

Mapping the evidence to determine the influence of stress, anxiety, and depression on wound healing in patients with diabetes-related foot ulcers: A scoping review

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ABSTRACT

Introduction: Diabetes-related foot ulcers (DFUs) are a severe complication of diabetes, affecting an estimated 6.3 % of individuals globally and significantly increasing healthcare burdens. Psychological factors such as stress, anxiety, and depression are common in DFU patients and are believed to impact wound healing through immune system disruptions and decreased self-care.

Objective: This scoping review evaluates current evidence on the influence of psychological distress on DFU healing, identifies research gaps, and underscores the importance of integrating mental health support in DFU management.

Methods: Following Joanna Briggs Institute guidelines and PRISMA-ScR reporting standards, a comprehensive literature search was conducted in MEDLINE, CINAHL, and PubMed. Studies with adult DFU patients reporting stress, anxiety, or depression and measurable wound outcomes were included.

Results: Ten studies were included, consistently demonstrating that psychological distress impairs DFU healing. Chronic stress was found to extend inflammation and weaken immune function, while anxiety and depression were associated with reduced self-care and directly impaired wound healing, further hindering recovery. These findings highlight the significant impact of psychological factors on the DFU healing process.

Conclusion: psychological distress, including stress, anxiety, and depression, may impair the healing process of diabetes-related foot ulcers (DFUs). However, the evidence is very low quality, making it difficult to draw definitive conclusions. This highlights the need for further high-quality research to clarify the role of mental health in DFU management.

1. Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by hyperglycaemia resulting from insufficient insulin production, action, or both [1]. This condition has reached epidemic proportions, with an estimated 537 million adults affected in 2021, a number projected to rise to 783 million by 2045 [1]. One of the most debilitating complications of diabetes is the development of diabetes-related foot ulcers (DFUs), which affect between 9.1 and 26.1 million people annually [2]. DFUs, as defined by the International Working Group on the Diabetic Foot (IWGDF), are foot ulcers in individuals with diabetes that are difficult to heal [3]. Peripheral neuropathy, a common consequence of

diabetes, causes a loss of protective sensation in the feet, making patients prone to minor injuries that often progress into chronic ulcers [6]. The presence of peripheral arterial disease further impairs blood flow, delays healing, and increases the risk of infection, often resulting in lower limb amputations, with DFUs accounting for over 85 % of such cases [4,5,7]. These ulcers significantly contribute to morbidity, disability, and mortality while placing a substantial burden on health-care systems due to frequent hospitalizations, prolonged treatments, and high recurrence rates [8]. Additionally, DFUs diminish patients' quality of life, not only due to physical limitations but also because of the psychological distress associated with chronic wounds [9–11].

There is strong evidence linking DFUs with various psychosocial

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challenges, particularly stress, anxiety, and depression [12–14]. These psychological factors are not only common in patients with DFUs but are also believed to influence wound healing processes directly [10,12]. Psychological distress can impair a person's ability to adhere to treatment regimens, which can delay recovery and increase the likelihood of complications [10,12]. Studies have shown that anxiety and depression can negatively affect self-management behaviours, such as foot care practices and adherence to medical advice, further increasing the risk of DFU development and delayed healing [13–15]. Additionally, living with a chronic wound can contribute to a cycle of emotional distress, frustration, and helplessness, which in turn exacerbates psychological conditions like anxiety and depression [15]. Elevated levels of depression and anxiety have been associated with poor glycaemic control, higher rates of DFU recurrence, and an increased risk of amputation [16, 17]. Addressing these psychological factors is crucial in managing DFUs, as interventions targeting mental health can improve not only psychological wellbeing but also wound-healing outcomes [18].

Stress is associated with delayed wound healing and poor glycaemic control in people with DM. Acute and chronic stress affect cortisol release, increasing glucose levels and complicating glycaemic control [10,19]. Cortisol's impact on wound healing prolongs the inflammatory phase, while glucocorticoid suppression of cytokines delays recovery [20,21]. Studies by Morris et al. (2011) and Chrousos (2009) show that stress exacerbates unhealthy behaviours, such as poor diet and alcohol consumption, which further impair healing [10,19]. Parvanah et al. (2014) conducted a pilot study on patients with (DFUs), revealing moderate to high stress during wound dressing changes, which negatively impacted wound healing outcomes [22]. The study had a small sample size of $N = 25$, leading to limited statistical power and the inability to conclusively determine the relationship between stress and delayed wound healing. Additionally, the study was conducted exclusively in Qatar, resulting in a lack of population diversity. This limited generalisability to other populations with different healthcare settings, ethnic backgrounds, and socio-cultural factors, which might influence the relationship between stress and wound healing outcomes [22]. Further research with larger, more diverse populations is needed to address these limitations [22].

Anxiety is defined as fear and worry affecting concentration and decision-making [23]. In 2019, the global prevalence of anxiety was 4 % [24]. The limbic system, including the amygdala, thalamus, and hippocampus, processes emotions, and heightened activity in this system is linked to anxiety [25]. Individuals with diabetes are twice as likely to develop anxiety disorders, which can worsen glycaemic control due to stress hormone activation, insulin resistance, and platelet aggregation [26]. A Pakistani study found that 57 % of type 2 diabetes patients experienced anxiety [27]. Anxiety also affects the healing of diabetes-related foot ulcers by impairing the immune system and increasing feelings of powerlessness [28]. A study showed that 39 % of patients with DFU reported anxiety symptoms [29].

Depression is a chronic mental disorder affecting mood and physical health, with symptoms including hopelessness and insomnia [30,31]. It increases the risk of chronic conditions like diabetes and cardiovascular disease [32]. Depression and diabetes often co-occur, with diabetes doubling the risk of depression [33]. Nouwen et al. (2010) conducted a systematic review and meta-analysis to examine type 2 diabetes mellitus (T2DM) as a risk factor for developing depression and found a 24 % increased risk of depression among individuals with T2DM. Similarly, Roy et al. (2012) reported that depression was three times more prevalent in individuals with type 1 diabetes and twice as prevalent in those with type 2 diabetes [34,35]. Depression has also been shown to impact the healing of diabetic foot ulcers (DFUs). Holt (2020) and Westby et al. (2020) reported that depressive symptoms increased the risk of ulcer development by 68 %, while Coli-King et al. (2020) demonstrated a correlation between anxiety, depression, and delayed wound healing [35,36]. Despite existing research, limitations like small sample sizes and lack of diversity hinder generalisability. Mapping the evidence on

the relationship between psychosocial factors and DFU outcomes is essential for developing holistic interventions that improve wound healing and patient well-being [35–38].

1.1. Review question

What is the evidence for the impact of stress and/or anxiety and/or depression on wound healing in patients with diabetes-related foot ulcers (DFUs)?

1.2. Objectives

The aims and objectives of this scoping review were to systematically explore the existing literature to examine the influence of psychological distress specifically stress, anxiety, and depression on wound healing outcomes in patients with diabetic foot ulcers (DFUs).

2. Methods

This review followed the Joanna Briggs Institute's methodology for scoping reviews, and the results were reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) [39,40].

2.1. Eligibility criteria

This scoping review included all research methodologies that presented primary data and met the eligibility criteria. Ethical approval was not required since this review is based on previously published data.

The inclusion criteria for this review encompassed studies published from the databases' inception to the present and were limited to those with adult participants aged 18 years or older. Eligible studies employed a variety of research designs, including Cross-Sectional studies, Prospective Cohort studies, Observational studies, and a Randomized Controlled Trial. The review focused specifically on individuals diagnosed with diabetes-related foot ulcers and psychological conditions such as depression, stress, or anxiety. Furthermore, studies were required to evaluate wound healing outcomes, such as wound size, healing time, infection rate, or other measurable wound-related parameters. The literature search was conducted in November and December 2024.

The exclusion criteria involved studies not published in English along with editorials, opinions and reviews. Additionally, articles that did not assess or report on depression, stress, or anxiety were excluded. The review also excluded studies that investigated the impact of psychological factors on wound healing in general, focusing solely on diabetes-related wound healing to ensure relevance and specificity to the research question.

2.2. Information sources

To identify potentially relevant documents, searches were conducted using databases including OVID MEDLINE, CINAHL, and PubMed. A general search in Google Scholar was also used to explore further references from included papers, and grey literature was examined. Keywords and MeSH terms were applied to locate relevant articles, and reference lists were reviewed to identify additional suitable studies (Table 1). Several preliminary searches were performed, and the final search strategy was established through team discussion and consensus.

2.3. Selection of sources

After conducting the search strategy, relevant citations were uploaded to EndNote version 20 to remove duplicates, and the remaining studies were transferred to Rayyan (<https://www.rayyan.ai/>) a web-based tool designed to streamline the literature review process

Table 1
Search strategy.

Concept	Search strategy
1-	Diabetic Foot MeSH terms: "Foot Ulcer/" OR "Diabetic Foot/" Keywords: (diabet* adj3 ulcer*) OR (diabet* adj3 (foot OR feet)) OR (diabet* adj3 wound*) OR (foot adj3 ulcer*)
2-	Psychological Factors MeSH terms: "Stress, Psychological" OR "Anxiety" OR "Depression" OR "Mental Health" Keywords: anxious* OR emotion* OR depress* OR mental stress* OR mental disorder* OR distress*
3-	Wound Healing MeSH terms: "Wound Healing/" OR "Ulcer Healing" Keywords: healing wound OR healing wounds OR ulcer healing OR ulcers healing

through title and abstract screening, tagging, and organisation. Study selection followed four steps: (1) importing references, (2) title and abstract screening, (3) full-text screening, and (4) data extraction. The screening was conducted between November and December 2024, with results in a PRISMA flowchart [Fig. 1].

Level 1 Screening (Title and Abstract Screening): The primary author and screening partner assessed titles and abstracts for eligibility, requiring more than one criterion failure to exclude a study. Discrepancies were resolved through team discussion (LA, AA, CMcI, CmacG,

EK, JH). A pilot test was conducted on ten randomly selected papers, with inclusion and exclusion decisions documented in Rayyan.

Level 2 Screening (Full-Text Screening): Full texts were reviewed for eligibility by the primary author and screening partner, with any discrepancies resolved by team consensus. Inclusion and exclusion decisions were documented in Rayyan, and a pilot test on five studies ensured screening accuracy. Two authors (LA, AA) extracted data and verified it by following a pilot exercise using Microsoft Excel. The data extraction process adhered to the guidance outlined in the JBI Manual for Evidence Synthesis, ensuring consistency and rigor. Extracted data included study information (authors, year, country, study design, setting, objectives) and concept details (sample size, outcome measures, recruitment strategy [39].

2.4. Population, concept and context

The Population, Concept, and Context (PCC) framework was applied as follows:

Population: Adults aged 18 and older with type 1 or type 2 diabetes who experience diabetes-related foot ulcers (DFUs), particularly those impacted by psychological factors like stress, anxiety, or depression.

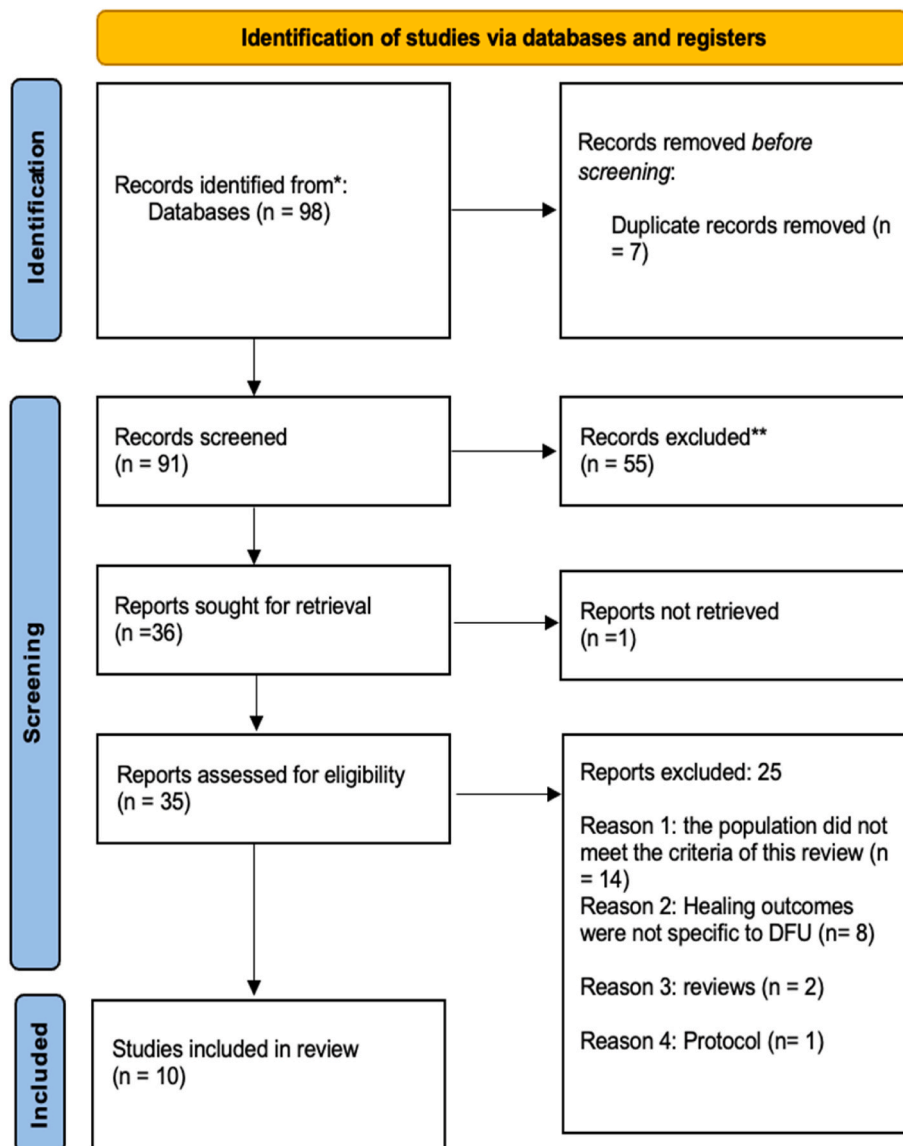


Fig. 1. Prisma flowchart.

Concept: Exploring the influence of psychological factors stress, anxiety, and depression on the healing outcomes of DFUs.

Context: The review considered evidence from diverse healthcare settings (e.g., hospitals, podiatry clinics) and geographic regions globally to ensure a comprehensive understanding of the topic by including a wide range of contexts and practices. However, the inclusion of only studies published in English was due to practical considerations, such as resource limitations and the reviewers' language proficiency, which may have restricted their ability to accurately assess non-English studies.

3. Results

3.1. Study selection

The primary search identified 98 studies. After the selection process, ten articles were included in the study [Fig. 1].

3.2. Critical appraisal of the included studies

The scoping review included ten articles published from 2006 to 2024. The general characteristics of those studies are outlined in the table. The primary origin of the studies includes Indonesia (n = 2), Pakistan (n = 1), Canada (n = 1), Australia (n = 1), Portugal (n = 3), Qatar (n = 1), the United Kingdom (n = 1), and Italy (n = 1) (see Table 2). The studies were primarily conducted in hospital-based multidisciplinary diabetic foot clinics and outpatient podiatry clinics, with fewer focusing on community or primary care settings.

3.2.1. Outcome measures and screening tool

The studies reviewed highlight the critical role of psychological factors, including stress, anxiety, and depression, in influencing the healing of diabetes-related foot ulcers (DFUs). Various study designs and methodologies were employed, as detailed in Table 1, to explore these associations. Prospective cohort studies by Da Silva et al. (2024) and Monami et al. (2008) assessed the impact of depression and stress on ulcer healing [46,49]. Da Silva et al. conducted a randomized controlled trial (N = 77) using the Beck Depression Inventory (BDI) and Perceived Stress Scale (PSS) to assess psychological distress, finding that higher baseline scores were associated with slower reductions in ulcer size. Similarly, Monami et al. conducted a prospective cohort study (N = 80) utilizing the Geriatric Depression Scale (GDS) to examine the impact of depressive symptoms on ulcer healing and recurrence. Vedhara et al. (2010) found that depression and confrontational coping styles predicted non-healing of (DFUs). Biologically, higher pro-MMP2 levels and greater cortisol awakening responses were linked to delayed healing [39]. Ahmedani et al. (2017) found that higher PHQ-9 scores were linked to delayed healing, lower ulcer healing rates, and increased amputation risk [48]. Cross-sectional studies, including Gayatri et al. (2020) and Pearson et al. (2014), identified links between psychological

Table 2
General demographics and characteristics of the included studies.

Study	Sample Size	Mean Age (Years)	Male (%)	Female (%)
Ahmedani et al. (2017)	105	57.0	60.0	40.0
Pearson et al. (2014)	60	54.0	55.0	45.0
Razjouyan et al. (2017)	25	59.3	70.0	30.0
Vedhara et al. (2010)	93	60.7	73.1	26.9
Monami et al. (2008)	80	58.0	65.0	35.0
Pereira et al. (2023)	153	58.0	55.0	45.0
Gayatri et al. (2020)	120	58.0	65.0	35.0
Da Silva et al. (2023)	77	56.0	50.0	50.0
Westby et al. (2020)	140	55.0	60.0	40.0
Ferreira et al. (2023)	153	57.0	55.0	45.0

distress and self-care practices, measured using tools like the Depression, Anxiety, and Stress Scale (DASS) and the Short Form Health Survey (SF-36) [42,47] (see Table 3). Ferreira et al. (2023) conducted a qualitative study with 153 participants, as part of a pilot randomized controlled trial, in diabetic foot clinics [50].

3.3. Evidence of the impact of stress on wound healing

Chronic stress can suppress immune function and delay tissue repair by interfering with inflammation regulation and cellular proliferation [41–43]. Research indicates that patients experiencing significant stress show delayed wound healing and a higher likelihood of chronic ulceration [44,45]. The study by Da Salvia et al. (2023) observed the effects of stress on immune cell ratios and circulating microRNAs over a **6-month period**, linking altered levels of microRNAs such as miR-21–5p, miR-155–5p, and miR-146a–5p to prolonged inflammation, impaired angiogenesis, and delayed wound healing [46].

3.4. Evidence of the impact of anxiety on wound healing

The study by Vedhara et al. (2010) found that patients with higher anxiety experienced slower reductions in ulcer size over 24 weeks compared to those with lower anxiety levels. A control group was not explicitly included for comparison in terms of anxiety levels, and the certainty of evidence was moderate. The p-value for anxiety's association with ulcer size reduction was 0.281, indicating that the effect was not statistically significant.

Similarly, Gayatri et al. (2020) observed that anxiety had significant indirect effects on healing through reduced self-care and increased discomfort, with a p-value <0.005, supporting a stronger association in their findings [41,42].

3.5. Evidence of the impact of depression on wound healing

Depression is prevalent in individuals with DFUs and correlates with poorer outcomes, increased mortality, and impaired adherence to medical advice [47,48]. Depression's effect on healing is mediated through both behavioural and biological mechanisms, such as diminished self-care and changes in hormonal balance [41,49]. Da Salvia et al. (2023) conducted a randomized controlled trial over six months, finding that psychological interventions targeting depressive symptoms improved immune regulation and stress markers. Key changes included reductions in inflammation and normalization of microRNAs (e.g., miR-21–5p, miR-155–5p), significantly enhancing wound healing (p < 0.05) (see Table 3) [46].

3.6. Psychological Interventions

Psychological Interventions aimed at reducing stress and improving mental well-being have shown promising results in promoting DFU healing. Ferreira et al. (2023) conducted a qualitative study within a three-arm pilot randomized controlled trial involving 153 participants from multidisciplinary diabetic foot clinics. The study found that relaxation interventions, including guided relaxation sessions, significantly reduced stress, improved emotional well-being, and enhanced adherence to treatment in DFU patients. Patients reported visible improvements in wound healing and overall quality of life, attributing progress partly to reduced stress levels. Similarly, Pearson et al. (2014), in a cross-sectional survey of 60 patients in podiatry clinics, observed that depressive symptoms were linked to poorer diabetes self-management and mental well-being. However, no significant association was found between depression and ulcer healing or recurrence at six months (p > 0.05) [47,50].

Table 3
Summary of the results.

Author/Year/Country	Research Question/Aims	Setting	Research Design	Screening tool/Outcome measure	Key findings
Setyawati & Sagita, 2024 Indonesia [43]	To explore the psychological impact on a patient with a nonhealing DFU.	Hospital	Case Report	Semi-structured interviews and clinical observations. Adherence to treatment protocols was assessed through semi-structured interviews, providing insights into patients' consistency with wound care practices	Case report of one patient. Psychological stress significantly influenced the patient's adherence to treatment, worsening wound healing. Counselling and stress management interventions led to improvements in adherence and wound condition.
Gayatri et al., 2020 Indonesia [42]	To identify relationships between wound severity, discomfort, and psychological issues in DFU patients in Indonesia	Three Hospitals and one podiatry clinic.	Cross-Sectional Study	Depression, Anxiety, and Stress Scale (DASS); Discomfort Evaluation of Wound Instrument (DEWI). Bates-Jensen Wound Assessment Tool (BWAT); psychological issues; discomfort levels (DEWI)	A sample size of (n = 140) patients with DFU. 74.3 % experienced immobilization, 69.3 % reported pain, and 63.6 % had sleep disturbances. Mean scores: discomfort (2.35 ± 0.33), depression (1.34 ± 0.41), stress (1.49 ± 0.48), anxiety (1.43 ± 0.40). Discomfort mediated the relationship between wound severity and psychological issues, with an indirect effect coefficient of 0.11 (p < 0.005).
Ahmedani et al., 2017 Pakistan [48]	To assess depression among DFU patients and compare ulcer outcomes between depressive and non-depressive participants	Hospital	Observational Perspective Study	Patient Health Questionnaire-9 (PHQ-9), assessing ulcer healing rates in terms of the number of days to complete healing , alongside amputation frequencies and glycaemic control (HbA1c levels)	The sample size of (n = 105), (75.2 % male, 24.8 % female). 50.4 % (n = 53) had depressive symptoms (PHQ-9 ≥ 9). Antidepressant treatment over 3 months led to a significant reduction in depression scores (P ≤ 0.05). Ulcer healing: 60 % healed in non-depressed vs. 40 % in depressed patients. No significant differences in minor/major amputation rates. Mean HbA1c was high in both groups (10.1 % ± 2.7).
Razjouyan et al., 2017 Qatar [44]	To examine the association between physiological stress (measured by heart rate variability) and wound healing speed in patients with diabetic foot ulcers (DFUs).	Wound Care Clinic	Observational study	Heart Rate Variability (HRV) metrics to assess stress levels and their relationship to wound healing speed , measured in days	25 patients (19 analysed; mean age 59.3 ± 8.3 years, 83 % male). Significant correlation between wound healing speed and HRV metrics: vagal tone (r = -0.705, P = 0.001) and stress response (r = 0.713, P = 0.001). Fast healers had lower stress (nLF: 41.7 % lower, P < 0.001) and higher relaxation (nHF: 99.1 % higher, P < 0.001). HRV parameters were stronger predictors of healing than demographic/clinical factors (AUC > 0.90 for HRV model).
Pearson et al., 2014 Australia [47]	To examine the prevalence of depressive symptoms, diabetes self-management, and quality of life in people with diabetes and foot ulcers.	Podiatry clinics	Cross- Sectional Study	Patient Health Questionnaire (PHQ); Summary of Diabetes Self-Care Activities (SDSCA); Short Form Health Survey (SF-36) Ulcer healing and recurrence rates; self-care activities; quality of life (SF-36)	(n = 60) participants (18+ years, both Type 1 and Type 2 diabetes). 51.7 % had depressive symptoms (PHQ > 4), 23.3 % mild (PHQ 5-9), and 28.3 % moderate-severe (PHQ > 9). 70.6 % on antidepressants still reported moderate-severe symptoms. Depression was linked to poorer diabetes self-care and lower mental health (MCS). No association with ulcer healing or recurrence at 6 months.
Ferreira et al., 2023 Potugal [50]	To explore the perspectives of patients and healthcare professionals on the suitability and acceptability of a relaxation intervention, its effects on well-being and DFU healing, and its integration into multidisciplinary care.	Podiatry Clinic	Qualitative Study Design	Semi-structured qualitative interviews explored patient-reported stress and well-being, adherence, emotional states, and DFU size changes	(n = 19) 8 patients (mean age 63.63 ± 10.97 years, 100 % male) and 11 healthcare professionals. Patients reported improved well-being and reduced stress after relaxation sessions. Healthcare professionals noted changes in patients' adherence, emotional state, and reduced DFU size. The COVID-19 pandemic affected feasibility, but the sessions were still seen as valuable.
Monami et al., 2008 Italy [49]	To assess the impact of depressive symptoms on healing and recurrence of diabetic foot ulcers (DFUs).	Hospital	Prospective Cohort Study	Geriatric Depression Scale (GDS). Time to complete healing; ulcer recurrence rates	(n = 80) type 2 diabetic patients (60+ years, chronic foot ulcers > 3 months). Patients with GDS scores ≥ 10 had higher risk of not healing within 6

(continued on next page)

Table 3 (continued)

Author/ Year/ Country	Research Question/Aims	Setting	Research Design	Screening tool/Outcome measure	Key findings
Pereira et al., 2023 Portugal [45]	To identify demographic, clinical, and psychological contributors to diabetic foot ulcer (DFU) healing and favourable healing processes, and to analyse the timing of interventions over six months.	Hospitals	Longitudinal cohort study	Brief Illness Perception Questionnaire (BIPQ); Newest Vital Sign (NVS) tool. Healing rates; psychological predictors (e.g., illness perceptions, health literacy)	months (RR: 3.57, 95 % CI: 1.05–12.2). Ulcer recurrence was significantly higher in patients with GDS scores ≥ 10 (RR: 3.55, 95 % CI: 1.13–11.25). Depression was an independent predictor for both delayed healing and recurrence (n = 153) (81 % male; mean age 64.42 \pm 10.52 years) 56.1 % achieved complete healing within six months; 83.6 % showed a positive healing process. Median time to complete healing was 112 days, and 30 days for healing. Predictors for healing included illness perceptions, while being female, adequate health literacy, and a first DFU predicted advantageous healing outcomes
Vedhara et al., 2010 UK [39]	To examine the effects of psychological distress, coping style, and biological mechanisms on diabetic foot ulcer healing over 24 weeks.	Podiatry Clinic	Prospective observational study	Hospital Anxiety and Depression Scale (HADS); Coping Strategies Questionnaire Ulcer healing over 24 weeks; cortisol levels; matrix metalloproteinases (MMPs)	(n = 93) patients with neuropathic or neuroischaemic ulcers (mean age 60 years, 68 men). Depression was associated with slower ulcer size reduction (p = 0.04, d = 0.31). Patients with unhealed ulcers showed lower evening cortisol and higher pro-MMP2 levels.
Da Silva et al., 2023 [46]	To evaluate the influence of psychological distress on physiological indicators of healing prognosis and the effectiveness of stress-reducing therapies for DFU healing.	Wound Care Clinic	Randomized-Controlled Trial	Beck Depression Inventory (BDI); Perceived Stress Scale (PSS) Reduction in ulcer size over 12 weeks; baseline and 12-week psychological assessments	Participants (N = 77, aged 18+) with chronic DFU were assessed. Initial Assessment: No significant differences were found in PEDIS scores, HbA1c, or inflammatory/angiogenic markers between those with (Group 3) and without psychological distress (Group 1). However, immune cell ratios were over twofold higher, and circulating microRNAs (miR-21–5p, miR-155–5p, miR-146a–5p, miR-221–3p) were significantly elevated in Group 3 (p < 0.05). Post-Intervention: Participants receiving stress-reducing interventions (Group 5) showed improved stress and anxiety scores (p < 0.01), with a 2.5-fold decrease in immune cell ratios, indicating enhanced healing potential

4. Discussion

The primary aim of this scoping review was to investigate whether stress, anxiety, and depression influence the healing of DFU. Through a systematic scoping review approach, the authors aimed to investigate the impact of stress, anxiety, and depression on the healing of (DFUs) and to highlight the importance of addressing patients' overall well-being in their management. The articles selected were rigorously screened by the authors, and ten eligible studies were included in this review.

4.1. Summary of findings

The findings across the reviewed studies suggest that these psychological conditions negatively influence wound healing in patients with DFU, primarily by affecting immune responses add citations, glycaemic control add citations, and adherence to self-care practices add citations. Chronic stress, for example, was associated with prolonged inflammation and impaired immune function, which delayed wound healing [43]. Anxiety, meanwhile, was frequently linked to decreased adherence to wound care practices, and depression was associated with higher

recurrence rates of DFUs and impaired healing due to hormonal and behavioural effects [43]. A critique of these findings highlights certain methodological limitations. For instance, most studies relied on self-reported questionnaires to assess psychological conditions, which can introduce biases, such as social desirability or recall bias, potentially compromising the reliability of data on stress, anxiety, and depression [48]. Additionally, the diversity of study design ranges from observational and cross-sectional studies to a few randomized controlled trials (RCTs) limits the strength of causal conclusions. Observational and cross-sectional studies, which lack the control of RCTs, make it difficult to establish causation, reducing confidence in whether psychological factors directly influence DFU healing.

4.2. Comparing the findings with the existing literature

The findings of this scoping review align with research in psychoneuroimmunology, which examines how psychological factors like stress, anxiety, and depression affect immune function and wound healing. Studies by Kiecolt-Glaser et al. (2002) and Christian et al. (2006), both experimental studies with N < 100 participants, demonstrated that stress raises cortisol levels, prolongs inflammation, and

slows tissue repair, especially in chronic conditions like diabetes. These studies found significant delays in wound healing ($p < 0.01$), supporting the review's identification of stress as a significant factor in delayed DFU healing [11,21].

The review also highlights the impact of anxiety on self-care, consistent with Gonzalez et al. (2008), a longitudinal study with $N = 211$, finding that anxiety reduced adherence to essential behaviours, such as wound care ($p < 0.01$) [13]. Similarly, Khuwaja et al. (2010), a cross-sectional study of $N = 300$, linked high anxiety levels to poorer glycaemic control, with significant associations ($p < 0.05$) [27]. The role of depression in delayed healing is supported by previous studies linking it to worse outcomes in chronic illnesses through biological mechanisms like hormonal dysregulation and behavioural impacts on self-care. Polikandrioti et al. (2020), in a mixed-methods study with $N = 120$ observed that those with depression had poorer glycaemic control ($p < 0.05$), reinforcing the need for mental health support [38]. These findings collectively emphasize the importance of integrating mental health care into DFU management to improve outcomes Walburn et al. (2009) conducted a meta-analysis which also found that stress delays healing across chronic wounds. Stress reduction can aid wound healing, suggesting that mental health integration could benefit DFU management [20]. The systematic reviews by Westby et al. (2020) and Yunding et al. (2022) align with this scoping review, supporting evidence that psychological conditions like stress, anxiety, and depression negatively impact diabetic foot ulcer (DFU) healing [52,53]. Westby et al. identified significant associations between psychological distress and delayed healing but highlighted the low quality of evidence due to small sample sizes and varied methodologies. Similarly, Yunding et al. found that stress impairs healing through cortisol elevation and immune dysregulation but noted the heterogeneity of studies and low certainty of evidence. Both reviews emphasize the need for high-quality, methodologically sound research to strengthen the evidence base and inform clinical practice.

4.3. Strengths and limitations

The process conforms to PRISMA-ScR guidelines and adheres to the JBI guidelines for scoping reviews, ensuring methodological rigor and transparency throughout the review [39]. The inclusion of diverse study types allowed a broad examination of the evidence. However, small sample sizes and single-site studies such as those in Indonesia and Pakistan, limit generalisability, as the findings may not reflect global DFU populations [42,48]. Additionally, inconsistent wound-healing measures and a lack of controls for confounders, such as glycaemic control, complicate comparisons and make it challenging to isolate the impact of psychological factors on healing [47]. There was also inconsistency in reporting ulcer types, such as incident versus recurrent DFUs, further contributing to the heterogeneity of the literature. This variability makes it difficult to draw definitive conclusions and highlights the need for standardised methodologies in future research [47].

4.4. Future research

Future research studies should focus on increasing sample size to improve generalisability and adopt standardised measures for psychological factors and wound healing. A core outcome set for diabetes-related foot ulceration (DFU) studies is being developed to standardize reporting on wound healing, time to healing, and quality of life. This will reduce heterogeneity, improve study comparability, and enhance evidence quality for DFU management [51].

More RCTs with adequate follow-up are necessary to determine causality and account for confounding factors, such as comorbidities [34]. Additionally, studies should investigate the physiological mechanisms, such as cortisol regulation, through which stress and depression impact healing to support targeted interventions [10]. The findings of such research could significantly influence future guidelines,

encouraging a holistic approach to managing DFU. This may involve integrating psychological assessments into standard clinical practice and ensuring mental health support is integral to treatment plans. By addressing the physical and psychological aspects of DFU, integration into future clinical guidelines could improve patient outcomes, reduce healing times, and alleviate healthcare burdens. The IWGDF Wound Healing Interventions Review found no RCTs on psychological interventions meeting inclusion criteria, highlighting a critical evidence gap. Addressing this will improve understanding and management of DFUs, emphasizing the importance of psychological care in treatment strategies [3].

5. Conclusion

This scoping review suggests that psychological distress, particularly stress, anxiety, and depression, may impair the healing of DFUs, but further definitive research is warranted. The findings highlight the potential importance of addressing psychological factors as a core component of DFU management. Chronic stress disrupts immune function and prolongs inflammation, while anxiety and depression reduce engagement in self-care and may directly affect wound healing. These observations underscore the need for a holistic approach, aligning with the biopsychosocial model, to integrate mental health support with physical care for improved DFU outcomes. To strengthen understanding and enhance patient care, further empirical research is essential, particularly high-quality RCTs with larger, more diverse populations and standardised measures of psychological distress and wound outcomes, to establish clearer causal relationships.

Author contribution

JH is guarantor of this study. LA, AA and JH drafted the manuscript. All authors contributed to the development of study concept and the data extraction criteria. LA, AA, EK and JH developed the search strategy for this study. CMcI and CMacG provided expertise on psychological conditions within the context of diabetes-related foot disease. LA, AA, CMcI, CMacG, JH and EK provided a Podiatric Medicine input. CMcI, CMacG, EK and JH provided experience and expertise in the evidence synthesis. All authors have read, provided feedback, and approved the final manuscript. All authors contributed to data interpretation and article drafts.

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Declaration of competing interest

The authors declare no conflicts of interest.

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