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NON-PHARMACOLOGICAL INTERVENTIONS FOR WOUND-RELATED PAIN IN CHRONIC LOWER LIMB ULCERS: A SYSTEMATIC REVIEW

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Abstract

Chronic lower extremity wounds impose significant physical, emotional, and socioeconomic burdens, with pain being a prevalent yet often neglected symptom. This systematic review examined the effectiveness of non-pharmacological interventions for wound-related pain in adults with chronic lower limb ulcers. A PRISMA-guided search was conducted across Scopus, PubMed, Web of Science, and ProQuest, including randomized controlled trials (RCTs) and quasi-experimental studies. Twelve RCTs published between 2011 and 2025 involving 1,078 participants were analyzed. Interventions ranged from single-session methods to multi-session therapies, behavioral programs, and modality-based treatments. Findings showed that stress balls and cold saline significantly reduced procedural pain, while electrical stimulation and motivational support provided sustained benefits. In contrast, virtual reality and heated saline offered limited pain relief but improved patient comfort. Overall, simple, low-cost approaches demonstrated promise for immediate relief, whereas structured behavioral and modality-based therapies supported longer-term pain management. These strategies, being safe and feasible, may complement standard wound care, particularly within nursing practice. Further high-quality, large-scale trials are warranted to refine their clinical application.

Keywords**:** *chronic wounds, non-pharmacological interventions, pain management.*

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INTRODUCTION

Chronic wounds create substantial physical, emotional, and socioeconomic burdens for patients and their families. These wounds persist beyond the typical healing period of four to six weeks, often remaining stuck in the inflammatory phase due to factors such as poor circulation, underlying medical conditions, or inadequate treatment (Olsson et al., 2019; Parasuraman & Perumal, 2021; Wilkinson & Hardman, 2020). Affecting roughly 4.5 million people worldwide, their prevalence is rising alongside aging populations and increasing rates of diabetes and obesity (Zhu et al., 2022). Notably, 15% of diabetic patients develop foot ulcers, with one in four at risk over their lifetime (Yazdanpanah et al., 2018).

Pain may now be regarded as the fifth vital sign, but its importance in managing chronic wounds remains underappreciated. This is particularly true for lower extremity wounds, where pain management remains inadequate. This underestimation may occur because diabetic neuropathy masks pain or because patients gradually adapt to persistent pain (Parveen, Hussain, Anwar, Elagib, & Kausar, 2025). In wound management, pain originates from tissue injury, inflammation, and nerve damage, while routine dressing changes frequently exacerbate the pain. Uncontrolled pain can lead to patient anxiety about wound care procedures, non-adherence to treatment schedules, and delayed wound healing (Woo, 2024).

Pain is highly prevalent in chronic wound patients, with both baseline wound pain and procedural pain being common. A study in China indicate that most chronic wound patients experience wound-related procedural pain, while many report wound baseline pain. Baseline pain typically reaches moderate intensity, but procedural pain, especially during debridement, often becomes severe (Wei et al., 2024). The rising economic burden of chronic wound management is further compounded by the substantial impact of wound-related pain on patients' quality of life. Recent study demonstrates that even low pain intensity can affect HRQoL (Ghadeer et al., 2025; Holloway et al., 2024).

While pharmacological options exist for pain management, they are frequently limited by delayed efficacy, inconsistent effectiveness, and potential side effects. In contrast, various non-pharmacological approaches such as music therapy, virtual reality, and psychological interventions have been proposed as complementary alternatives. However, these methods remain underutilized in clinical practice, and evidence supporting their effectiveness remains fragmented, highlighting the need for more comprehensive research in this area (Woo, 2024). Early studies (particularly in the 2000s) primarily focused on pharmacological interventions for pain management. Only in the past decade have non-pharmacological approaches gained significant attention. This shift reflects an evolving paradigm in wound care, where pain management during dressing changes has gradually moved from pharmacological dominance to increasing exploration of complementary non-pharmacological strategies. Contemporary studies are investigating non-pharmacological interventions including music therapy, VR, and guided imagery, though current evidence shows variable effectiveness in pain control during wound procedures. While numerous RCTs have assessed non-pharmacological interventions, inconsistent outcomes and methodological limitations (including small samples and population diversity) hinder both data synthesis and clinical application.

This systematic review aimed to evaluate the effects of nonpharmacologic treatments on wound-related pain in people with diabetic or chronic ulcers on the foot or leg. It also sought to compare these treatments with standard wound care without nonpharmacologic therapies. Additionally, the review aimed to identify the key components of nonpharmacologic pain management interventions to provide recommendations for optimizing pain management strategies based on the existing evidence. The research questions of the review were: “What is the effect of nonpharmacologic treatments on wound-related pain in adults with diabetic or chronic ulcers on the foot or leg compared to those receiving only wound care without nonpharmacologic therapies?".

METHODS

Design

This study was designed according to the systematic review method and conducted according to Preferred Reporting for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2021). The review protocol was registered on the international Prospective Register of Systematic Reviews (PROSPERO) website (CRD420251142866). The review was carried out through formulation of review questions, establishment of inclusion criteria, and design of a research strategy. This process continued with the screening and selection of studies, critical appraisal, data extraction, and data synthesis (Tufanaru, Munn, Aromataris, Campbell, & Hopp, 2020). The PICOT framework, which stands for population, intervention, comparison, outcome, and type of study, was used to guide the review process, as presented in Table 1 (Tufanaru et al., 2020). We included in this review only RCTs published in English. As the review focused on exploring nonpharmacologic treatments for wound-related pain, only studies whose

intervention targeted wound-related pain were included.

Table 1. Inclusion and Exclusion Criteria.

	Inclusion	Exclusion
Populations	Adult with diabetic/chronic ulcer on foot or leg, age >18	
Intervention/Exposure	Nonpharmacologic treatments which have effect on pain	Pharmacologic intervention
Comparison	Undergoing wound care and not receiving nonpharmacological therapies	
Outcome	Wound-related pain	
Study Designs	Randomized controlled trials, quasi-experimental studies	Letter to editor, Commentaries, Qualitative studies, Abstract only, Case series, case reports, reviews, Discussion papers, cohort studies
Publication year	January 2011 to March 2025	
Language	English	

Databases and Search Strategy

This research includes studies published in Scopus, Web of Science, Sciencedirect and Pubmed databases between 2011-2025. The keywords and subject headings used were as follows:

Table 2. Search Strategies.

Database	Search Strategy
Scopus	(TITLE-ABS-KEY (diabetes OR diabetic OR chronic) AND TITLE-ABS-KEY (wound OR ulcer OR ulceration) AND TITLE-ABS-KEY (pain) AND TITLE-ABS-KEY (leg OR foot OR limb) AND TITLE-ABS-KEY ("dressing change" OR "wound care" OR "wound cleansing" OR care OR debridement))
Web of Science	diabetes OR diabetic OR chronic (All Fields) AND wound OR ulcer OR ulceration (All Fields) AND pain (All Fields) AND leg OR foot OR limb (All Fields) AND "dressing change" OR "wound care" OR "wound cleansing" OR care OR debridement (All Fields)
Pubmed	((("diabetic" OR "diabetes" OR "chronic") AND ("Wound" OR "ulcer" OR "ulceration")) AND ("pain")) AND ("leg" or "foot" or "limb")) AND ("dressing change" OR "wound care" OR "wound cleansing" OR "care" OR "debridement")
Proquest	summary("diabetic" OR "diabetes" OR "chronic") AND summary("wound" OR "ulcer" OR "ulceration") AND summary("pain") AND fulltext("leg" OR "foot" OR "limb") AND fulltext("dressing change" OR "wound care" OR "wound cleansing" OR "care" OR "debridement")

Study Selection and Data Extraction

The screening process was performed in two steps: title and abstract screening followed by full-text screening. Nested knowledge software (Covidence) was used for de-duplication and screening. Studies screened by two reviewers, all disagreements were resolved by discussion or consultation with a third reviewer, and consensus was reached in all cases. Data extraction was performed by one reviewer, followed by a double-check conducted by other two reviewers to ensure accuracy and consistency. For each included article, the data extracted included the author's name, year of publication, study design, country, age of participants, sample size, intervention setting, participants' demographic data (total participants, wound type, wound location, wound care type, and age) intervention details (intervention types between groups, intervention provider, frequency and length of intervention and follow-up), and outcomes. This comprehensive approach allowed for a detailed analysis of the studies' key characteristics and demographic information, providing a robust foundation for the systematic review.

Quality Assessment

To assess the quality of each included study, a meticulous quality assessment was performed using the Joanna Briggs Institute (JBI) tool. The JBI assessment covers various aspects, including the representativeness of the sample, the appropriateness of the study's methodology, the validity and reliability of the measures used, and the adequacy of response rates.

Data Synthesis

Data were analyzed and narratively summarized, then displayed in tables outlining the objective, population, sample, intervention, measurement tools, outcomes, and methodological quality. Additionally, a figure was created for visual representation.

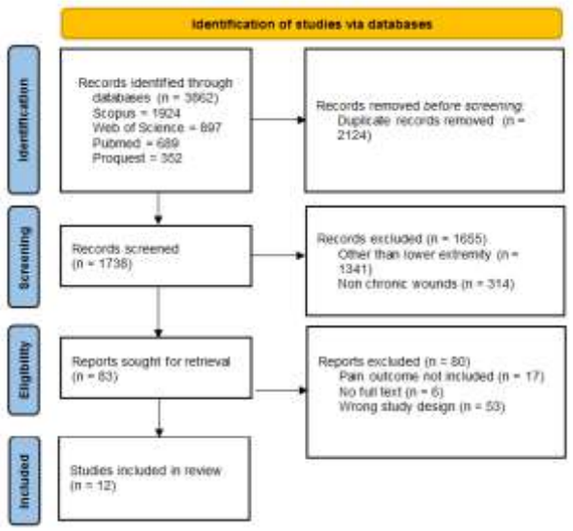

Figure 1. Flowchart of steps for inclusion of articles in the systematic review according to PRISMA, 2021.

RESULTS AND DISCUSSION

General Characteristics of the Included Studies

The initial search across Scopus, Web of Science, PubMed, and ProQuest databases yielded 3,862 records. After removing 2,124 duplicate records, 1,738 articles underwent title and abstract screening, resulting in the exclusion of 1,655 records (1,341 for non-lower extremity wounds and 314 for non-chronic wounds). Subsequently, 83 full-text articles were assessed for eligibility, with 80 excluded due to irrelevant pain outcomes (n=17), unavailability of full text (n=6), or inappropriate study designs (n=53). Finally, 12 randomized controlled trials (RCTs) met the inclusion criteria and were included in the systematic review (Figure 1).

The 12 studies comprised a total of 1,078 participants, with sample sizes ranging from 16 to 336 individuals. The largest study enrolled 336 participants (172 in the intervention group and 164

in the control group), while the smallest study included 16 participants (8 per group). Geographically, the studies were conducted in Turkey (n=3, 25%) (Aslan, Tosun, Altınok Ersoy, & Ozen, 2025; Belhan, Muhan, Aksoy, Ozker, & Unver, 2025; Turan, Özbay, & Avşar, 2025), China (n=2, 16.7%) (Ma et al., 2024; Zhou, Zhang, Zhong, & Zhang, 2024), Brazil (n=2, 16.7%) (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015), the United States (n=1, 8.3%) (Kelechi, Mueller, Spencer, Rinard, & Loftis, 2014), Italy (n=1, 8.3%) (Santamato et al., 2012), Australia (n=1, 8.3%) (Michailidis, Bergin, Haines, & Williams, 2018), and a multicountry trial (US, Germany, UK, Canada; n=1, 8.3%) (Galiano, Snyder, Mayer, Rogers, & Alvarez, 2019).

All 12 included studies were two-arm randomized controlled trials, comparing a non-pharmacological intervention group with a standard care control group. The standard care across studies typically involved routine wound management, such as sharp debridement, saline cleansing, hydrogel dressings, or antimicrobial agents, often combined with offloading techniques for diabetic foot ulcers. The sample criteria across all studies included diabetic foot ulcers (n=12, 100%). In addition, five of the twelve studies also specified general chronic foot wounds as part of their sample criteria (n=5, 41.7%) (Belhan et al., 2025; Galdino-Júnior et al., 2024; Kelechi et al., 2014; Ma et al., 2024; Santamato et al., 2012). Neuropathic characteristics were explicitly noted in diabetic ulcer studies, with patients often exhibiting peripheral neuropathy (Galiano et al., 2019; Kelechi et al., 2014).

Intervention Durations and Methods

The interventions varied widely in duration and methodology. Short-term single-session interventions included stress ball use (20–30 minutes during debridement) (Aslan et al., 2025), cold saline application (5–15 minutes) (Turan et al., 2025), and heated saline irrigation (immediate effect measured) (Galdino-Júnior et al., 2024). Multi-session protocols ranged from 3 weeks (15 sessions of Frequency Rhythmic Electrical Modulation System [FREMS]) (Santamato et al., 2012) to 6 months (e.g., weekly low-frequency ultrasonic debridement) (Michailidis et al., 2018). Psychological and behavioral interventions, such as motivational support (Kelechi et al., 2014; Zhou et al., 2024) and virtual reality (VR) (Belhan et al., 2025), were administered during wound care visits (single or multiple sessions), while physical modalities like low-level laser therapy (LLLT) (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015), shockwave therapy (Galiano et al., 2019), and electrical stimulation required repeated applications (e.g., 12–16 sessions over 4 weeks) (Ma et al., 2024). VR and stress ball interventions targeted procedural pain during dressing changes, whereas LLLT and FREMS aimed at both pain relief and tissue repair. Heterogeneity in intervention frequency (daily to weekly) and delivery (clinician-administered vs. patient-applied) reflected the diversity of approaches.

The interventions were delivered by a variety of healthcare professionals, included wound care specialist nurses administering cold saline irrigation (Turan et al., 2025), trained nurses applying heated saline solutions (Galdino-Júnior et al., 2024), wound-ostomy-continence (WOC) nurses delivering motivational and exercise-based interventions (Kelechi et al., 2014) and general nurses delivering motivational behavior rehabilitation (Zhou et al., 2024). Other interventions were performed by physicians (e.g., electrical stimulation (Santamato et al., 2012) and shockwave therapy (Galiano et al., 2019)), physiotherapists (e.g., low-level laser therapy) (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015), and podiatrists (Michailidis et al., 2018). In two studies, patients self-administered interventions at home under medical supervision, such as stress ball use (Aslan et al., 2025) and pulsed electrical stimulation (Ma et al., 2024). Virtual reality interventions were facilitated by researchers or clinic staff (Belhan et al., 2025), highlighting the diversity in delivery approaches across non-pharmacological therapies.

Pain Assessment Tools Across Studies

The Visual Analogue Scale (VAS) was the most frequently used tool to assess pain, employed in 10 out of 12 studies (83%) (Aslan et al., 2025; de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015; Galiano et al., 2019; Kelechi et al., 2014; Ma et al., 2024; Michailidis et al., 2018; Santamato et al., 2012; Turan et al., 2025; Zhou et al., 2024). The Numeric Pain Rating Scale (NPRS) was the second most common (n=2, 16.7%) (Belhan et al., 2025; Galdino-Júnior et al., 2024). One article used multiple pain assessment tools, such as the Leg Pain Questionnaire (LPQ) (Kelechi et al., 2014) alongside VAS. VAS was predominantly applied to measure both baseline and procedural pain intensity, often during or immediately after wound care interventions. Self-reported scales were favored due to their simplicity and reproducibility, though one study combined VAS with infrared thermometry to correlate pain with wound temperature changes.

Efficacy of Nonpharmacologic Therapies

A statistically significant reduction in pain was reported in 7 out of 12 studies (58%) (Aslan et al., 2025; Feitosa et al., 2015; Kelechi et al., 2014; Ma et al., 2024; Santamato et al., 2012; Turan et al., 2025; Zhou et al., 2024). The most effective interventions included stress ball application (100% pain reduction during debridement) (Aslan et al., 2025), cold saline irrigation (mean VAS

reduction: 3.2 points) (Turan et al., 2025), and electrical stimulation (FREMS: 50% faster pain relief vs. control) (Santamato et al., 2012). Behavioral interventions, such as nurse-directed motivational support (Kelechi et al., 2014), also showed significant pain improvement ($p<0.05$). Conversely, virtual reality (VR) (Belhan et al., 2025) and heated saline solution failed to demonstrate significant pain reduction despite improving patient comfort (Galdino-Júnior et al., 2024). Although it was not proven to reduce pain, shockwave therapy was reported not to increase pain (Galiano et al., 2019). LLLT did not significantly reduce pain compared to the control group, although some patients reported regained sensitivity (de Alencar Fonseca Santos et al., 2018). In the FLUD study, there was no significant difference in pain between the two groups; however, pain was reported to increase during debridement but returned to baseline afterward in both groups (Michailidis et al., 2018).

Two studies (16.7%) reported no significant pain reduction: VR glasses during dressing changes ($p>0.05$) (Belhan et al., 2025) and heated saline irrigation (mean NPRS difference: 0.3 points, $p=0.41$) (Galdino-Júnior et al., 2024). VR's ineffectiveness was attributed to low patient immersion, particularly among older adults, while heated saline's minimal impact may reflect its focus on comfort rather than analgesia. Notably, low-level laser therapy (LLLT) yielded mixed results, with one study reporting pain improvement (VAS drop: 9 to 5) (Feitosa et al., 2015) and another showing no significant difference, possibly due to varying laser parameters or small sample sizes (de Alencar Fonseca Santos et al., 2018).

Table 3. Methodological quality of studies according to the Joanna Briggs Institute's critical appraisal checklist.

Article	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Score
Article 1	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Article 2	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Article 3	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	85%
Article 4	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Article 5	Y	Y	Y	Y	Y	Y	Y	Y	Y	-	-	-	-	100%
Article 6	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Article 7	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Article 8	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	92%
Article 9	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%
Article 10	Y	U	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	77%
Article 11	Y	U	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	77%
Article 12	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	85%

*Y = yes; N = no; U = unclear; NA = not applicable

Methodological Quality Assessment

The quality assessment of the 12 articles was conducted using the JBI critical appraisal tools, with Articles 1–4 and 6–12 evaluated as randomized controlled trials (RCTs) and Article 5 as a quasi-experimental study. For the RCTs, most articles (Aslan et al., 2025; Belhan et al., 2025; Galdino-Júnior et al., 2024; Ma et al., 2024; Michailidis et al., 2018; Santamato et al., 2012; Turan et al., 2025; Zhou et al., 2024) scored 11 out of 13, indicating high quality, with consistent adherence to randomization (Q1), allocation concealment (Q2), baseline similarity (Q3), and appropriate statistical analysis (Q12). However, blinding of participants (Q4) and treatment deliverers (Q5) was often unclear or not reported, and some studies did not treat groups identically outside the intervention (Q6). Article 8 achieved a almost perfect score of 12 (Galiano et al., 2019), demonstrating rigorous methodology. Articles 10 and 11 scored lower (10/13) due to unclear allocation concealment (Q2) and treatment group comparability (Q4) (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015). However, pre- and post-intervention measurements (Q5) were not consistently reported across RCT studies. For the quasi-experimental study (Kelechi et al., 2014), the score was 9 out of 9 applicable items. Overall, the majority of the articles exhibited strong methodological quality, with minor limitations in blinding and treatment standardization. The findings support the reliability of the included studies for synthesis.

Discussion

Nonpharmacological approaches to wound-related pain in patients with chronic leg ulcers can be grouped into four broad categories. Single-session interventions such as stress ball distraction, virtual reality application, and cold or heated saline irrigation, are designed to provide immediate pain relief during dressing changes or debridement (Aslan et al., 2025; Belhan et al., 2025; Galdino-Júnior et al., 2024; Turan et al., 2025). Multi-session interventions, including electrical stimulation, laser therapy, shockwave therapy, structured behavioral programs, and low-frequency ultrasound debridement are performed repeatedly over several days or weeks to achieve sustained pain reduction and wound healing (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015; Galiano et al., 2019; Kelechi et al., 2014; Ma et al., 2024; Michailidis et al., 2018; Santamato et al., 2012; Zhou et al., 2024). Physiological and behavioral interventions, such as nurse-directed motivational support, goal setting, or physical exercise, aim to influence patient behavior and self-management capacity alongside clinical care (Kelechi et al., 2014; Zhou et al., 2024). Modality-based interventions, such as low-level laser therapy (LLLT), frequency rhythmic electrical modulation system (FREMS), extracorporeal shockwave therapy (ESWT), and low-frequency ultrasound debridement (LFUD), employ physical modalities or devices to accelerate tissue repair while alleviating pain (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015; Galiano et al., 2019; Ma et al., 2024; Michailidis et al., 2018; Santamato et al., 2012).

Single-session interventions

Two articles highlights the nuanced differences between heated and cold saline irrigation

as single-session interventions.

Table 4. Characteristics of Studies Included in the Review.

no	Study title / Authors / Country	Population, sample and age	Intervention	Measures	Results related to pain
1	The effect of a stress ball on pain and anxiety during sharp debridement in patients with diabetic foot ulcers: A randomized controlled, single-blind study / Aslan et al., 2025 / Turkey	Inpatients with diabetic foot ulcers undergoing first-time sharp debridement. T: 38 (59.02 ± 9.96) C: 38 (56.39 ± 8.51)	Experimental Group: Use of a stress ball during debridement. Control group: Routine debridement without additional intervention. Both before, during, and after debridement. Patients in the intervention group used the stress ball 5 minutes before the procedure, throughout the debridement (20–30 min), and stopped immediately after the procedure. No long-term or repeated interventions were conducted—only one debridement session per patient was evaluated.	Descriptive Information Form. Diabetic Foot Meggit-Wagner Classification. Visual Analogue Scale (VAS) for pain. State Anxiety Inventory (STAI) for anxiety.	The use of a stress ball significantly reduced pain during and after sharp debridement in diabetic foot ulcer patients. It is a simple, cost-effective non-pharmacological intervention.
2	Examining the effect of virtual reality application on pain and anxiety in the care of chronic wounds on the leg / Belhan et al., 2025 / Turkey	Patients with chronic leg wounds. T: 36 (62.39 ± 13.41) C: 35 (64.29 ± 11.31)	Experimental Group: Virtual reality glasses (Oculus Quest 2) with nature videos and relaxing music during wound care (once per visit). Control group: Standard wound care without VR (once per visit). Both during wound care (single session). September 2022 to July 2024.	Numeric Pain Intensity Scale (pain). Spielberger State Trait Anxiety Inventory (anxiety). Virtual Reality Symptom Questionnaire (VR-related symptoms).	VR did not significantly reduce pain or anxiety during chronic wound care, possibly due to older age limiting engagement. No adverse effects were noted.
3	The impact of cold application on pain and comfort during the process of diabetic foot care / Turan, Özbay and Avşar, 2025 / Turkey	Patients with diabetic foot ulcers (DFUs) receiving wound cleansing care with sharp debridement. T: 34 (60.64 ± 9.67) C: 34 (62.35 ± 8.90)	Experimental Group: Cold 0.9% NaCl solution (+4°C to +8°C). Control group: Lukewarm 0.9% NaCl solution (+18°C to +24°C). Both applied once during wound care; single session (5-15 minutes).	Visual Analogue Scale (VAS) for pain. Short General Comfort Questionnaire (SGCQ).	Cold application significantly reduced pain during diabetic foot care, enhancing patient comfort and treatment adherence.
4	Effects of low-frequency pulsed electrical stimulation at the common peroneal nerve on chronic refractory wounds of the lower limb: A randomized controlled trial / Ma et al., 2024 / China	Patients with chronic lower limb wounds. T: 24 (57.96 ± 13.28) C: 24 (60.21 ± 12.12)	Experimental Group: Wearable low-frequency pulsed electrical stimulation (ES) at the common peroneal nerve, 60 min per session, 3 sessions daily for 4 weeks + SWC. ES and SWC were applied concurrently (at the same time). Control group: SWC only, twice a week for 4 weeks. Both performed at home during treatment	PAR: Wound area measurement. VAS: Pain intensity. BWAT: Wound status. Wound-Qol: Quality of life.	The study found that electrical stimulation significantly reduced pain (VAS scores) in the treatment group compared to the control group, correlating with improved quality of life.
5	The Effect of a Nurse-Directed Intervention to Reduce Pain and Improve	Patients with painful lower legs and critically colonized/infect	Experimental Group: MECALF (Motivational Enhancement + CALF exercises), delivered by WOC nurses during weekly	Leg Pain Questionnaire (LPQ). Visual Analog Scale (VAS).	Both interventions reduced pain, but the CALF group (handout-only) showed a slightly

	Behavioral and Physical Outcomes in Patients With Critically Colonized/Infected Chronic Leg Ulcers / Kelechi et al., 2014 / United States	ed chronic leg ulcers. T: 12 (64.8 ± 16.1) C: 9 (65.8 ± 14.6)	visits for 6 weeks. Control group: CALF handout (exercise brochure/written instructions for exercises) provided at baseline, no nurse-directed intervention	Dynamometer (strength). Goniometry (range of motion). Readiness Ruler (motivation). Questionnaire for Physical Activity and Exercise (self-efficacy). Timed Up and Go (TUG), Timed Chair Standing Test (TCST), CHAMPS (physical activity)	greater reduction in pain intensity. The MECALF group reported improved confidence and perceived benefits in leg function, but no significant statistical difference in pain outcomes compared to the control group.
6	Effectiveness of the Frequency Rhythmic Electrical Modulation System for the Treatment of Chronic and Painful Venous Leg Ulcers in Older Adults / Santamato et al., 2012 / Italy	Older adults (>65 years) with chronic and painful venous leg ulcers. T: 10 (73.1 ± 5.6) C: 10 (72.7 ± 5.5)	Experimental Group: Frequency Rhythmic Electrical Modulation System (FREMS) (25 min/session) + topical treatment. Control group: Topical treatment alone. Both performed 15 sessions over 3 weeks (5 sessions/week).	Visitrack™ digital planimetry (ulcer area). Visual Analog Scale (VAS) for pain.	FREMS combined with topical treatment significantly reduced pain and ulcer area in older adults with venous leg ulcers compared to topical treatment alone, with faster pain relief observed in the FREMS group.
7	Effect of Heated Saline Solution on Pain Intensity, Wound Bed Temperature, and Comfort during Chronic Wound Dressing Changes: Crossover Randomized Clinical Trial / Galdino-Júnior et al., 2024 / Brazil	Adults (≥18 years) with chronic wounds (duration ≥8 weeks). T: 15 (60.3 ± 15.1) C: 17 (58.4 ± 11.9)	Experimental Group: Heated saline solution (39.8 ± 0.6 °C), single application per session. Control group: Room temperature saline solution (27.1 ± 1.1 °C), single application per session. Immediate effect measured post-cleaning; washout period: 10 minutes. Single session with two cleanings (10-minute washout between); performed during wound care at the clinic	Numeric Pain Rating Scale (0–10). Infrared thermometer.	Heated saline did not reduce pain but improved comfort and slightly increased wound bed temperature, suggesting utility for patient preference despite no significant clinical impact on pain.
8	Focused shockwave therapy in diabetic foot ulcers: secondary endpoints of two multicentre randomised controlled trials / Galiano et al., 2019 / Multicountry (US, Germany, UK, Canada)	Patients with neuropathic diabetic foot ulcers (DFUs), grades 1A or 2A (University of Texas grading scheme). T: 172 (60.4 ± 10.4) C: 164 (56.2 ± 9.4)	Experimental Group: Focused ESWT (dermaPACE System), 4–8 sessions over 2–12 weeks. Control group: Sham ESWT + standard care. Study 1: 2-week treatment phase, 24-week follow-up. Study 2: 12-week treatment phase, 24-week follow-up.	Wound tracings, photography, Aranz SilhouetteStar device, VISITRAK depth probe. Visual Analog Scale (VAS) for pain assessment.	ESWT did not increase pain; trends suggested reduced pain in the active group, though not statistically significant. Inflammation modulation by ESWT was implied but not directly measured.
9	Effect of Rehabilitation Intervention Based on Motive Behavioral Conversion Concept on Healing, Self-management, and	Diabetic foot ulcer patients post-artificial dermal transplantation. T: 50 (59.36 ± 6.52) C: 50 (58.85 ± 6.47)	Experimental Group: Motivation-behavioral transformation (education, goal-setting, psychological support, self-management training); frequency: regular follow-ups (e.g., monthly phone calls). Control group: Conventional	VAS (pain intensity). Self-care ability assessment (diet, blood glucose, exercise, foot care). DSQL (quality of life).	Intervention group reported significantly less pain post-intervention, attributed to motivational support and self-management,

	Quality of Life in Patients with Diabetic Foot Ulcers after Artificial Dermal Transplantation / Zhou et al., 2024 / China		rehabilitation (blood sugar management, infection prevention, routine foot care). Post-surgery, during wound care; follow-up for 6 months	HAMA (anxiety), SDS (depression).	enhancing recovery and comfort.
10	Effects of Low-Power Light Therapy on the Tissue Repair Process of Chronic Wounds in Diabetic Feet / de Alencar Fonseca Santos et al., 2018 / Brazil	Patients with chronic wounds on their feet due to diabetes mellitus complications. T: 9 (48.33 – 12.09) C: 9 (53.11 – 8.85)	Experimental Group: LLLT (660 nm, 30 mW, 6 J/cm²). Control group: Physiological solution + hydrogel. Both performed for every 48 h for 4 weeks (16 sessions), during wound care at the clinic	PUSH scale (wound healing). VAS (pain). ImageJ software (wound area measurement).	LLLT did not significantly reduce pain compared to control, but some patients reported regained sensitivity.
11	Effects of the Low-Level Laser Therapy (LLLT) in the process of healing diabetic foot ulcers / Feitosa et al., 2015 / Brazil	Type II diabetic patients with lower limb ulcers. T: 8; C: 8). Age: Not specified in the text	Experimental Group: LLLT (632.8 nm, 30 mW, 4 J/cm²). Control group: Daily asepsis with saline solution only. 3 times/week for for 4 weeks (12 sessions). Performed during wound care at the hospital.	Wound size: ImageJ® software. Pain: Visual Analog Scale (VAS, 0-10).	LLLT significantly reduced pain (VAS score dropped from 9 to 5) in diabetic foot ulcer patients, while the control group reported no improvement. This suggests LLLT's analgesic effect.
12	Healing rates in diabetes-related foot ulcers using low frequency ultrasonic debridement versus non-surgical sharps debridement: a randomised controlled trial / Michailidis et al., 2018 / Australia	Individuals with diabetes-related foot ulcers (DRFUs) managed by podiatry. T: 5; C: 5). Age: Not specified in the text	Experimental Group: Low frequency ultrasonic debridement (LFUD), weekly. Control group: Non-surgical sharps debridement (NSSD), weekly. 6 months, weekly treatments, measurements taken before, during, and after debridement	EQ-5D-5L for quality of life. 100 mm Visual Analogue Scale (VAS) for pain. Digital photography and wound measurements for healing progress.	Pain levels increased during debridement but returned to baseline afterward in both groups. No significant difference in pain between LFUD and NSSD was observed. Quality of life improved as ulcers healed.

The study by Turan et al. (2025) demonstrated that cold 0.9% NaCl solution (4–8 °C) applied during sharp debridement of diabetic foot ulcers significantly reduced pain intensity and increased patient comfort compared with room-temperature irrigation. In contrast, Galdino-Júnior et al. (2024) reported that heated saline (approximately 39.8 °C) did not significantly reduce pain intensity in chronic wound care compared with room-temperature saline, although patients consistently rated the heated solution as more comfortable and expressed a preference for its use.

The analgesic benefit of cold irrigation aligns with prior studies in other clinical contexts. For instance, in post-tonsillectomy patients, cold-water irrigation resulted in significantly lower pain scores compared with room-temperature irrigation (Liu et al., 2023). Similarly, in dental procedures, patients reported cold saline irrigation to be more comfortable and soothing than room-temperature alternatives (Dayanan, Ozupek, & Seyrek, 2023; Ernst, Gershoff, Miller, Tilden, & Weiss, 2003). The physiological mechanism underlying these findings is well established: cold reduces inflammation and tissue perfusion, thereby limiting nociceptor activation, while also producing a localized numbing effect that decreases pain perception (Allison et al., 2024).

On the other hand, heated irrigation has been shown to improve patient satisfaction in procedures, where warm saline significantly reduced intra- and post-procedural pain (Baradwan et al., 2022). Yet, evidence from chronic wound care suggests that while warming enhances comfort, it does not consistently reduce pain intensity (Galdino-Júnior et al., 2024; Wang et al., 2021). Cold saline irrigation appears more effective for immediate analgesia during painful wound procedures, whereas heated saline may be prioritized when the goal is to maximize patient comfort and satisfaction during less painful interventions.

Other single-session intervention showed beneficial effects. Aslan et al. (2025) found that giving patients a simple stress ball to squeeze before and during debridement dramatically

reduced procedural pain (100% pain reduction reported during the one debridement session). Patients using the stress ball had significantly lower pain scores during and immediately after the debridement procedure, and no adverse effects were noted. The use of stress balls during various medical procedures has been shown to effectively reduce pain and anxiety, enhancing patient comfort and satisfaction. This simple, cost-effective intervention can be widely recommended across different clinical settings to improve patient experiences during painful procedures (Karatas & Gezginci, 2023; Öz & Demirci, 2024).

In contrast, some single-session approaches had little or no effect on pain. In a trial of virtual reality (VR) distraction during dressing changes, Belhan et al. (2025) found no significant difference in pain or anxiety between the VR group and usual care. The authors noted that many older patients had trouble engaging with the non-interactive VR content, which likely limited its analgesic benefit. Non-interactive VR was generally found to be easy to use and inexpensive, with minimal adverse effects. However, willingness to use VR varied widely among older adults, suggesting that preconceptions and education about VR could influence engagement levels (Jansen, de Zande, de Korne, & Andringa, 2025). The effectiveness of non-interactive VR for pain management is less clear, with some studies indicating non-significant effects (Corbel, Le Cerf, Breaud, & Corveleyn, 2025). Meanwhile, immersive VR interventions were well accepted and enjoyed by older adults, with minimal side effects reported (Benham, Kang, & Grampurohit, 2019).

Multi-session interventions

Multi-session therapies showed better effect on pain. Repeated applications appear to enhance analgesic outcomes by allowing cumulative physiological and psychological benefits to build over time. Electrical stimulation, laser therapy, shockwave therapy, structured behavioral programs, and low-frequency ultrasound debridement share the principle that multiple exposures reinforce neural modulation, tissue repair processes, and coping mechanisms, which are less likely to emerge from a single exposure. In this sense, the frequency of administration serves not only to maintain the therapeutic signal but also to reduce fluctuations in pain intensity between dressing changes and wound care procedures (de Alencar Fonseca Santos et al., 2018; Feitosa et al., 2015; Galiano et al., 2019; Kelechi et al., 2014; Ma et al., 2024; Michailidis et al., 2018; Santamato et al., 2012; Zhou et al., 2024).

While extended treatment protocols suggest cumulative benefits, the current body of evidence remains insufficient to establish definitive superiority of multi-session approaches over single-session strategies in wound-related pain. The studies conducted thus far vary considerably in their treatment schedules, with some applying interventions several times per day and others weekly, making it difficult to isolate the optimal dosing pattern. This inconsistency underscores the importance of investigating how session frequency and duration specifically contribute to analgesic effects. Multi-session therapies point to a promising direction for achieving sustained pain relief in chronic wound care, yet treatment frequency optimization remains an important research gap. Clarifying whether daily, bi-weekly, or weekly schedules yield the most effective and practical outcomes would provide critical guidance for clinical protocols. Until such evidence is consolidated, the advantage of multi-session over single-session interventions for pain relief should be interpreted as a cautious trend rather than a definitive conclusion.

Physiological and behavioral interventions

Physiological and behavioral interventions also showed promise, particularly when delivered over time. Kelechi et al. (2014) evaluated a nurse-directed program of Motivational Enhancement plus exercise (the “MECALF” intervention) versus an exercise brochure alone in patients with chronic leg ulcers. The nurse-led MECALF patients reported better confidence, exercise adherence, and perceived leg function benefits than brochure-only controls, even though formal pain scores were similar. Zhou et al. (2024) tested a “motivation-behavioral conversion” rehabilitation program after surgical wound care. Patients in the intervention arm received education, goal-setting, psychological support and self-management training over six months, whereas controls received standard foot-care instructions. The intervention group achieved significantly greater pain relief and better self-care behaviors and quality of life at 6 months.

Other research corroborates that sustained, nurse-facilitated physical activity programs can mitigate pain symptoms in chronic leg ulcer patients. A structured physical activity program integrated into standard nursing care was evaluated in a randomized multicenter trial and not only aimed to enhance wound healing but also specifically assessed pain as a secondary outcome, suggesting potential benefits in pain reduction through increased exercise adherence and mobility (Herraiz-Ahijado, Folguera-Álvarez, Verdú-Soriano, Mori-Vara, & Rico-Blázquez, 2023). Additionally, a supervised exercise training as an adjunctive therapy for venous leg ulcer patients demonstrated improved lower leg function and patient adherence over time, outcomes which may indirectly contribute to pain relief by enhancing calf muscle pump efficiency and reducing stasis-

related discomfort (Probst, Allet, Depeyre, Colin, & Buehrer Skinner, 2019).

These findings indicate that structured psychosocial or behavioral support often delivered by trained nurses, can reduce wound pain and improve other outcomes. Such programs likely work in part by improving adherence to care and promoting healing, which indirectly lessens nociceptive signals. The MECALF and Zhou studies highlight that even when pain does not differ greatly in numerical scores, patients may feel more empowered and comfortable with an active rehabilitation approach.

Modality-based interventions

Among modality-based therapies, three stood out. The FREMS plus standard dressing care led to significantly faster pain relief and greater ulcer reduction compared to dressings alone (Santamato et al., 2012). These results suggest FREMS has an analgesic effect on chronic wound pain, likely through enhancing microcirculation and modulating neural pain pathways. ESWT accelerated healing and had no negative pain effects (Galiano et al., 2019). LLLT had mixed results point to a need for standardization, but one included trial showed that LLLT significantly reduced pain (Feitosa et al., 2015). In summary, FREMS and ESWT both consistently showed pain improvements or at least pain-neutral outcomes, while LLLT's impact on pain was equivocal. We note that all these modalities though can accelerate tissue repair while alleviating pain, they require specialized equipment and operator training.

Ease of application

Safety, cost, and feasibility are important considerations. None of the trials reported serious adverse events from the interventions. The nonpharmacological therapies were generally safe: for example, the stress ball had no reported side effects (Aslan et al., 2025), and even VR caused only minor, transient symptoms in a small number of patients (Turan et al., 2025). Simple interventions are inexpensive and easy to integrate. A stress ball or chilled saline is virtually cost-free, requires minimal training, and can be supervised by nursing staff during routine wound care. By contrast, high-tech modalities entail higher costs and more training. Devices like shockwave generators, laser units, FREMS machines, or VR headsets involve substantial capital investment and skilled operators. For instance, wound care nurses or therapists administering ESWT or LLLT must be trained to set parameters safely. Nurse-led programs like MECALF rely on specialized wound care nurses (WOCNs) who are trained in motivational interviewing and exercise prescription.

Cost-effectiveness was not formally studied in these studies, but one can infer that low-cost methods (stress ball, irrigation) are highly economical given their efficacy. High-tech approaches may improve healing and reduce long-term costs (e.g. fewer clinic visits or complications) but would need formal economic evaluation. In practice, wound care nurses play a key role in implementing any of these interventions. Nurses can screen patients for suitable therapies, instruct them on devices (or operate them), and monitor for discomfort. Importantly, professional training is required for safe use of sophisticated modalities: for example, nurses must know how to operate laser or shockwave equipment and recognize contraindications. All authors noted the need for clear protocols and training. Overall, the interventions ranged from very simple (stress ball, saline irrigation, nurse coaching) to complex (device-based therapies), and their adoption in clinical settings will depend on balancing expected benefit with resource availability and staff expertise.

CONCLUSION

This systematic review highlights the potential of various non-pharmacological interventions to effectively manage pain in patients with chronic lower extremity wounds. Simple, low-cost methods such as stress balls and cold saline irrigation demonstrated significant immediate pain relief during procedural care and can be integrated into routine wound care, particularly in low-resource settings. While multi-session therapies like electrical stimulation and behavioral programs showed durable benefits. Although some interventions, such as virtual reality and heated saline, did not significantly reduce pain, they were well-tolerated and improved patient comfort. The findings underscore the importance of integrating these adjunctive therapies into standard wound care protocols, particularly in nursing practice, to enhance pain management and overall patient outcomes. Future research should focus on larger, more rigorous trials to further validate these approaches and optimize their clinical application.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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