

Efficacy and Safety of Negative Pressure Wound Therapy in Diabetic Foot Ulcers: A Cross-Sectional Analysis of Overlapping Meta-Analyses

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Objective: Negative pressure wound therapy (NPWT) is a key intervention for diabetic foot ulcers (DFUs). However, the body of meta-analytic evidence is fraught with conflicting findings, creating significant clinical uncertainty. This study was designed to harmonize the discordant evidence, identify the most methodologically robust meta-analysis, and formulate a clear, evidence-based recommendation for the clinical use of NPWT.

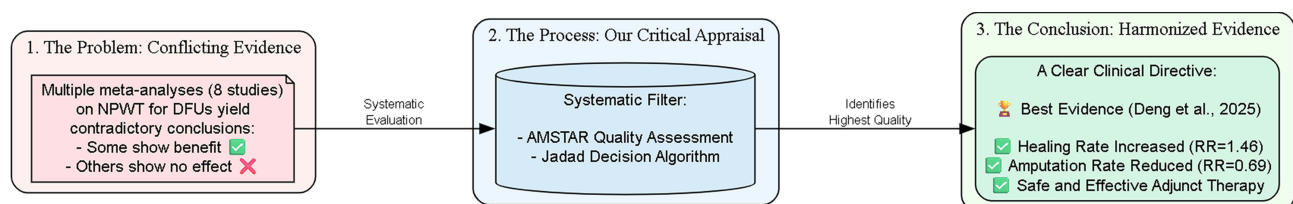
Methods: We conducted a comprehensive search of the PubMed, Embase, and Cochrane Library databases to identify all pertinent meta-analyses. The methodological quality of each included review was rigorously assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) instrument. The Jadad decision algorithm was then employed to systematically select the most reliable and robust evidence.

Results: Eight meta-analyses met the inclusion criteria, with AMSTAR scores ranging from 6 to 9. The formal application of the Jadad decision algorithm identified the meta-analysis by Deng et al as the definitive source of best available evidence. This meta-analysis demonstrated that NPWT significantly improved wound healing rates (risk ratio = 1.46) and decreased amputation rates (risk ratio = 0.69) relative to conventional therapy, while also shortening granulation tissue formation time without increasing adverse events.

Conclusion: The highest-quality evidence, harmonized through this appraisal, confirms that NPWT is a safe and effective adjunctive therapy for DFUs. Its demonstrated ability to accelerate healing while reducing amputations provides a strong evidence base for consideration as a key component of standard clinical practice.

Keywords: diabetic foot ulcer, negative pressure wound therapy, vacuum-assisted closure, systematic review, meta-analysis

Graphical Abstract



Introduction

Diabetic foot ulcers (DFUs) stand as a severe and pervasive complication of diabetes mellitus, with a lifetime incidence that affects up to a quarter of this patient population.^{1,2} These chronic wounds are a significant source of patient morbidity, precipitating frequent hospitalizations, a diminished quality of life, and a high risk of lower-extremity amputation and subsequent mortality.^{3,4} The established standard of care for DFUs necessitates a comprehensive, multidisciplinary strategy, integrating glycemic control, meticulous wound debridement, infection management, pressure off-loading, and the application of appropriate dressings.⁵

Although conventional therapy (CT) utilizing moist dressings remains a fundamental treatment component, its efficacy is often constrained, frequently resulting in protracted healing trajectories and a persistent risk of severe complications.^{3,6} Conventional wound management typically relies on passive dressings like gauze, cotton, films, and hydrocolloids. While these aim to protect the wound and maintain a moist environment, they possess inherent limitations.^{3,7,8} For instance, simple gauze dressings can adhere to the wound bed, causing secondary tissue trauma upon removal, and they offer suboptimal exudate management.^{3,7-9} More advanced options like hydrocolloids improve moisture retention but are primarily passive barriers that do little to actively stimulate the complex biological processes required for healing in compromised wounds like DFUs.¹⁰ These limitations have driven the field toward the development of advanced, active therapeutic modalities designed to modulate the wound environment and promote regeneration.⁷⁻⁹ This paradigm shift is evident in the extensive research into strategies such as the use of electrospun biomaterials that mimic the extracellular matrix, the incorporation of nanoparticles (eg, cerium oxide, titanium nanorods) to provide antioxidant and pro-angiogenic properties, and the development of systems for the controlled release of bioactive agents like nitric oxide and plant-derived compounds.¹¹⁻¹⁴ In this context, negative pressure wound therapy (NPWT), also known as vacuum-assisted closure (VAC), has emerged as a leading advanced therapeutic modality.⁶ NPWT operates by applying a controlled sub-atmospheric pressure to the wound environment, which is believed to foster healing through multiple mechanisms, including the management of exudate, reduction of tissue edema, enhancement of local perfusion, and stimulation of granulation tissue proliferation.^{6,15}

Reflecting its clinical significance, a substantial number of systematic reviews and meta-analyses have been published to synthesize the evidence on NPWT versus conventional therapy for DFUs.¹⁶⁻²³ However, this body of literature is characterized by disparate and often contradictory conclusions, resulting in a state of clinical equipoise.²⁴ This discordance is particularly evident for critical clinical outcomes and arises from key differences between reviews, including variations in study inclusion criteria, the date of literature searches, and the methodological quality of the reviews themselves.²⁴⁻²⁶ For example, regarding the pivotal issue of amputation, the meta-analysis by Chen et al²⁰ found no statistically significant benefit for NPWT over standard care. This stands in stark contrast to other comprehensive reviews that have reported a significant reduction in amputation risk with NPWT.²² Similarly, the effect of NPWT on ulcer depth reduction remains a point of contention; a meta-analysis by Liu et al¹⁷ demonstrated a significant advantage for NPWT, whereas a subsequent analysis by Angulo et al²³ reported no significant difference between the two therapies. This fractured evidence landscape creates considerable uncertainty for practitioners aiming to implement evidence-based medicine and impedes the formulation of a definitive, standardized therapeutic protocol.^{2,3}

To resolve this ambiguity, the present study undertakes a formal critical appraisal of these overlapping meta-analyses. Our objective was to systematically deconstruct and harmonize the available evidence, apply the validated Jadad decision algorithm to identify the highest-quality and most dependable meta-analysis, and, consequently, provide a clear, evidence-based clinical recommendation on the role of NPWT in the treatment of diabetic foot ulcers.

Methods

Search Strategy

This cross-sectional analysis was designed in accordance with the methodologies of previously published similar studies,²⁷⁻³⁰ and structured according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.³¹ A comprehensive literature retrieval was performed on June 18, 2025, to identify all meta-analyses published up to that date, across the PubMed, Embase, and Cochrane Library databases. Search terms included negative,

vacuum, NPWT, VAC, diabetic, foot, DFU, systematic review, and meta-analysis. The search was executed independently by two authors without language restrictions. To ensure comprehensiveness, the reference lists of included articles were manually screened for additional potential meta-analyses. Initial screening involved a review of titles and abstracts, with full-text articles being obtained for closer inspection when necessary. Any disagreements were resolved through discussion, with a third author serving as an arbitrator.

Eligibility Criteria

Inclusion parameters were as follows: (1) the study population consisted exclusively of patients with DFUs; (2) studies compared an intervention group (treated with NPWT or VAC) against a control group (treated with conventional therapy); (3) reported at least one quantifiable clinical outcome, such as healing time, healing rate, adverse events, or amputation rate; (4) the study was a meta-analysis.

Exclusion parameters were: (1) studies that were not meta-analyses (eg, narrative reviews, meeting abstracts, correspondence, or systematic reviews without a pooled analysis); (2) studies involving non-diabetic foot trauma; (3) articles lacking quantifiable outcome measures; (4) retracted articles.

Data Extraction

A standardized data collection form was used by two authors working independently to extract the following information from each eligible meta-analysis: first author, publication year, journal, number of primary studies included, number of randomized clinical trials (RCTs), search strategy details, methodological information (eg, software used, sensitivity analysis), I^2 values, and principal meta-analytic results. A third author was consulted to resolve any discrepancies in extracted data.

Quality Assessment

The methodological quality of each included meta-analysis was appraised using two standardized instruments: the Oxford Levels of Evidence³² and the Assessment of Multiple Systematic Reviews (AMSTAR) tool.²⁵ The AMSTAR instrument is a validated 11-item tool recognized for its reliability and validity in evaluating the quality of systematic reviews²⁶ and is widely applied in this context.^{27–30} Two reviewers independently performed the quality appraisal, with disagreements resolved by consensus discussion or adjudication by a third reviewer.

Application of Jadad Decision Algorithm

The Jadad decision algorithm was utilized to systematically navigate the sources of discordance among the included reviews.²⁴ This algorithm provides a structured framework for comparing meta-analyses based on differences in their clinical question, inclusion criteria, data extraction processes, quality appraisal, and statistical methods. It has been effectively used in prior studies to select the best evidence from a pool of conflicting meta-analyses.^{27–30} Three authors independently applied the algorithm to reach a consensus on which meta-analysis offered the most reliable evidence.

The application of the algorithm by three independent authors proceeds as follows: First, an assessment is made as to whether the included meta-analyses address the same clinical question (Step A). If they do, the degree of overlap among the primary trials included in each review is evaluated, typically by creating an evidence matrix (Step C). Depending on the degree of trial overlap and the similarity of study quality (Step D), the algorithm guides the user to compare specific aspects such as data extraction and synthesis (Step E) or to select the review with the highest overall quality (Step F). If the included trials are not the same, the algorithm directs an assessment of the selection criteria used by each review (Step G). Based on this assessment, the process may involve a focused comparison of search strategies (Step H) or, if criteria differ, a broader assessment of methodological quality, language restrictions, and the quality of primary trials to identify the most robust review (Step I). A consensus is reached among the authors to determine the final selection.

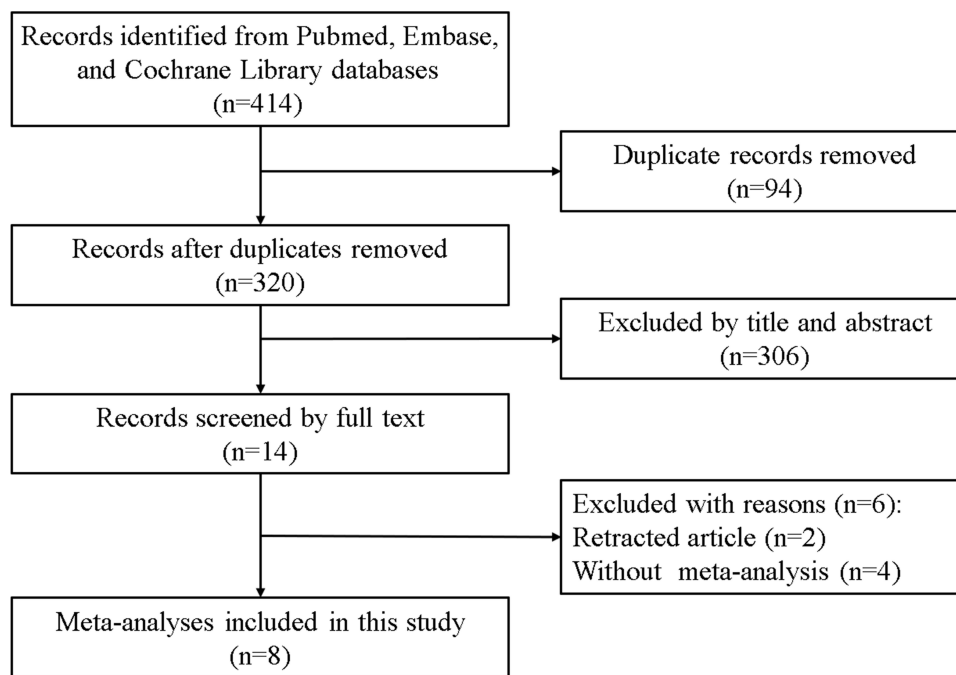


Figure 1 Visual summary of the study identification and screening pathway.

Results

Literature Search

The study selection process is illustrated in [Figure 1](#). An initial search yielded 414 records. After screening and eligibility assessment, eight meta-analyses were included in this critical appraisal.^{16–23} [Table 1](#) summarizes the characteristics of these studies, which were published between 2014 and 2025. The included meta-analyses drew upon primary trials published from 2000 to 2021, with each review including between 8 and 14 primary studies ([Table 2](#)).^{33–71}

Search Methodology

The search parameters varied across the included reviews. Three meta-analyses restricted their search to English-language publications,^{16,17,23} three imposed no language restrictions,^{18,21,22} and the remaining two did not specify their language criteria.^{19,20} Only two studies reported searching for unpublished literature (ie, no restriction on publication status).^{18,21} PubMed, Embase, and the Cochrane Library were consistently used across all reviews, while the inclusion of other databases like Web of Science was inconsistent. The search methodology for each study is detailed in [Table 3](#).

Table 1 Summary of Key Attributes of the Included Meta-Analyses

First Author	Date of Publication	Journal	Date of Last Literature Search	No. of Included Studies	No. of Included RCTs
Zhang J ¹⁶	2014	<i>Plastic and Reconstructive Surgery</i>	2013.02	8	8
Liu S ¹⁷	2017	<i>Therapeutics and Clinical Risk Management</i>	2016.06	11	11
Liu Z ¹⁸	2018	<i>Cochrane Database of Systematic Reviews</i>	2018.01	8	8
Huang Q ¹⁹	2019	<i>Journal of Foot & Ankle Surgery</i>	2017.10	10	10
Chen L ²⁰	2021	<i>Annals of Palliative Medicine</i>	NA	9	9
Dalmedico MM ²¹	2024	<i>Wounds</i>	2021.05	14	14
Deng YX ²²	2025	<i>World Journal of Diabetes</i>	2024.09	9	9
Angulo AR ²³	2025	<i>Journal of Wound, Ostomy and Continence Nursing</i>	2021.12	12	8

Table 2 Primary Trials Included in Each Meta-Analysis

First Author (Year)	Zhang J (2014) ¹⁶	Liu S (2017) ¹⁷	Liu Z (2018) ¹⁸	Huang Q (2019) ¹⁹	Chen L (2021) ²⁰	Dalmedico MM (2024) ²¹	Deng YX (2025) ²²	Angulo AR (2025) ²³
McCallon SK (2000) ³³	+	+		+				
Eginton MT (2003) ³⁴	+	+						
Etöz A (2004) ³⁵	+							
Armstrong DG (2005) ³⁶	+	+		+			+	
Sun J (2007) ³⁷		+						
Akbari A (2007) ³⁸				+		+		
Etoz A (2007) ³⁹						+		
Blume PA (2008) ⁴⁰	+	+	+	+		+	+	
Mody GN (2008) ⁴¹			+					
Sepúlveda G (2009) ⁴²	+	+		+			+	
Novinščak T (2010) ⁴³			+				+	
Riaz M (2010) ⁴⁴							+	
Paola L (2010) ⁴⁵							+	
Karatepe O (2011) ⁴⁶	+	+	+			+		+
Nain PS (2011) ⁴⁷	+	+	+	+	+		+	
Ulusal AE (2011) ⁴⁸				+		+		
Ravari H (2013) ⁴⁹		+		+	+			+
Zhu X (2014) ⁵⁰			+	+				
Lone AM (2014) ⁵¹					+		+	
Vaidhya N (2015) ⁵²		+	+		+	+		+
Sajid MT (2015) ⁵³		+			+			
Shi F (2015) ⁵⁴				+				
Yan W (2015) ⁵⁵				+				
Sun Y (2015) ⁵⁶						+		
Galstyan GR (2016) ⁵⁷						+		
Zaitseva EL (2016) ⁵⁸						+		
Zhang X (2017) ⁵⁹			+					
Chiang N (2017) ⁶⁰					+			
Dsouza C (2017) ⁶¹						+		
Borys S (2018) ⁶²					+			
Bayoumi A (2018) ⁶³						+		
Hu C (2018) ⁶⁴						+		
Potula VS (2018) ⁶⁵						+		
Hu X (2018) ⁶⁶						+		
James SMD (2019) ⁶⁷					+		+	+
Seidel D (2020) ⁶⁸					+		+	+
Alamdari N (2021) ⁶⁹								+
Maranna H (2021) ⁷⁰								+
Sheen N (2021) ⁷¹								+

Note: + indicates inclusion of the primary trial in the respective meta-analysis.

Table 3 Summary of Literature Search Strategies Employed by Each Meta-Analysis

First Author (Year)	Restriction of Publication Language	Restriction of Publication Status	Search Database				
			PubMed	Embase	Cochrane Library	Web of Science	Others
Zhang J (2014) ¹⁶	Yes	Yes	+	+	+		
Liu S (2017) ¹⁷	Yes	Yes		+	+		+
Liu Z (2018) ¹⁸	No	No		+	+		+
Huang Q (2019) ¹⁹	NA	NA	+	+	+		+
Chen L (2021) ²⁰	NA	Yes	+	+	+		+
Dalmedico MM (2024) ²¹	No	No	+		+	+	+

(Continued)

Table 3 (Continued).

First Author (Year)	Restriction of Publication Language	Restriction of Publication Status	Search Database				
			PubMed	Embase	Cochrane Library	Web of Science	Others
Deng YX (2025) ²²	No	NA	+	+	+	+	
Angulo AR (2025) ²³	Yes	Yes	+	+		+	+

Note: + indicates the database was included in the search strategy.

Methodological Quality

According to the Oxford Levels of Evidence, seven meta-analyses were classified as Level II evidence, as they exclusively included RCTs.^{16–22} One study was deemed Level III evidence due to its inclusion of both RCTs and cohort studies (Table 4).²³ The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework was used in two reviews to assess the certainty of evidence.^{18,21} The most commonly used statistical software was RevMan. AMSTAR scores for the included reviews ranged from 6 to 9, with a median score of 7.5, indicating generally moderate to high methodological quality (Table 5).

Heterogeneity Assessment

The I^2 statistic was used in all included reviews to quantify inter-study heterogeneity for their pooled outcomes (Table 6). Three of the meta-analyses conducted sensitivity analyses to explore the impact of methodological quality on their results (Table 4).^{16,17,20}

Results of Jadad Decision Algorithm

The Jadad decision algorithm was applied to determine which of the eight meta-analyses provided the best available evidence.²⁴ The pooled results from all included studies are visualized in Figure 2. The specific application of the algorithm to the eight included meta-analyses proceeded as follows (Figure 3): All studies were determined to address the same clinical question (Step A: Yes). Examination of the primary trial evidence matrix (Table 2) revealed that the studies did not include the same trials (Step C: No). A further assessment of the search strategies and methodological details (Tables 3 and 4) showed that the selection criteria were not the same (Step G: No). This path led to Step I, which mandates the selection of the best evidence based on a comprehensive comparison of methodological quality, search comprehensiveness, and the quality of included primary trials. Based on this final assessment, the 2025 meta-analysis by Deng et al²² was selected (Figure 3). This review demonstrated a statistically significant improvement in wound healing rate (risk ratio = 1.46, 95% confidence interval 1.22–1.76) and a reduction in amputation rate with NPWT (risk ratio = 0.69, 95% confidence interval 0.50–0.96). Additionally, it found that the time to granulation tissue formation was significantly shortened. The incidence of adverse

Table 4 Key Methodological Details of the Included Meta-Analyses

First Author (Year)	Study Design	Level of Evidence	Software	GRADE use	Sensitivity Analysis
Zhang J (2014) ¹⁶	RCT	Level II	STATA	No	Yes
Liu S (2017) ¹⁷	RCT	Level II	RevMan	No	Yes
Liu Z (2018) ¹⁸	RCT	Level II	RevMan	Yes	No
Huang Q (2019) ¹⁹	RCT	Level II	Revman	No	No
Chen L (2021) ²⁰	RCT	Level II	Revman	No	Yes
Dalmedico MM (2024) ²¹	RCT	Level II	Revman	Yes	No
Deng YX (2025) ²²	RCT	Level II	STATA	No	No
Angulo AR (2025) ²³	RCT or cohort study	Level III	Revman	No	No

Abbreviations: RCT, Randomized Controlled Trial; GRADE, Grading of Recommendations, Assessment, Development and Evaluations.

Table 5 Results of the AMSTAR Methodological Quality Assessment

Items	Zhang J (2014) ¹⁶	Liu S (2017) ¹⁷	Liu Z (2018) ¹⁸	Huang Q (2019) ¹⁹	Chen L (2021) ²⁰	Dalmedico MM (2024) ²¹	Deng YX (2025) ²²	Angulo AR (2025) ²³
1. Was an a priori design provided?	0	0	0	0	0	1	0	0
2. Was there duplicate study selection and data extraction?	1	1	1	1	1	1	1	1
3. Was a comprehensive literature search performed?	1	1	1	1	1	1	1	1
4. Was the status of publication (ie, grey literature) used as an inclusion criterion?	0	0	1	0	0	1	0	0
5. Was a list of studies (included and excluded) provided?	0	1	1	0	1	0	1	0
6. Were the characteristics of the included studies provided?	1	1	1	1	1	1	1	1
7. Was the scientific quality of the included studies assessed and documented?	1	1	1	1	1	1	1	1
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	0	0	1	1	0	1	1	0
9. Were the methods used to combine the findings of studies appropriate?	1	1	1	1	1	0	1	1
10. Was the likelihood of publication bias assessed?	1	0	0	0	1	0	1	0
11. Was the conflict of interest stated?	1	1	1	1	1	1	1	1
Total scores	7	7	9	7	8	8	9	6

Table 6 Reported Statistical Heterogeneity (I^2) for Key Outcomes in Each Meta-Analysis

Items	Zhang J (2014) ¹⁶	Liu S (2017) ¹⁷	Liu Z (2018) ¹⁸	Huang Q (2019) ¹⁹	Chen L (2021) ²⁰	Dalmedico MM (2024) ²¹	Deng YX (2025) ²²	Angulo AR (2025) ²³
DFU healing time	0.0%	0%		0%				
DFU healing rate	0.0%	37%	0%	24%	0%		0%	
Number of DFU closed or covered with surgery			28.39%					
DFU depth reduction		0%				100%		96%
DFU area reduction	0.0%	40%		0%				
Granulation tissue formation time					0%		28.4%	95%
Hospital length of stay								78%
Adverse events	0.0%	0%		36%	0%		19.6%	
Infection rate								22%
Pain reduction								0%
Amputation rate	0.0%	0%	0%		0%		25.7%	38%
Major amputation rate	0.0%							
Minor amputation rate	0.0%							

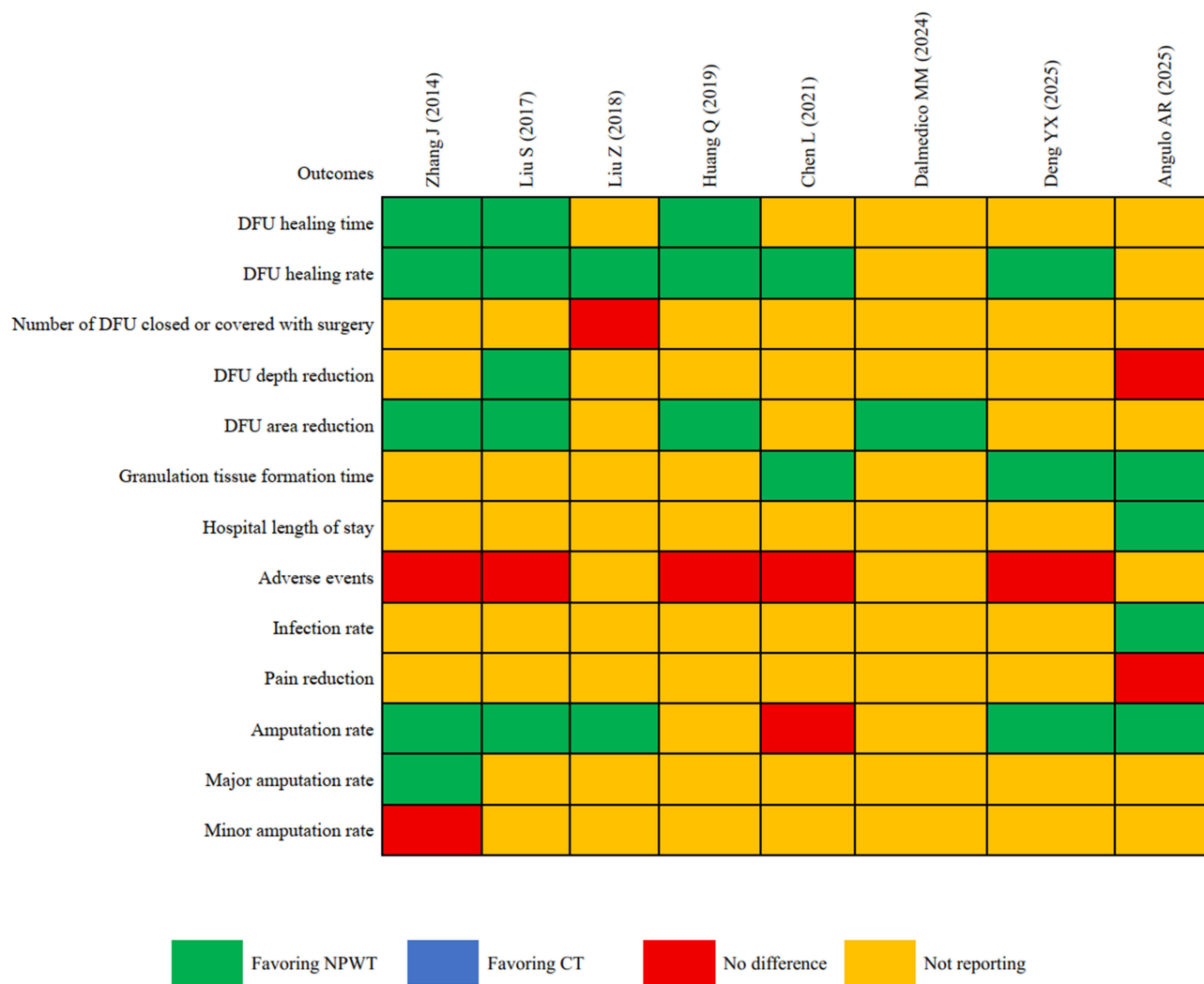


Figure 2 Comparative summary of findings from the included meta-analyses.

events, however, was not significantly different between NPWT and control groups. Therefore, NPWT is a safe and effective therapy that enhances healing and reduces amputations in patients with DFUs.

Discussion

This study represents, to our knowledge, the first critical appraisal designed to synthesize and harmonize the overlapping body of meta-analytic evidence on NPWT for DFUs. In a clinical area characterized by multiple, often contradictory, high-level meta-analyses, such an investigation is essential for providing clarity and guiding evidence-based practice.^{27–30} This methodological approach is particularly valuable in modern evidence-based medicine, where clinicians are often overwhelmed by an ever-increasing volume of publications.^{24–26} Instead of requiring practitioners to individually appraise multiple complex reviews with varying conclusions, our work provides a single, methodologically vetted directive, thereby enhancing the practical application of evidence at the point of care. Through a comprehensive evaluation of eight meta-analyses and the formal application of the Jadad decision algorithm, our work identifies the 2025 meta-analysis by Deng et al²² as the most methodologically robust and reliable source of evidence currently available. This selection was not an arbitrary choice, but the direct result of a systematic process that evaluated multiple quality-related domains. Specifically, the selection of Deng et al²² was predicated on its superior AMSTAR score, its comprehensive search strategy which did not impose language bias, and its inclusion of a greater number of recent and high-quality RCTs, making it the most up-to-date and methodologically sound synthesis available.

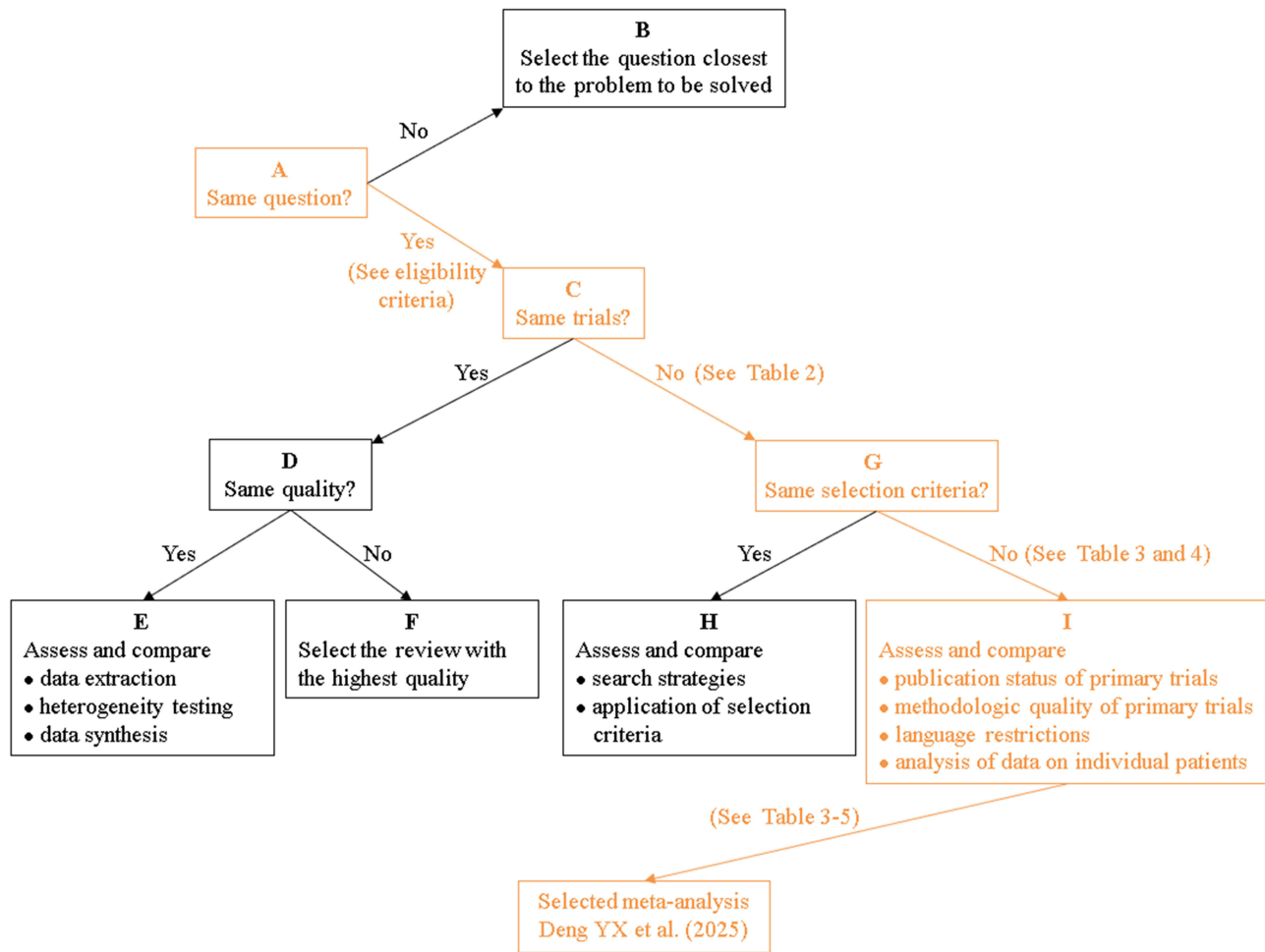


Figure 3 Schematic representation of the Jadad decision algorithm application.

The central conclusion derived from this best-evidence analysis is that NPWT confers substantial clinical benefits over conventional therapy in the management of DFUs.²² The evidence demonstrates that NPWT leads to a significantly higher rate of complete wound closure and a clinically important reduction in the risk of amputation.²² Moreover, NPWT accelerates a critical phase of healing by markedly shortening the time to granulation tissue formation.²² Importantly, these therapeutic gains are not accompanied by an increased risk of adverse events, underscoring a favorable safety profile for the intervention.²² However, the conclusion of a favorable safety profile must be interpreted with some caution. While the best-evidence analysis found no significant increase in overall adverse events, safety reporting across the primary trials included in these meta-analyses is often inconsistent and incomplete.²² Important adverse events like bleeding or periwound maceration may be underreported, a common limitation in wound care trials that should be acknowledged.²²

The discordance among the eight included meta-analyses is attributable to several identifiable factors. Chronological differences in publication are a key contributor; earlier reviews, such as those by Zhang et al and Liu et al,^{16,17} were unable to incorporate the findings of more recent RCTs, which were included in the later, more comprehensive analysis by Deng et al.²² Furthermore, variations in methodological quality, reflected by AMSTAR scores spanning from 6 to 9, likely influenced the results. Meta-analyses with lower scores may have employed less rigorous inclusion criteria or statistical methods, leading to less precise or potentially biased effect estimates.^{24,25} As our detailed examination in the introduction revealed, these methodological differences manifested as conflicting conclusions on key outcomes like amputation rates and ulcer depth reduction.^{17,20,22,23}

From a clinical standpoint, these findings carry significant weight. The confirmation that NPWT accelerates healing and reduces amputations provides a strong evidence-based rationale for its integration into DFU treatment algorithms.^{3,22} A more

rapid formation of healthy granulation tissue facilitates earlier consideration of definitive wound closure procedures, such as skin grafting, which may in turn reduce the length of hospital stay and lower overall healthcare costs.^{1,3,6,22} The demonstrated reduction in amputation risk is paramount, as limb preservation is a primary objective of DFU care, with profound implications for patient mobility, quality of life, and survival.^{2,3,6} The robust safety profile of NPWT should provide clinicians with confidence in its application, assuming appropriate patient selection and monitoring protocols are followed.

While our analysis confirms the efficacy of NPWT as a crucial advanced therapy, it is important to contextualize this finding within the rapidly evolving field of wound care materials science.^{7,9} Recent advancements in biofabrication, such as the development of electrospun Janus nanofibers, offer novel therapeutic possibilities.^{7–9,72} As reviewed by Yu et al,⁷² these multi-functional dressings can be engineered to possess different properties on each side (eg, hydrophobic outer layer for protection and hydrophilic inner layer for exudate management), allowing for a combination of effects such as simultaneous antibacterial action and promotion of cell growth. This goes beyond the primarily mechanical function of NPWT. Therefore, the future of DFU management may involve not just the optimization of existing methods like NPWT, but also the integration or combination of these therapies with such advanced, multi-functional biomaterials to achieve synergistic healing effects.

Furthermore, the future of wound dressing development is increasingly focused on sustainability and “green” approaches, as highlighted in a recent comprehensive review by Verma et al.¹⁰ This involves a shift towards utilizing natural biopolymers such as cellulose, chitosan, and alginates, which offer advantages like biocompatibility, biodegradability, and derivation from renewable resources.¹⁰ This trend towards “green” biomaterials complements the development of advanced mechanical therapies like NPWT. Future research may therefore explore hybrid systems that combine the proven mechanical benefits of NPWT with bioactive, sustainable biopolymer dressings to optimize healing outcomes in a more environmentally conscious manner.

This study, however, is subject to certain limitations. First, and most fundamentally, while our method’s principal value lies in providing a clear, high-level directive, this comes at the cost of the granular detail found in primary studies. Nuances regarding specific patient subgroups, wound characteristics, or variations in NPWT application protocols are inevitably lost in a cross-sectional analysis of meta-analyses. Second, our approach means our findings are based on aggregate data from previously published studies rather than a *de novo* analysis of primary trial data, and the validity of our conclusion is therefore contingent upon the quality of the source reviews. If all existing meta-analyses are flawed, our conclusion, though representing the best available evidence, will still inherit those limitations. Third, the potential for publication bias in the primary literature remains a concern, as studies with null or negative findings may be under-represented, which could skew the results of the meta-analyses we evaluated. Finally, this cross-sectional analysis is inherently retrospective; new primary trials may have been published after the search cutoff dates of the included meta-analyses, representing a potential evidence lag.

Conclusion

In summary, this critical appraisal identified the highest-quality evidence, which demonstrates that NPWT is a safe and effective intervention for DFUs, significantly enhancing wound healing rates, accelerating granulation tissue formation, and reducing the incidence of amputations compared to CT. The primary innovation of this study lies in its methodological approach, which was predicated on the premise that a systematic, quality-based appraisal of overlapping meta-analyses could resolve the clinical uncertainty arising from a landscape of conflicting reports. Our final conclusion, derived from the most robust available evidence, aligns with prior meta-analyses that reported a benefit for NPWT, while providing a methodological explanation for the discordance with those that found no significant effect. By harmonizing these findings, this study provides a clear and compelling rationale for the routine consideration of NPWT as an effective adjunct to standard multidisciplinary care for DFUs. Future research should now focus on direct head-to-head comparisons between NPWT and other advanced wound therapies and evaluate long-term, patient-centered outcomes such as quality of life and treatment burden.

Abbreviations

AMSTAR, Assessment of Multiple Systematic Reviews; CT, Conventional therapy; DFUs, Diabetic foot ulcers; GRADE, Grading of Recommendations, Assessment, Development and Evaluations; NPWT, Negative pressure wound therapy; RCTs, Randomized clinical trials; VAC, Vacuum-assisted closure.

Data Sharing Statement

Data are available on reasonable request to the corresponding author.

Author Contributions

Ying Du and Tiangang Zhai: Data curation, methodology, investigation, validation, formal analysis, writing—original draft; Zhujun Sheng, Weinan Xie, and Zhiwei Jia: Methodology, investigation, visualization, formal analysis, writing—review and editing; Tianlin Wen, Xiyan Zhao, and Xiaolin Tong: Conceptualization, supervision, writing—review and editing. All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare no conflicts of interest in this work.

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