirability bias and reporting bias, especially in studies using only patient-reported outcomes, with self-reported questionnaires.

RCTs (RoB 2)

The RCTs in this review had a low-to-moderate risk of bias on most of the assessed domains in general and none of the RCTs were rated as critical risk of bias (Figures 4 and 5). Low risk associated with the randomization process was noted in both the studies by Bogner et al and Abbas et al where both studies reported on random allocation of interventions and similar baseline characteristics across intervention groups.[26,27]

Bias due to deviations from intended interventions was noted as low because interventions such as collaborative depression care and cognitive behavioral therapy (CBT) were implemented in a consistent manner based on study protocols. Outcome measurement bias was also evaluated as low because validated assessment tools (PHQ-9, SHAI, SF-36 and RV-DQOL) were used.

Some concerns regarding missing outcome data were identified in Abbas et al noted some issues with missing outcome data due to participant attrition over time as well as the imbalanced completion rates among the study groups.[27]

There was low risk of selective reporting bias, although low numbers of reported long-term outcomes did lower the certainty of sustainability of interventions and short follow-up duration did lower the certainty of financial sustainability.

Overall, the methodological quality of the randomized evidence used in this review and the quality of the evidence to support the association between depression, anxiety, and QoL in DM patients is of reasonably high reliability.

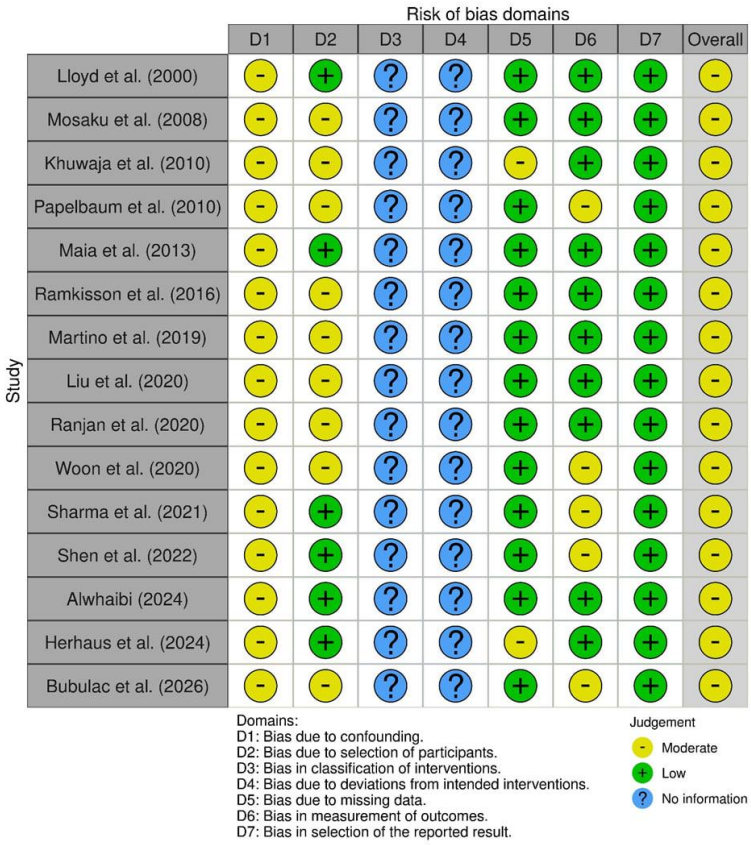

Figure 2: Risk of bias assessment of non-randomized studies using ROBINS-I: traffic light plot.

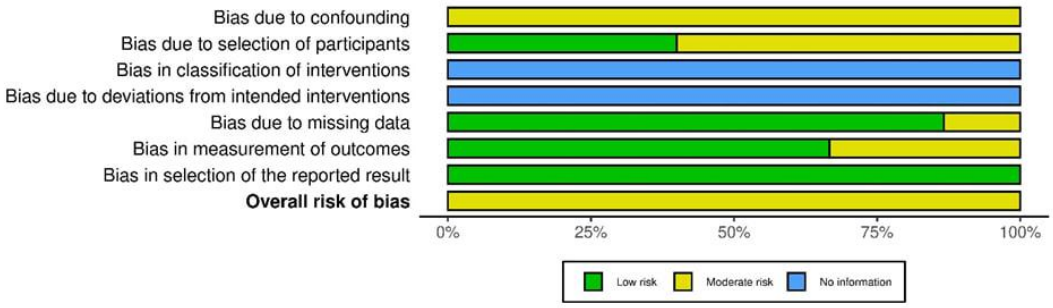

Figure 3: Summary of risk of bias judgments for non-randomized studies (ROBINS-I).

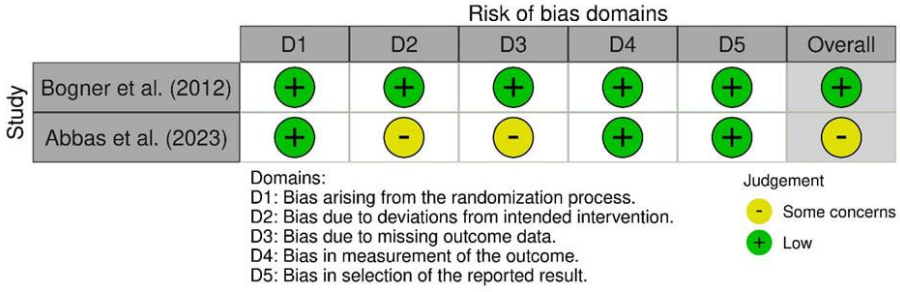

Figure 4: Risk of bias assessment of RCTs using RoB 2: traffic light plot.

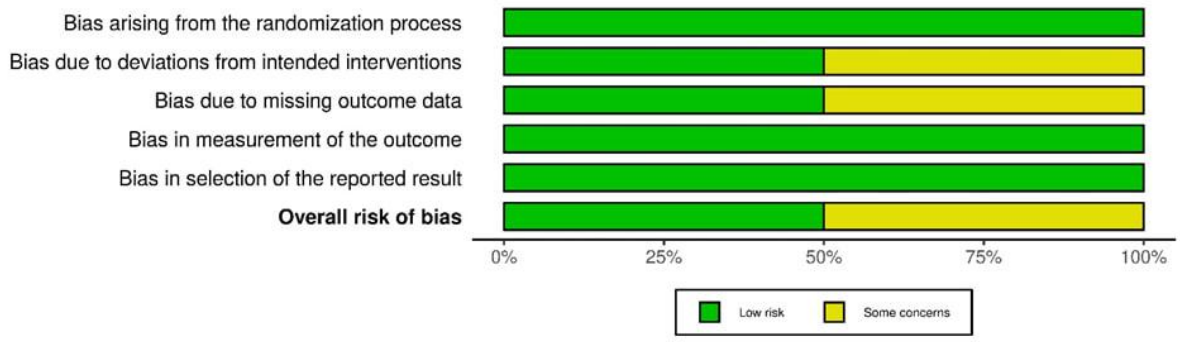

Figure 5: Summary of risk of bias judgments for RCTs (RoB 2).

RESULTS

In total, 17 studies were included in this systematic review, which included cross-sectional, prospective observational, retrospective studies, and RCTs, and were conducted in various geographic areas such as the United Kingdom, Pakistan, Brazil, the United States, South Africa, Italy, the Netherlands, India, Malaysia, Nepal, China, Germany, Romania, and Nigeria. Participant numbers ranged from 45 to 5,259. The studies included were predominantly T2DM while some studies included both T1DM and T2DM patients. Participants were mostly middle aged or elderly with mean ages from 50 to 66 years. Studies included both males and females and, in some cohorts, there was a higher number of females. The duration of diabetes ranged significantly from study to study from 1 day after diagnosis to >19 years. There were variable reports on HbA1c levels and diabetes-related complications including hypertension, cardiovascular disease, neuropathy, nephropathy, retinopathy, renal disease, and obesity. The vast majority of studies were done in outpatient clinics or tertiary care hospital settings, with a smaller proportion in the community or using data from national surveys (Table 2).

The HADS, PHQ-9, BDI/BDI-II, Zung Self-Rating Depression Scale (SDS), and ICD-10 diagnostic codes were the most frequently used instruments to assess depression. The anxiety assessment instruments comprised the Hamilton Anxiety Rating Scale (HAM-A), GAD-7, STAI, Zung Self-Rating Anxiety Scale (SAS) and Short Health Anxiety Inventory (SHAI). Prevalences of depression varied from 8% to 57.8% and anxiety 9% to 57.9% across the studies included. Some studies have reported severity scores [mean] and not prevalence. Moderate to severe depression and anxiety symptoms were frequently reported and some studies have found that patients with diabetes also had comorbid anxiety and depression. RCTs mainly reported the baseline as well as the post-intervention symptom scores, while observational studies often reported prevalence estimates, mean scores, correlations, or categorized symptom severity levels. Reporting format, classification of severity, and psychometric thresholds varied greatly between studies (Table 3).

The most commonly-used QoL tools were short form-36 health survey (SF-36), EuroQol-5 dimensions (EQ-5D), the WHOQOL-BREF, the DQOL, and ADDQoL. There were also a few studies that utilized disease-specific and/or regional questionnaires, including the Revised Version Diabetes QoL questionnaire (RV-DQOL), problem areas in diabetes (PAID), and AsianDQOL. QoL outcomes were presented as total scores, subscale scores, utility index, or stratified scores. Studies differed in their assessment of physical, psychological, social and environmental domains. Several studies found that higher psychological symptom burden or poorer diabetes-related morbidity was associated with poorer QoL scores. Some studies reported pre- and post- intervention measurements of QoL after psychological and/or behavioral interventions. A large variation in scoring systems, reporting formats and dimensions investigated was found, which varied according to study objectives, populations and clinical settings in the literature included (Table 4).

Depression and anxiety showed significant negative correlation with QoL over the included studies in patients with DM. Several studies reported significant inverse correlations between depressive symptoms and QoL outcomes, including Mosaku et al ($r=-0.90$, $p=0.001$), Ramkisson et al ($\rho=-0.579$, $p<0.05$), Shen et al ($r=-0.690$, $p<0.001$), and Bubulac et al ($r\approx-0.55$, $p<0.001$).[13,17,22,25] Anxiety also showed significant negative relationships with QoL, with correlations ranging from moderate to strong, including findings from Ramkisson et al ($\rho=-0.632$, $p<0.05$], Shen et al ($r=-0.646$, $p<0.001$), and Bubulac et al ($r\approx-0.48$ to -0.46, $p<0.001$).[17,22,25] Depression and anxiety were identified as independent predictors of impaired QoL in several studies, and bidirectional associations between psychological symptoms and health-related QoL were also reported. Symptoms of depression and anxiety were often linked to poor QoL outcomes, low well-being and poor physical, psychological and social functioning. Results of intervention studies also showed that QoL measures improved with decreases in depression and anxiety scores after CBT or collaborative care interventions (Table 5).

Table 2: Characteristics of included studies.

Authors (Year)	Countries	Study design	Sample size	Diabetes type	Mean age / age range (in years)	Female	Diabetes duration (in years)	HbA1c	Major complications reported
Lloyd et al 2000[12]	UK	Cross-sectional	109	T1DM/ T2DM	34–61	34-48%	8-16	≥9% in subset	Retinopathy, neuropathy, nephropathy, CAD
Mosaku et al 2008[13]	Nigeria	Cross-sectional	80 diabetics	T1DM/ T2DM	54.6	53.7%	8	FBG 7.1 mmol/L	HTN, CVD, renal disease, ulcers
Khuwaja et al 2010[14]	Pakistan	Cross-sectional	889	T2DM	Mostly >50	57.5%	>5 common	NR	HTN, IHD
Papelbaum et al 2010[15]	Brazil	Cross-sectional	100	T2DM	53.5	39%	12.4	8.7±2.2%	NR
Bogner et al 2012[26]	USA	RCT	180	T2DM	57	~68%	10-12	~7.1%	NR
Maia et al 2013[16]	Brazil	Cross-sectional	210	T1DM/ T2DM	59.4	61.4%	NR	NR	NR
Ramkisson et al 2016[17]	South Africa	Cross-sectional	401	T2DM	53.7	60.6%	10.3	NR	Severe complications excluded
Martino et al 2019[18]	Italy	Cross-sectional	45	T2DM	65.3	70%	11.6	7.1±0.9%	Micro/ macrovascular disease
Liu et al 2020[11]	Netherlands	Longitudinal	131	T1DM/ T2DM	54	49.6%	19.4	NR	NR
Ranjan et al 2020[19]	India	Cross-sectional	123	T2DM	50.2	13%	88.7 months	NR	NR
Woon et al 2020[20]	Malaysia	Cross-sectional	300	Mostly T2DM	63	47%	14	7.6%	HTN, dyslipidemia, renal disease
Sharma et al 2021[21]	Nepal	Cross-sectional	296	T2DM	59.5	59.5%	≥3	NR	Multiple comorbidities
Shen et al 2022[22]	China	Cross-sectional	620	T2DM	Mostly >50	47.9%	NR	8.15±2.04%	HTN, neuropathy, retinopathy
Abbas et al 2023[27]	Pakistan	RCT	90	T2DM	23-50	55.6%	3-5 common	NR	HTN, obesity
Alwhaibi 2024[23]	USA	Retrospective cross-sectional	5,259	T2DM	52.9	49.3%	NR	NR	NR
Herhaus et al 2024[24]	Germany	Cross-sectional survey	2,386	Mixed diabetes	66.2	56%	NR	NR	NR
Bubulac et al 2026[25]	Romania	Cross-sectional	400	T1DM/ T2DM	54.2	55.2%	9.8	NR	NR

*CAD: coronary artery disease, CVD: cardiovascular disease, FBG: fasting blood glucose, HbA1c: glycated hemoglobin, HTN: hypertension, IHD: ischemic heart disease, NR: not reported, RCT: randomized controlled trial, T1DM: type 1 diabetes mellitus, T2DM: type 2 diabetes mellitus.

Table 3: Depression and anxiety assessment in included studies.

Authors (Year)	Depression tool	Depression findings	Anxiety tool	Anxiety findings
Lloyd et al 2000[12]	HADS-D	Moderate-severe depression: 8%; mild: 17%	HADS-A	Moderate-severe anxiety: 25%; mild: 18%
Mosaku et al 2008[13]	SDS	Depression in diabetics: 20%	STAI-1	Anxiety in diabetics: 20%
Khuwaja et al 2010[14]	HADS	Depression: 43.5%	HADS	Anxiety: 57.9%
Papelbaum et al 2010[15]	BDI	Mean BDI: 15.2±10.6	NR	NR
Bogner et al 2012[26]	PHQ-9	Baseline score ~10; all participants depressed	NR	NR
Maia et al 2013[16]	HADS-D/ MINI	Overall depression: ~45.2%	HADS-A	Overall anxiety: ~51.9%
Ramkisson et al 2016[17]	HADS-D	Depression features: 46%	HADS-A	Anxiety features: 32%
Martino et al 2019[18]	BDI-II	Median BDI-II: 13	HAM-A	Median HAM-A: 25
Liu et al 2020[11]	HADS-D	Depression: 19.8–23.4%	HADS-A	Anxiety: 27.5–27.9%
Ranjan et al 2020[19]	HADS-D	Depression above cutoff: 17.1%	HADS-A	Anxiety above cutoff: 10.6%
Woon et al 2020[20]	BDI-II	Depression: 20%	GAD-7	Anxiety: 9%
Sharma et al 2021[21]	PHQ-9	Depression: 57.8%	GAD-7	Anxiety: 49.7%
Shen et al 2022[22]	SDS	Depression: 41.3%	SAS	Anxiety: 45.0%
Abbas et al 2023[27]	PHQ-9	Pre-intervention mean: 15.85	SHAI	Pre-intervention mean: 29.81
Alwhaibi 2024[23]	ICD-10-CM codes	Depression: ~9.7%	ICD-10-CM codes	Anxiety: ~8.4%
Herhaus et al 2024[24]	PHQ-9	Mean PHQ-9: 5.80	GAD-7	Mean GAD-7: 4.03
Bubulac et al 2026[25]	BDI	Mean BDI: 14.7±11.4	STAI-Y1/STAI-Y2	Anxiety scores significantly higher in DM group

*BDI: Beck depression inventory, BDI-II: Beck depression inventory-II, HADS: Hospital Anxiety and Depression Scale, HADS-A: Hospital Anxiety and Depression Scale-Anxiety subscale, HADS-D: Hospital Anxiety and Depression Scale–Depression subscale, ICD-10-CM: International Classification of Diseases 10th Revision Clinical Modification, MINI: Mini International Neuropsychiatric Interview, NR: not reported, PHQ-9: Patient Health Questionnaire-9, SAS: Zung Self-Rating Anxiety Scale, SDS: Zung Self-Rating Depression Scale, SHAI: Short Health Anxiety Inventory, STAI: State-Trait Anxiety Inventory, STAI-Y1: State-Trait Anxiety Inventory Form Y1, STAI-Y2: State-Trait Anxiety Inventory Form Y2.

Table 4: QoL assessment and outcomes in included studies.

Authors (years)	QoL instrument	QoL domains/measures	Main QoL findings
Lloyd et al 2000[12]	DQOL	Satisfaction, impact, worry	Lower QoL associated with psychological distress
Mosaku et al 2008[13]	WHOQOL-BREF	Physical, psychological, social, environmental	Lower QoL in diabetic participants compared with controls
Khuwaja et al 2010[14]	EQ-5D	Mobility, self-care, usual activities, pain/discomfort, anxiety/depression	Reduced QoL scores in participants with anxiety/depression
Papelbaum et al 2010[15]	SF-36	Physical and mental health domains	Lower SF-36 scores observed with depressive symptoms
Bogner et al 2012[26]	SF-12	Physical and mental component summary	QoL improved following collaborative care intervention
Maia et al 2013[16]	WHOQOL-BREF	Physical, psychological, social, environmental	Significant impairment in psychological and physical domains
Ramkisson et al 2016[17]	DQOL	Diabetes-related QoL domains	Poorer QoL associated with depressive and anxiety symptoms
Martino et al 2019[18]	ADDQoL	Diabetes-specific life impact	Reduced QoL in participants with higher psychological burden
Liu et al 2020[11]	EQ-5D	Health utility and self-rated health	Lower QoL associated with anxiety and depressive symptoms
Ranjan et al 2020[19]	QOLID	Role limitation, physical endurance, emotional health	Emotional health and general health domains commonly affected
Woon et al 2020[20]	AsianDQOL	Diet, memory, finance, energy, relationships	QoL impairment observed in multiple diabetes-related domains
Sharma et al 2021[21]	WHOQOL-BREF	Physical, psychological, social, environmental	Poor QoL reported across all major domains
Shen et al 2022[22]	EQ-5D-5L	Mobility, self-care, usual activities, pain/discomfort, anxiety/depression	Lower health utility scores with psychological symptoms
Abbas et al 2023[27]	RV-DQOL	Satisfaction and diabetes-related concerns	Improved QoL after CBT intervention
Alwhaibi 2024[23]	HRQoL measures	General health-related QoL	Lower HRQoL reported in participants with depression/anxiety
Herhaus et al 2024[24]	PAID / WHO-5	Diabetes distress and emotional well-being	Emotional well-being scores reduced in psychologically distressed patients

Continued.

Authors (years)	QoL instrument	QoL domains/measures	Main QoL findings
Bubulac et al 2026[25]	SF-36	Physical and mental health domains	Significant reduction in mental health-related QoL

*ADDQoL: Audit of diabetes-dependent QoL, AsianDQOL: Asian Diabetes QoL, CBT: cognitive behavioral therapy, DQOL: Diabetes QoL Measure, EQ-5D: EuroQol 5-Dimensions, EQ-5D-5L: EuroQol 5-Dimensions 5-Levels, HRQoL: health-related QoL, PAID: Problem Areas in Diabetes, QOLID: QoL Instrument for Indian Diabetes Patients, RV-DQOL: Revised Version Diabetes QoL questionnaire, SF-12: Short Form-12 Health Survey, SF-36: Short Form-36 Health Survey, WHO-5: WHO-5 Well-Being Index.

Table 5: Association between depression, anxiety, and QoL in included studies.

Authors (years)	Depression-QoL association	Anxiety-QoL association	Combined depression and anxiety effect on QoL
Lloyd et al 2000[12]	QoL not assessed; depression associated with poor glycemic control in men (p=0.02; R^2=0.16)	QoL not assessed; anxiety associated with glycemic control (NS)	Combined effect observed on glycemic control (R^2=0.19)
Mosaku et al 2008[13]	Significant negative correlation with well-being (GWB r=−0.90, p=0.001)	Significant negative correlation with well-being (GWB r=-0.45, p=0.001)	Comorbid anxiety and depression associated with reduced well-being
Khuwaja et al 2010[14]	Depression associated with female sex, older age, HTN, IHD, and metabolic factors	Anxiety associated with physical inactivity, HTN, IHD, and metabolic factors	QoL not measured
Papelbaum et al 2010[15]	BDI positively correlated with PAID score (r=0.503, p<0.001)	NR	NR
Bogner et al 2012[26]	NR	NR	NR
Maia et al 2013[16]	Depression strongly associated with impaired QoL in T1DM and T2DM (OR=8.42-10.27, p<0.0001)	Anxiety strongly associated with impaired QoL (OR=18.19-19.60, p<0.0001)	Depression and anxiety comorbidity significantly associated with poor QoL
Ramkisson et al 2016[17]	WHO-5 negatively correlated with HADS-D (ρ=−0.579, p<0.05)	WHO-5 negatively correlated with HADS-A (ρ=-0.632, p<0.05)	Both independently associated with reduced well-being
Martino et al 2019[18]	BDI-II independently predicted lower MCS (β=-0.48, p=0.02)	HAM-A independently predicted lower PCS and MCS	Anxiety and depression explained unique HRQoL variance
Liu et al 2020[11]	Bidirectional negative association with EQ-5D (B=-0.03, p<0.001)	Bidirectional negative association with EQ-5D (B=-0.03, p<0.001)	Combined symptoms associated with lower QoL across EQ-5D dimensions
Ranjan et al 2020[19]	Negative correlations with physical, psychological, and social QoL domains	Negative correlations with physical and psychological domains	Both negatively associated with physical and psychological QoL
Woon et al 2020[20]	Higher physical and social QoL protective against depression	Higher psychological QoL protective against anxiety	Co-morbid anxiety and depression associated with lower QoL across domains
Sharma et al 2021[21]	NR	NR	NR
Shen et al 2022[22]	Strong negative correlation with QoL (r=-0.690, p<0.001)	Strong negative correlation with QoL (r=-0.646, p<0.001)	31.6% had concurrent anxiety and depression symptoms
Abbas et al 2023[27]	CBT significantly reduced PHQ-9 scores with improved QoL	CBT significantly reduced SHAI scores with improved QoL	Both symptoms improved following CBT intervention
Alwhaibi 2024[23]	Depression associated with lower MCS and PCS scores	Anxiety associated with lower MCS and PCS scores	Combined depression and anxiety showed strongest reduction in HRQoL
Herhaus et al 2024[24]	Lower EQ-5D-5L mediated association between diabetes and depression	Lower EQ-5D-5L mediated association between diabetes and anxiety	HRQoL fully mediated diabetes-depression and diabetes-anxiety associations
Bubulac et al 2026[25]	Moderate negative correlation between BDI and EQ-5D VAS (r≈−0.55, p<0.001)	Moderate negative correlations for state and trait anxiety (r≈-0.48 to -0.46, p<0.001)	Psychological variables remained strongest HRQoL correlates

*BDI: Beck Depression Inventory, CBT: cognitive behavioral therapy, EQ-5D: EuroQol 5-Dimensions, EQ-5D-5L: EuroQol 5-Dimensions 5-Levels, GWB: General Well-Being, HADS-A: Hospital Anxiety and Depression Scale-Anxiety subscale, HADS-D: Hospital Anxiety and Depression Scale–Depression subscale, HAM-A: Hamilton Anxiety Rating Scale, HRQoL: health-related quality of life, HTN: hypertension, IHD: ischemic heart disease, MCS: Mental Component Summary, NR: not reported, OR: odds ratio, PAID: Problem Areas in Diabetes, PCS: Physical Component Summary, PHQ-9: Patient Health Questionnaire-9, PWB: Positive Well-Being, SHAI: Short Health Anxiety Inventory, WHO-5: World Health Organization-Five Well-Being Index.

DISCUSSION

The findings of this systematic review are consistent and strong, showing a negative correlation between depression, anxiety and QoL in patients with DM in diverse clinical settings across 17 studies from 14 countries. The prevalence of depression and anxiety in the studies included ranged from 8% to 57.8% and 9% to 57.9%, respectively, and depression and anxiety were related to the decline in each of the four QoL domains, physical, psychological, social and environmental, independently. There were negative correlations with psychological symptom severity and QoL on several validated instruments such as EQ-5D, SF-36, WHOQOL-BREF, and DQOL. However, the association remained clinically significant in intervention trials that included CBT and collaborative care models as well as reductions in depressive and anxiety symptoms, which further strengthened the clinical relevance of this association. Overall, these results highlight the significant triple burden of diabetes, depression and anxiety and the need for integrated psychological treatment in standard diabetes care.

The rates for depression and anxiety in the current review are comparable to previous systematic reviews. The high degree of variance is a result of considerable diversity in study populations, geographic settings, psychometric measures used, and thresholds for diagnosis. This variability reflected that reported by the European Depression in Diabetes (EDID) Research Consortium, which showed that depressive symptoms were found in all the studies included in the analysis, regardless of the instrument used.[9] A recent meta-analysis of 61 studies with 19537 participants further demonstrated that depression and diabetes had significant relationships with glycemic poor control and lower self-care behaviors indicating the downstream effects of psychological distress on metabolic and function outcomes in diabetic patients.[10] Some studies in this review found strong associations between diabetes and mental health. For example Mosaku et al (r=-0.90), Shen et al (r=-0.690), and Bubulac et al (r≈-0.55). These connections are much stronger than those found in the general population.[13,22,25] This is likely because managing chronic diabetes is very stressful. In developing countries many people with diabetes also have depression or anxiety. For example in Pakistan Khuwaja et al found that 57.9% of people with diabetes had anxiety and 43.5% had depression.[14] In Nepal, Sharma et al found that 57.8% of people with diabetes had depression.[21] In China Shen et al found that 41.3% of people, with diabetes had depression.[22] These countries have a psychological burden. A study of countries found that being female having complications and having a low socioeconomic status were linked to depressive symptoms.[28]

The negative correlation between psychological symptoms and QoL reported across all the included studies is not surprising and can be explained by a clear pathophysiological framework that relates depression, anxiety and diabetes. While distinct, both conditions have overlapping biological mechanisms such as dysregulation of hypothalamic-pituitary-adrenal (HPA) axis function, chronic systemic inflammation and impaired neurotransmitter signaling, leading to a vicious cycle that exacerbates psychological distress through the effects on glycemic control and worsens metabolic control through the effects on psychiatric symptoms.[29] A comprehensive review showed that the odds of having major depressive disorder (MDD) are 38% to 67% higher in people with T2DM and the odds of having T2DM are 15% to 33% higher in people with MDD; chronic low-grade inflammation was identified as one of the common mechanisms linking MDD and T2DM.[30] Recent studies have also brought up other emerging immune-inflammatory pathways that could serve as further links between T2DM and mood disorders such as toll-like receptor 4 (TLR4) signaling, advanced glycation end-products (AGEs) and gut-brain axis dysfunction.[31] In addition, diabetes has been independently linked with the psychological impact of vascular complications such as neuropathy, nephropathy and retinopathy. A large cross-sectional study of 6,960 diabetes patients was reported as having significant association between diabetic peripheral neuropathy, neuropathic pain, and impact on both mental health and QoL.[32] Likewise, research in diabetic retinopathy has shown that there is a striking increase in the prevalence of emotional disturbances in patients with severe retinopathy and advanced retinopathy status [higher anxiety and depression scores] which further reduces health-related QoL as a result of visual impairment and fear of blindness.[33] This relationship between diabetes, depression, and anxiety can therefore be seen as a psychosocial response, as well as a neuroendocrine and inflammatory process that needs to be addressed simultaneously from both biological and psychological perspectives.[34]

The results of the intervention studies in this review, specifically the studies conducted by Abbas et al and Bogner et al emphasize the therapeutic effect of the structured psychological interventions for enhancing QoL of diabetic patients with depression and anxiety.[26,27] A scoping review of RCTs on CBT-based interventions for T2DM provided similar results, with most studies showing benefits in reducing depressive symptoms, diabetes-related distress and overall QoL.[35] Systematic review results from a review of 28,307 participants also showed that CBT and collaborative care and health education models both showed significant improvements in depression outcomes, with CBT showing a consistent improvement across all systematic reviews, and collaborative care showing similar improvements.[36] A previous experimental study also showed that group-based CBT significantly decreased depression symptoms ($F=72.17$, $p<0.001$) and increased QoL ($F=8.82$, $p<0.05$) among women who suffered from T2DM.[37] Furthermore, a more recent RCT that investigated the effects of CBT-based intervention in T2DM patients with metabolic

syndrome found significant benefits in depression symptoms, levels of anxiety, diabetes self-care behaviors, and QoL, thus demonstrating the multidimensional advantages of psychotherapeutic interventions.[38]

The longitudinal and bidirectional evidence found in this review, especially from Liu et al and Herhaus et al is particularly compelling as this is beyond a mere cross-sectional association.[11,14] Liu et al found that the changes in scores for depression and anxiety were bidirectionally associated with changes in the EQ-5D utility scores, and according to Herhaus et al lower HRQoL fully mediated the associations between diabetes and depression and anxiety scores.[11,24] The overall literature supports these bidirectional effects: a meta-analysis revealed that people with pre-existing anxiety disorders are 19% more likely to develop diabetes, and people with diabetes are 41% more likely to develop anxiety disorders.[39] Alwhaibi found that the association between depression and anxiety had an additive and potentially synergistic effect on health-related QoL as a combination of depression and anxiety resulted in the largest decrease in both mental component summary (MCS) and Physical Component Summary (PCS) scores.[23] The authors of this review also found that mental health outcomes in T2DM were compromised during and before the COVID-19 pandemic, with comorbid anxiety and depression being one of the strongest predictors of poor psychological health outcomes.[40] Further evidence of the compounded effect of psychological comorbidity was reported by Maia et al (OR=18.19-19.60) who reported the notably high odds ratios associated with impaired QoL in individuals with both anxiety and depression, and a systematic review of patient empowerment in T2DM reported significant inverse associations between self-efficacy and perceived competence with anxiety and depression, suggesting that psychological resilience may provide a buffer against impaired QoL.[16,41]

The present review's results regarding depression and anxiety symptoms in females, older population and complication burdened groups are consistent with data from various observational sources from a sociodemographic perspective. Female sex was often found to be a stand-alone risk factor for depression and anxiety among diabetics, and this was considered as a result of hormonal sensitivity, higher care giving responsibilities and socioeconomic disadvantage among the women, especially in the low- and middle-income country settings.[14] A cross-sectional study of 583 diabetic patients in India also found that lower socioeconomic status and higher symptom severity were both associated with lower levels of life satisfaction; women also experienced higher depression and symptom burden than men.[42] The clinical significance of these findings is great. Psychological screening and management continue to be vastly under-used in the day-to-day management of diabetes: in England, only 10% of all diabetes departments used any psychological screening tool and only 80% had guidelines for managing patients with psychological comorbidities.[43] The American Diabetes Association (ADA) Standards of Care now state that 1 in 4 people with diabetes is suffering from depression and strongly recommend regular psychological screening of all people with diabetes, highlighting the need for a multidisciplinary, integrated approach to care.[44] A systematic review of 64 controlled trials also found that overall, integrated mental health/diabetes care models resulted in sustained improvement in depression and anxiety health outcomes, decreased diabetes specific distress, and modest, but statistically meaningful, decrease in HbA1c when compared to usual care.[45] The findings as a whole support the need for systematic integration of validated screening tools (PHQ-9, GAD-7 and HADS) and structured pathways for psychological referral into all diabetes care settings, especially in settings with lower health system resources where the number of people requiring mental health services and the number of people receiving services is highest.

Strengths and limitations

There are a number of important strengths of this systematic review. It systematically reviewed the results of 17 studies across a range of countries and healthcare contexts, securing wide international coverage and enhancing the scope for generalizability of results. A variety of study designs, including cross-sectional studies, longitudinal studies, retrospective analysis and RCTs were considered in the review, enabling assessment of both observational associations and intervention outcomes. Methodological rigor and transparency were improved by standardized PRISMA guidelines and a prospectively registered PROSPERO protocol. In addition, the majority of the studies included employed validated psychometric or quality-of-life questionnaires, which increased the reliability of the reported results. There are a few limitations as well. There was a lot of variation in the sample characteristics, psychometric instruments, instruments to measure QoL, severity classification, and reporting methods between studies, making direct comparisons between them difficult and making meta-analysis impossible. Causality could not be determined in most of the studies included because of their cross-sectional design. Another potential source of variation may have been the self-reported questionnaires used, potentially leading to reporting or measurement bias. Additionally, only English-language studies were considered, which could have led to language and publication bias.

Future research and clinical implications

Large-scale prospective cohort studies and well-designed RCTs would be beneficial to better elucidate the temporal and causal relationships between depression, anxiety, and diabetes and their impact on QoL. The development of useful and more standardized psychometric and QoL assessment tools would aid comparability between studies and future meta-analyses. There needs to be further

research on the impact of diabetes duration, glycemic control, diabetes complications, socioeconomic factors, and cultural factors on psychological outcomes as well. The results of this review have clinical implications for routine psychological screening for diabetes care, particularly the use of validated questionnaires like the PHQ-9, GAD-7 and HADS. Early diagnosis and treatment of depression and anxiety can help promote better outcomes for diabetes and treatment adherence as well as better QoL. Psychological counseling, CBT, and behavioral interventions may be of further benefit for the psychological distress in diabetic patients in multidisciplinary care models.

CONCLUSION

This systematic review showed that there was a consistent correlation between depression, anxiety and poor QoL in DM patients in various populations and health care systems. The studies included in this review revealed that depressive and anxiety symptoms were prevalent in diabetic individuals and were often correlated with deterioration of physical, psychological and social health status. Several studies found a significant negative correlation between psychological symptom severity and the QoL. Longitudinal and intervention studies confirmed bidirectional links between mental health and health-related QoL. Depression and anxiety were also demonstrated to both independently and together lead to decreased well-being, decreased functioning and decreased health utility scores. The evidence from the studies presented is consistent, despite the different study designs and assessment tools used, in favor of incorporating psychological assessment and mental health management into the routine care of individuals with diabetes. Targeted psychological interventions and early diagnosis could have important implications for both mental health and QoL in people with DM.

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