Review Article

The Bidirectional Relationship between Type 1 Diabetes and Depression according to Patient Health Questionnaire: A Systematic Review

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ABSTRACT

The aim of this study is to examine the bidirectional type 1 diabetes (T1D) & depression relationship, using the Patient Health Questionnaire (PHQ) to measure depressive symptomatology. A total of 760 pertinent publications were found after a comprehensive search across four databases. 375 full-text publications were examined after duplicates were eliminated using Rayyan QCRI and relevance was checked; seven studies finally satisfied the requirements for inclusion. We included seven studies with a total of 2518 patients, and less than half of them 1112 (44.1%) were males. Emotional distress from managing T1D, along with chronic hyperglycemia, fatigue, and related complications, intensifies mental health challenges. Sociodemographic factors like age and disease duration, as well as biological mechanisms such as inflammation, further influence this interplay. These findings underline the importance of integrated care that simultaneously addresses both physical and psychological health in T1D patients. This review emphasizes the bidirectional relationship between T1D and depression, where depressive symptoms worsen diabetes outcomes, and managing T1D exacerbates mental health challenges. Using the PHQ as a reliable tool to measure depression, the findings highlight the need for an integrated treatment approach that includes routine depression screening, psychological therapies, and collaborative care among clinicians. Future research should prioritize longitudinal studies to explore causality and understand the biological mechanisms linking T1D and depression.

Keyword: Acute stroke; Management; Pre-hospital delay; Systematic review.

Introduction

Adults with T1D are more likely to experience depression than the general population [1], and those who experience depression also typically have lower health outcomes [2]. T1D is becoming more common in younger people [3]. When compared to the background rate, the mortality rate for people with T1D is four times higher for men and nine times higher for women [4].

It is appropriate to inquire about the prevalence of depression in younger patients and its effects on their physical and mental health for these two reasons. High personal expenses and significant financial ramifications for health services are associated with such issues.

Access this article online	
Quick Response Code:	Website: www.smh-j.com
	DOI: 10.54293/smhj.v5i1.125

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Received: 25 Nov 2024 **Accepted:** 10 Dec 2024

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Please cite this article as: Al-Anzi MA, Bakhsh JI, Alrehaili LAM, Al-Johani AS, Aldalbahi SSG, Aljohara Abdulwahhab S Alwahhabi, Alqahtani AS, Saud Sheher Mohammed Alkahtani, Almansour ABM, Aljahdali ESO. The Bidirectional Relationship between Type 1 Diabetes and Depression according to Patient Health Questionnaire: A Systematic Review. SMHJ [Internet]. 2025;5(1):50-58.

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The etiology of inadequate metabolic control during adolescence and early adulthood has been linked to a number of factors, including physiological (insulin resistance increases insulin requirements) [5], social (family conflict) [6], and individual (risk taking and co-morbid psychological conditions like anxiety and depression) [7]. According to research, depressed symptoms can be more common in the initial years following diagnosis [8], when the "honeymoon period" is over, and beyond ten years [9]. Due to different diagnostic methods for evaluating depression, there have also been observed discrepancies in the prevalence of depression among people with diabetes as compared to those without. Instead of fulfilling the diagnostic criteria for depression based on a systematic clinical assessment, elevated scores on self-report measures, like the PHQ-9, may indicate diabetes distress or depressive symptoms [10]. The bidirectional association between T1D and depression is a public health issue that should not be overlooked, given the effects it has on the quality of life, disease control and healthcare economics. T1D is an autoimmune, chronic disease with lifelong management and often with physical, emotional and psychological burden. Depression, in turn, can have detrimental effects on self-care behaviors, glycemic control, and treatment adherence, ultimately worsening T1D complications. Recognition of this interaction is crucial as T1D patients are at a greater risk of developing depressive symptoms compared with the general population, and depression in turn has been shown to influence physiological and behavioural responses, which in turn can exacerbate diabetes outcomes [9, 10]. Despite the clinical and social relevance of this issue, little is known to date about a comprehensive integration of the evidence concerning the bidirectional impact of these conditions. The PHQ is a common instrument for screening and measuring depressive severity in clinical and experimental environments. Examining the evidence through a systematic review will clarify how depression, as measured by PHQ, interacts with T1D over time. This knowledge is of fundamental importance for guiding interventions to enhance not only mental health but also diabetes status. The aim of the present systematic review is to examine the bidirectional T1D & depression relationship, in particular by examining the use of the PHQ to measure depressive symptomatology.

Methods

Search strategy: The PRISMA and GATHER criteria were adhered to in the systematic review. To locate pertinent research on the bidirectional T1D & depression relationship, in particular by examining the use of the PHQ. Four electronic databases were searched by the reviewers: SCOPUS, Web of Science, Cochrane, and PubMed. We eliminated any duplicates and uploaded all of the abstracts and titles that we could find using electronic searches into Rayyan. After that, all of the study texts that met the requirements for inclusion based on the abstract or title were gathered for a thorough examination. Two reviewers independently assessed the extracted papers' suitability and discussed any discrepancies.

Study population—selection. The PEO (Population, Exposure, and Outcome) factors were implemented as inclusion criteria for our review: (i) Population: Patients with T1D, (ii) Exposure: Patients who have been evaluated for depressive symptoms using the PHQ, (iii) Outcome: The bidirectional impact between T1D and depression.

Data extraction: Data from studies that satisfied the inclusion requirements were extracted by two objective reviewers using a predetermined and uniform methodology. The following information was retrieved and recorded: (i) First author (ii) Year of publication, (iii) Study design, (iv) Country, (v) Sample size, (vi) Age, (vii) Gender, (viii) DM duration (years), (ix) Mean PHQ score (x) Prevalence of depression, (xi) Main outcomes.

Quality review: Since bias resulting from omitted factors is frequent in studies in this field, we used the ROBINS-I technique to assess the likelihood of bias since it enables a thorough examination of confounding. The ROBINS-I tool can be used for cohort designs where individuals exposed to different staffing levels are tracked over time and is designed to assess non-randomized studies. Each paper's risk of bias was evaluated independently by two reviewers, and any differences were settled by group discussion [11].

Results

760 papers were found using the given search technique (Figure 1). 375 trials were assessed using the title and abstract after duplicates (n = 385) were eliminated. Only 60 of these full-text articles were left for thorough evaluation while 311 of them did not meet qualifying requirements. Seven in all met the eligibility standards for analysis using Evidence Synthesis. (Table 1) included seven studies with a total of 2518 patients, less than half of them 1112 (44.1%) were males. Regarding study designs, all of the included studies were cross-sectional study [13-19]. Two studies were implemented in the USA [13, 15], two in Germany [18, 19], one in Saudi Arabia [14], one in Norway [16], and one in Kuwait [17]. The earliest study was conducted in 2006 [15] and the latest in 2023 [14, 16]. The prevalence of depression among patients with T1D ranged from 10.9% [15] to 33.3% [13]. Individuals with T1D who exhibited depressive symptoms, as identified by the PHQ tool, tended to have poorer glycemic control and were less

likely to adhere to necessary self-care behaviors, such as regular blood glucose monitoring. Because of the poor adherence, it is a risk factor of complications, thereby demonstrating the negative impact of depression to diabetes control [13, 14, 18]. Screening for depression in T1D patients is highlighted, in particular for those with additional medical conditions or poorly controlled diabetes. There is evidence that early treatment of depressive symptoms reduces adverse health effects on physical health. In addition, because emotional distress associated with diabetes care frequently overlaps with clinical depression, diagnosis and treatment are difficult. Emotional distress due to the chronic stress of diabetes could partly account for the prevalence of depressive symptoms among people with diabetes [15, 17]. Studies further highlight physical symptoms of chronic hyperglycemia, like fatigue and pain that are known to produce depressive symptoms. This underlines the importance of chronic hyperglycemia and its related complications in worsening mental illnesses. In addition, depressive symptoms seem to be modulated by a range of sociodemographic as well as biological determinants such as age, gender, and disease duration [19]. Further, young adults with early-onset and protracted T1D exhibit a relation between depression and impaired metabolic control [18]. (Table 2) summarizes bias assessments from various studies, most studies exhibit low to moderate bias levels, indicating generally reliable outcomes, although some, like Herder et al.[19], who present critical biases that could significantly impact their findings.

Discussion

The results highlight the complex and bidirectional link between T1D and depression. Depressive symptoms, determined by the PHQ, have been demonstrated to be very common in the T1D population. These symptoms are related to impaired glycemic control, lower treatment adherence, and higher propensity to diabetes-related complications. Johnson et al. reported that although there is currently insufficient data to determine if depression is more common in young adults with T1D than in adults, those with higher levels of depression also had higher HbA1c levels [20]. There is proof of associations between depression and more severe HbA1c levels and other health outcomes. This indicates importance to be sensitive to the possibility of depression while evaluating suitable measures, even though it is unclear whether depression is more common among patients with T1D than in the general population. According to the American Diabetes Association, normal best practices should include yearly psychiatric assessment [21]. The significance of including psychological support in the diabetes team is also emphasized in a recent report published by NHS Diabetes and Diabetes UK [22]. It has been demonstrated that routine screening may be established in diabetic clinics, despite the difficulties in implementing screening [23]. On the one hand, we found that the load of chronic (e.g., T1D) conditions, involving adherence to intensive self-management routines and continuous surveillance, triggers the development and exacerbation of depressive symptoms. These findings point to the complex interaction between the psychological and physiological factors of chronic disease management. Sociodemographic factors, such as younger age and longer disease duration, appear to exacerbate the risk of depression, while biological factors like systemic inflammation may also play a critical role in this relationship. These results highlight the need to treat mental health as a critical aspect of diabetes care. Buchberger et al. also found that patients with T1D had a significant prevalence of anxiety and depression symptoms, which had a detrimental effect on glycemic control and diabetes care [24]. The co-morbidity of diabetes and depression has sparked numerous studies in the past ten years due to the detrimental effects on both individual health and health care systems. Three potential explanations for the relationship between diabetes and depression were suggested by two separate reviews in 2015 [25]: either both conditions share a same etiology, diabetes raises the prevalence or risk of developing depression in the future, or depression raises the prevalence or risk of developing diabetes in the future. Compared to patients with T2D, those with T1D require a different and more complex approach to managing their condition. They require regular glycemic monitoring, dietary and physical activity modifications, and insulin dosage adjustments. T1D and depression have a very close chronological relationship; the diagnosis of T1D and the associated treatment burden occur during a time when the person is more susceptible to depression [26]. The age at which T1D start occurs is significantly earlier than that of T2D. Depression is two to three times more common in children and adolescents with diabetes than in those without the disease [27]. Depression and poorer socioeconomic status are linked to poor glycemic control in pediatric T1D patients, and the likelihood of depression in these children rises as glycemic control deteriorates [28]. Though there aren't many studies on the topic, one significant review shows a biological connection between T1D and depression; elevated circulating cytokines linked to autoimmune diabetes, insulin deficiency impacting neurogenesis and neurotransmitter metabolism, the effects of both iatrogenic hypoglycemia and chronic hyperglycemia, and hyperactivity in the HPA axis [29].

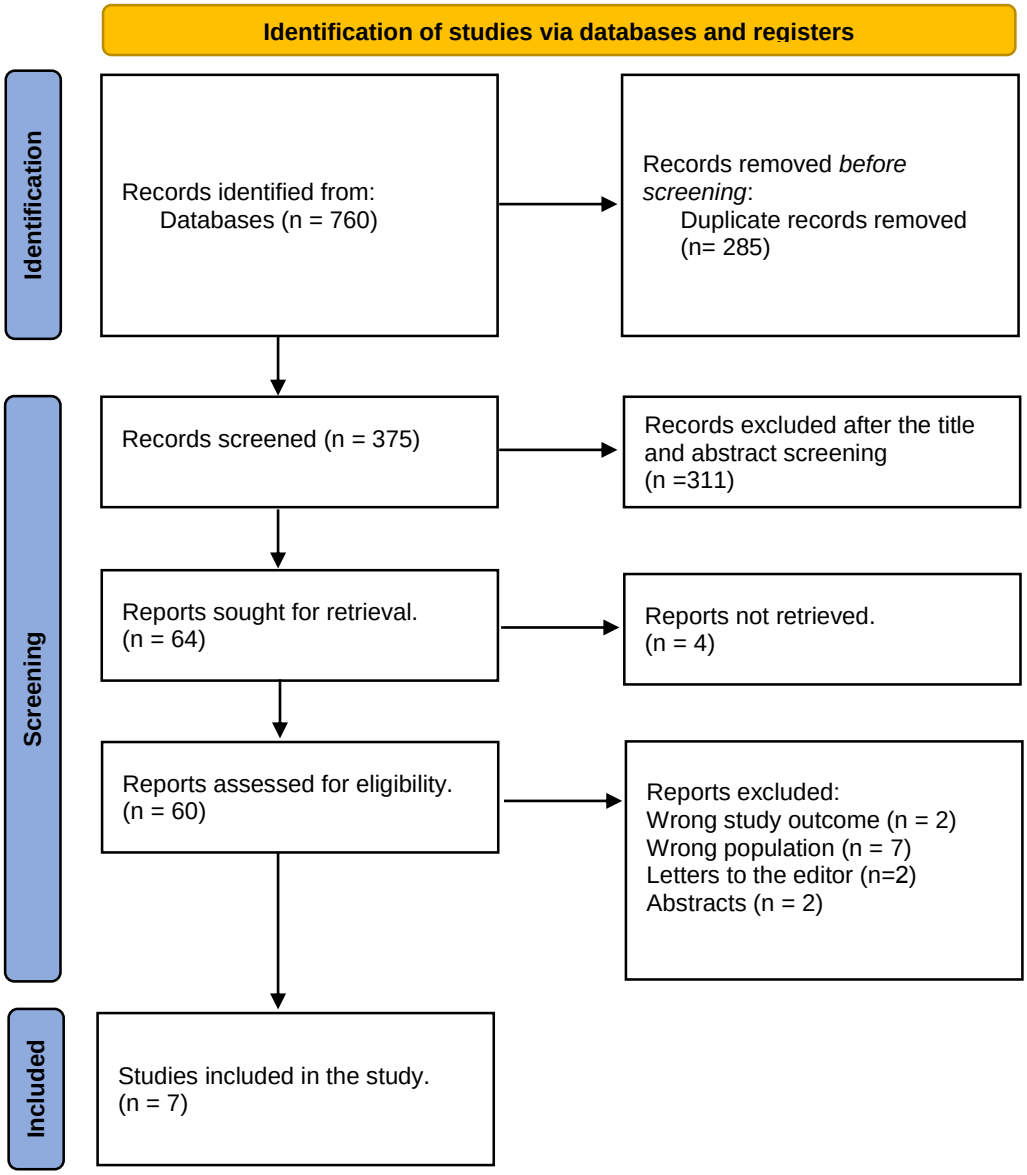

Figure 1: PRISMA flowchart [12].

Table 1: Outcome measures of the included studies.

Study ID	Study design	Country	Sociodemographic	Mean DM duration	Mean PHQ score	Depression prevalence	Main outcomes
Dalal et al., 2008 [13]	Cross-sectional	USA	N: 249 Age range: 18-72 Males: 101 (40.6%)	21.6 (14.4)	5.9 (8.1)	83 (33.3%)	Adults with T1D who scored as depressed on the PHQ-9 had lower glycemic control and were less likely to regularly check their blood glucose levels, which increased their risk of complications from the disease.
Aldossari et al., 2023 [14]	Cross-sectional	Saudi Arabia	N: 365 Males: 167 (45.8%)	0->5	NM	NM	Screening is advised for individuals with diabetes mellitus who have several comorbidities, glycemic non-control, serious complications of diabetes, and no lifestyle changes, as well as those receiving combination therapies with metformin, in order to mitigate the detrimental effects of undiagnosed depression.
Fisher et al., 2006 [15]	Cross-sectional	USA	N: 368 Mean age: 43.3 Males: 163 (44.3%)	25.6 (14.1)	4.5 (4.3)	40 (10.9%)	In this varied sample of persons with T1D, they discovered a very low prevalence of severe depressive illness and present depression. Given the high prevalence of diabetes distress, emotional distress related to managing a requesting chronic disease and other life stressors may account for a large portion of what has been classified as depression in adults with T1D, rather than underlying psychopathology.
Molvær et al., 2023 [16]	Cross-sectional	Norway	N: 104 Mean age: 64 Males: 52 (50%)	45-67	6.3 ± 4.9	NM	Chronic hyperglycemia over an extended period of time may negatively impact pain and fatigue in

							individuals with T1D. Several hypoglycemic episodes were linked to male depression.
AlOzairi et al., 2024 [17]	Cross-sectional	Kuwait	N: 832 Mean age: 29 Males: 382 (45.9%)	13.5 (8.4)	NM	231 (27.8)	Most individuals with T1D have symptoms of depression in addition to diabetes distress. There may be mutual prediction between diabetes distress and depressive symptoms, as evidenced by their substantial association.
Bächle et al., 2015 [18]	Cross-sectional	Germany	N: 211 Mean age: 19.3 Males: 85 (40.3%)	15.7 (1.1)	5.3 (4.4)	50 (23.9%)	It was discovered that ED and depression symptoms were connected in young adults with early-onset, long-duration T1D. These symptoms were also linked to poorer metabolic control, especially in men.
Herder et al., 2017 [19]	Cross-sectional	Germany	N: 389 Mean age: 38.1 Males: 162 (41.6%)	15.2 (11.2)	8.9 (5)	NM	Instead of a universal immune activation in diabetics with depressed symptoms, this study demonstrated distinct relationships between biomarkers of preclinical inflammation and depressive symptoms in T1D patients.

***NM=Not-mentioned.**

Table 2: Risk of bias assessment using ROBINS-I.

Study ID	Bias due to confounding	Bias in the selection of participants	Bias in the classification of interventions	Bias due to deviations from the intended interval	Bias due to missing data	Bias in the measurement of outcomes	Bias in the selection of reported result	Overall bias
Dalal et al., 2008 [13]	Low	Mod	Low	Low	Low	Mod	Low	Low
Aldossari et al., 2023 [14]	Low	Mod	Low	Low	Low	Low	Low	Low
Fisher et al., 2006 [15]	Low	Mod	Mod	Mod	Low	Mod	Low	
Molvær et al., 2023 [16]	Mod	Mod	Low	Low	Low	Low	Mod	Moderate
AlOzairi et al., 2024 [17]	Mod	Mod	Mod	Mod	Low	Low	Low	Moderate
Bächle et al., 2015 [18]	Mod	Mod	Mod	Low	Low	Low	Mod	Moderate
Herder et al., 2017 [19]	Crit	Crit	Low	Low	Mod	Low	Low	Critical

Strengths and limitations: This review has several strengths. It is aimed at work using the PHQ, which is a well validated, standardized measure of depressive symptoms and allows for comparability in findings. Additionally, the inclusion of diverse populations from different countries and age groups provides a comprehensive understanding of the relationship between T1D and depression. Most useful is the focus on the bidirectional nature of this relationship, which allows us to obtain a more integrative view of how the two conditions affect each other. However, there are also limitations. A number of the studies in review are cross sectional which limits inference of causality between T1D and depression. There are also few longitudinal data which could further add insights on how this relationship changes with time. Heterogeneity of the studies, such as differences in population, location and PHQ scoring thresholds, could impede the generalizability of the results. In addition, although a handful of studies investigate biological pathways (e.g., systemic inflammation), very few studies examine alternative pathways that could account for the relationship between T1D and depression.

Conclusion

This review highlights the significant bidirectional relationship between T1D and depression, with depressive symptoms playing a crucial role in worsening diabetes outcomes, while the challenges of managing T1D contribute to mental health deterioration. Depending on the PHQ as a tool for the measurement of depression, the foundation upon which this information is based is reliable to know the incidence and extent of depression in T1D patients. Aimed at this continuum it is needed an integrated approach to treatment which includes standardized depression screening, psychological therapies, and partnerships between clinicians. Future work should focus on longitudinal designs in order to question causality and to better understand the biological basis of this relationship. These endeavors will build an even stronger base from which effective interventions to promote mental and physical health improvement in people with T1D can be developed.

Conflict of Interest

None

Funding

None

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