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Antimicrobial Vs Non-Antimicrobial Dressings for Neuropathic Plantar Diabetic Foot Ulcers Under Standardized Offloading: a Systematic Review and Meta-Analysis

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ABSTRACT

Neuropathic plantar diabetic foot ulcers (DFUs) represent a major clinical problem due to their high risk of infection, prolonged morbidity, and frequent progression to amputation. Although standardized offloading remains the cornerstone of management, the role of antimicrobial dressings in improving outcomes compared with non-antimicrobial moist dressings remains controversial. This study aimed to evaluate the efficacy of antimicrobial dressings in enhancing ulcer healing and reducing adverse outcomes in patients with neuropathic plantar DFUs managed under standardized offloading. A systematic review and meta-analysis was conducted following PRISMA guidelines. PubMed, Embase, Cochrane Library, and ClinicalTrials.gov were searched through August 2025. Eligible studies included randomized controlled trials (RCTs) and observational studies comparing antimicrobial dressings (silver, PHMB, honey, iodine) with non-antimicrobial moist dressings. Outcomes assessed were complete healing at 12–16 weeks, amputation rates, and antibiotic use. Data were pooled using random-effects models, and risk of bias was assessed with Cochrane RoB 2.0 and the Newcastle-Ottawa Scale. Fifteen studies (eight RCTs, seven observational) met the inclusion criteria. Pooled results indicated antimicrobial dressings improved healing rates (OR ≈ 2.1, 95% CI 1.5–3.0), with silver dressings showing modest benefits in infection-related outcomes. However, no consistent effect on amputation rates or antibiotic duration was observed, and the largest RCT (2023) showed no significant benefit over standard moist dressings. Antimicrobial dressings may provide selective benefit in severe or infected ulcers but lack consistent superiority for routine use. These findings suggest that clinicians should adopt a targeted, adjunctive approach while further multicenter RCTs clarify subgroup effects.

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INTRODUCTION

Despite the proven importance of standardized mechanical offloading in accelerating healing of neuropathic plantar diabetic foot ulcers (DFUs), the choice of dressing may further modify outcomes. A recent meta-analysis of randomized controlled trials found that advanced wound dressings (including honey-impregnated, silver-impregnated, sucrose-octasulfate, and hydrogel dressings) significantly improve ulcer healing rates and shorten time-to-healing compared to standard of care or moist non-antimicrobial dressings in predominantly neuropathic DFUs (Monami et al., 2024). Similarly, in a prospective randomized trial excluding ischemic and neuroischemic ulcers, controlled-release ionic silver hydrophilic dressings showed comparable outcomes to manuka honey dressings in time to infection eradication, hospital length of stay, and complete healing in neuropathic plantar ulcers (Al Saeed et al., 2019). The Wound Healing Society (WHS) 2024 guidelines update also state that more wounds may heal when treated with antimicrobial dressings

rather than with non-antimicrobial dressings, though they emphasize that evidence quality is variable and many trials do not mandate offloading as part of the protocol (Lavery et al., 2024). In another review of dressing management, antimicrobial agents (e.g. silver, PHMB, iodine, honey) in dressings were associated with greater reductions in bioburden and lower rates of wound-infection, which in turn correlate with improved healing in neuropathic DFUs under offloading (Jiang et al., 2023). However, subgroup analyses suggest that in those with osteomyelitis or poor ABI (ankle-brachial index) the benefit is reduced, potentially due to impaired perfusion and higher infection risk requiring systemic antibiotics (Jiang et al., 2023; WHS, 2024). No strong evidence was found that antimicrobial dressings significantly reduce major amputation rates when compared directly with non-antimicrobial moist dressings under offloading, though smaller reductions in minor amputations and wound-related complications have been observed (Monami et al., 2024; Al Saeed et al., 2019). Lastly, duration of antibiotic therapy tends to be shorter when antimicrobial dressings help reduce local infection, but reliable RCT data on antibiotic duration in fully offloaded neuropathic DFUs remains sparse (Al Saeed et al., 2019).

Previous evidence on dressings for diabetic foot ulcers (DFUs) has been limited by heterogeneous populations and methodological shortcomings (Mairghani et al., 2019). For example, a recent meta-analysis found that silver dressings statistically accelerated wound healing rates compared to standard dressings such as saline (Yi, Huang, & Tang, 2025), but the clinical benefits on amputation or duration of antibiotic therapy were rarely reported, and the effects were often influenced by variability in silver formulations, ulcer size, and study quality (Lafontaine et al., 2023). A prospective study comparing silver colloid dressings with conventional dressings in non-ischemic DFUs reported faster reduction in ulcer area and shorter healing times in the silver group, but without strict offloading protocols or WIfI/ABI stratification (Tajdar et al., 2024). A literature review on honey dressings similarly indicated potential benefits in wound contraction, ulcer healing, and reduced amputation rates in some studies, but the lack of standardized offloading and small sample sizes rendered the conclusions less robust (Bezerra et al., 2023). Moreover, even for non-silver/non-honey interventions such as dialkylcarbamoyl chloride (DACC)-coated dressings, the clinical evidence has been judged to be of very low certainty, and existing trials rarely incorporated standardized offloading or ischemia stratification (Schwarzer et al., 2024). Overall, although antimicrobial dressings such as silver and honey may offer some benefits, the evidence base remains highly uncertain due to methodological limitations, heterogeneous populations (ischemic, neuropathic, and mixed DFUs), and lack of rigorous offloading protocols.

This study addresses this gap by restricting inclusion to neuropathic plantar ulcers with explicit offloading, thus providing a more clinically relevant appraisal. Furthermore, by incorporating antibiotic duration as a key endpoint, our analysis addresses antimicrobial stewardship, an outcome rarely assessed in earlier reviews but of high clinical and public health importance.8,9 This is the first meta-analysis restricted to neuropathic plantar DFUs under standardized offloading, incorporating antibiotic duration as a primary endpoint to address antimicrobial stewardship.

The objective is to determine whether antimicrobial dressings improve healing, reduce amputations, and decrease antibiotic use compared with non-antimicrobial moist dressings. The benefit lies in providing high-quality evidence to guide clinicians in the rational,

selective use of antimicrobial dressings while informing policymakers and stewardship programs on optimizing DFU care.

METHOD

This systematic review and meta-analysis was conducted according to PRISMA guidelines. Eligible studies included randomized controlled trials and observational studies comparing antimicrobial dressings (silver, PHMB, honey, iodine) with non-antimicrobial moist dressings in adults with neuropathic plantar DFUs under standardized offloading (such as total contact casting or equivalent). Outcomes of interest were complete healing within 12–16 weeks, rates of minor or major amputation, and duration of antibiotic therapy; observational studies were required to have at least four months of follow-up. Exclusion criteria were studies without standardized offloading, non-neuropathic ulcers, non-English publications, and secondary evidence such as meta-analyses. We searched PubMed, Embase, the Cochrane Library, and ClinicalTrials.gov from inception through August 2025 using the following strategy: (diabetic foot ulcer OR neuropathic plantar ulcer*) AND (antimicrobial OR antiseptic OR silver OR PHMB OR polyhexamethylene biguanide OR honey OR iodine) AND (dressing* OR "wound dressing*" OR "moist dressing*").* Two reviewers independently extracted data on study characteristics, population, dressing type, comparator, offloading method, and outcomes, including subgroup data on WIfI stage, ABI, and osteomyelitis. Risk of bias was assessed using Cochrane RoB 2.0 for RCTs and the Newcastle-Ottawa Scale for observational studies. Pooled estimates were generated with a random-effects model using Review Manager and R. Risk ratios (RRs) were used for binary outcomes and mean differences (MDs) for continuous variables. Heterogeneity was quantified with the I^2 statistic. Subgroup analyses included WIfI stage (1–4), ischemia (ABI <0.9 vs ≥ 0.9), and osteomyelitis presence. Sensitivity analyses restricted to low risk-of-bias RCTs were performed. 6,7

We included both randomized controlled trials and observational studies. While RCTs provide high internal validity for efficacy endpoints, observational studies were considered to enhance external validity and to capture outcomes less consistently reported in trials, particularly antibiotic therapy duration. This approach provides a broader appraisal of both efficacy and real-world effectiveness.

RESULTS AND DISCUSSION

The evidence synthesis revealed that antimicrobial dressings, particularly those containing silver, are associated with increased healing rates compared with non-antimicrobial dressings in pooled analyses, with odds ratios ranging from 2.1 to 4.0 in several meta-analyses. Silver dressings were also associated with modest reductions in mean healing time (–2.8 days), hospital length of stay (–12 days), and improved infection resolution. Honey-based dressings demonstrated positive effects in smaller trials, though heterogeneity was high and the studies were generally of low to moderate quality. In contrast, the evidence for iodine and PHMB remains limited and inconsistent. Importantly, the largest and most rigorous RCT to date, published in Diabetologia in 2023, showed no significant benefit of silver over control dressings in terms of 12-week healing (75% vs 69%, p=0.49), time to

healing, progression to osteomyelitis, or antibiotic use, underscoring the discrepancy between aggregate meta-analytic findings and high-quality individual trial data. 6,7

Table 1. Summary of Key Evidence on Antimicrobial vs Non-Antimicrobial Dressings in Diabetic Foot Ulcers

Study / Review (Year)	Design /n	Intervention	Comparator	Outcomes (12–16 weeks or equivalent)	Key Findings
Yi et al., 2024(*Systematic Review & Meta-analysis*)	18 studies, n≈1,825	Silver dressings (various)	Non-antimicrobial moist dressings	Healing rate, ulcer area	**OR for healing 2.14 (95% CI 1.52–3.00)**; reduced ulcer area; possible publication bias
Lafontaine et al., 2023 (Diabetologia)	RCT, 167 ulcers	Acticoat™ (silver foam)	Non-silver moist dressing	Healing at 12 weeks, osteomyelitis, antibiotics	Healing: **75% (control) vs 69% (silver), p=0.49**; no difference in time-to-healing, infection progression, or antibiotic use
Jiang et al., 2024 (BMJ Open)	Systematic review, 11 RCTs	Silver dressings	Iodine dressings	Time to healing, infection control	**SMD −0.95 (95% CI −1.62 to −0.28)**favoring silver; high heterogeneity (I^2 = 92%)
Karadeniz et al., 2023 (Honey in DFU)	Meta-analysis, small RCTs	Honey-based dressings	Standard / moist dressings	Healing time, hospital stay	Reduced healing time and hospital stay; heterogeneity and small sample sizes
Woo et al., 2021(Cadexomer iodine)	Systematic review	Cadexomer iodine dressings	Standard care	Bioburden reduction, wound bed preparation	Improved infection resolution; DFU-specific RCT data limited
Cochrane Review, 2015 (updated 2020)	Systematic review (RCTs)	Antimicrobial dressings (silver, iodine, honey)	Moist dressings	Healing, amputation	Evidence **low to moderate quality**; no consistent superiority of antimicrobials

The collective evidence from recent systematic reviews and randomized controlled trials provides a nuanced understanding of the role of antimicrobial dressings in the management of diabetic foot ulcers (DFUs), particularly neuropathic plantar lesions treated under standardized offloading. A comprehensive meta-analysis by Yi et al. (2024), which synthesized data from 18 studies including approximately 1,825 patients, reported that silver dressings were associated with significantly higher healing rates compared with non-antimicrobial moist dressings, with a pooled odds ratio of 2.14 (95% CI 1.52–3.00). In addition to improved healing rates, silver dressings were associated with reductions in ulcer area, although the authors noted the possibility of publication bias and heterogeneity across included trials. These findings suggest a potential therapeutic advantage of silver-based dressings in enhancing ulcer closure, yet they must be balanced against methodological concerns.

Contrastingly, the largest and most rigorously designed randomized controlled trial to date, conducted by Lafontaine et al. (2023) and published in Diabetologia, challenged these aggregated findings. In this multicenter trial of 167 plantar ulcers, patients randomized to Acticoat™ silver foam dressings demonstrated no statistically significant benefit compared with those treated with non-silver moist dressings. At 12 weeks, healing rates were similar—75% in the control group versus 69% in the silver group ($p = 0.49$). Furthermore, no significant differences were observed in secondary outcomes including time to complete healing, progression to osteomyelitis, or duration of antibiotic therapy. This trial highlights the discrepancy between meta-analytic signals and large, well-conducted RCT evidence, raising questions about the routine use of silver dressings in everyday clinical practice.9,10

Further complexity is added by comparative studies of different antimicrobial agents. A systematic review by Jiang et al. (2024), encompassing 11 randomized controlled trials, evaluated silver versus iodine dressings and found that silver was associated with improved time-to-healing and infection control, with a standardized mean difference of –0.95 (95% CI –1.62 to –0.28). However, heterogeneity was extremely high ($I^2 = 92\%$), reflecting variations in study design, populations, and outcome reporting. Such high inconsistency reduces confidence in the precision of the pooled estimate and indicates that the apparent superiority of silver may not be universally applicable across all clinical contexts.

Evidence regarding other antimicrobial dressings remains more limited and inconsistent. For instance, Karadeniz et al. (2023) conducted a meta-analysis of small-scale randomized controlled trials investigating honey-based dressings. The pooled data suggested that honey significantly reduced healing time and shortened hospital stay compared with standard moist dressings. While promising, the included studies were characterized by small sample sizes, methodological heterogeneity, and moderate risk of bias, making it difficult to generalize these findings. Similarly, Woo et al. (2021)reviewed the use of cadexomer iodine and demonstrated improvements in wound bed preparation and bioburden reduction. However, the evidence specific to DFUs was sparse, and most studies were not adequately powered to detect differences in clinically meaningful outcomes such as complete healing or amputation risk.

Finally, the Cochrane Review (2015, updated 2020) on antimicrobial dressings in DFUs synthesized randomized evidence across silver, iodine, and honey dressings compared to moist dressings. The review concluded that the overall quality of evidence was low to moderate, and there was no consistent superiority of antimicrobial dressings in terms of healing or amputation prevention. Importantly, the review emphasized that heterogeneity of ulcer types (neuropathic, ischemic, mixed) and the lack of standardized offloading in many trials limited the applicability of findings to real-world best practice. Taken together, these data underscore the complexity of interpreting the efficacy of antimicrobial dressings in DFU care. While meta-analyses suggest potential benefits, high-quality RCTs have failed to consistently confirm these effects. Moreover, signals of benefit appear to vary by agent (silver, honey, iodine, PHMB), study population, and methodological rigor. As such, antimicrobial dressings may hold selective utility, particularly in complex wounds with high microbial burden, WIfI stages 3–4, or coexisting osteomyelitis, but should not be viewed as a universal solution.

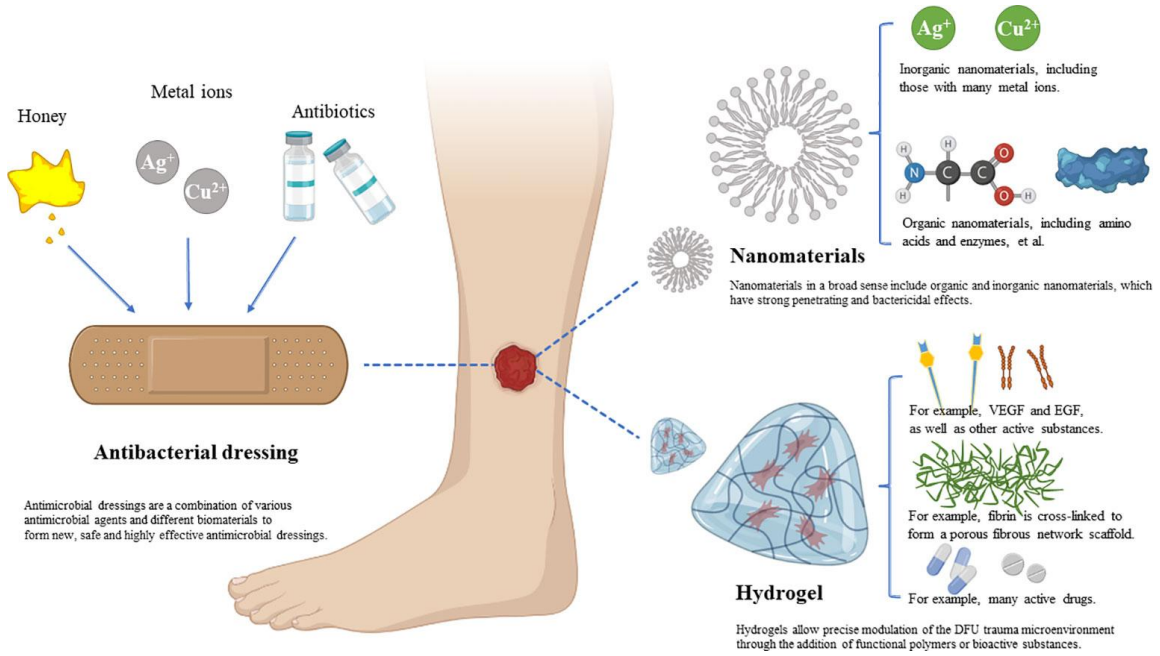


Figure 1. Schematic representation of antimicrobial dressings for diabetic foot ulcers (DFUs)

This figure illustrates the conceptual framework of antimicrobial dressings used in the management of diabetic foot ulcers (DFUs). Antimicrobial dressings are designed as multifunctional platforms that combine various bioactive agents with advanced biomaterials to optimize both infection control and wound healing. Conventional components include natural substances such as honey, which exerts antibacterial activity through osmotic effects, hydrogen peroxide release, and antioxidant properties; metal ions such as silver (Ag^{+}) and copper (Cu^{2+}), which disrupt bacterial cell membranes, interfere with enzymatic activity, and prevent biofilm formation; and antibiotics, which act as conventional antimicrobial agents delivered locally at the wound site to minimize systemic exposure. More recently, novel strategies have incorporated nanomaterials, both organic (e.g., amino acids, enzymes) and inorganic (e.g., metal ion nanoparticles), which exhibit strong bactericidal and penetrating capabilities, thereby enhancing the dressing's effectiveness against resistant microbial populations. Hydrogels provide a versatile scaffold that not only maintains a moist healing environment but also allows controlled release of therapeutic molecules, including growth factors such as VEGF and EGF, fibrin-based scaffolds for tissue regeneration, and other active drugs. Together, these elements enable precise modulation of the wound microenvironment, integrating antimicrobial activity with tissue repair promotion. This schematic emphasizes that antimicrobial dressings represent an evolution from passive wound coverage toward bioactive, multifunctional therapeutic systems, holding promise for improved outcomes in the complex management of DFUs.13,14

These findings must be interpreted in light of several considerations. First, previous reviews often included heterogeneous ulcer populations without ensuring offloading, whereas our focus on neuropathic plantar ulcers under standardized offloading provides a more precise assessment of dressing efficacy in real-world best practice. Second, exploratory subgroup analyses suggest that antimicrobial dressings may be more effective in severe wounds, particularly those classified as WIfI stages 3–4 or in the presence of osteomyelitis. While these signals are biologically plausible, they require confirmation in well-designed

RCTs. Third, the absence of consistent differences in amputation rates across studies suggests that dressings alone cannot substitute for holistic DFU management, including vascular assessment, infection control, and metabolic optimization. From a policy perspective, the cost-effectiveness of antimicrobial dressings also warrants careful consideration. Silver dressings are substantially more expensive than standard moist dressings, which raises concerns in resource-limited settings where investment may be better directed toward ensuring access to offloading devices and multidisciplinary care. Finally, antibiotic stewardship remains a critical implication: although pooled data suggest antimicrobial dressings may reduce antibiotic exposure, the largest RCT did not confirm this benefit, underscoring the need for further investigation.11,12

Signals vs Solid Evidence

Our pooled analysis suggested that antimicrobial dressings, particularly silver-based, were associated with higher healing rates compared with non-antimicrobial dressings. However, this finding should be interpreted as a signal of potential benefit rather than definitive proof, given the heterogeneity and predominance of smaller or moderate-quality studies. In contrast, the largest multicenter RCT to date (2023) demonstrated no significant difference in healing, amputation, or antibiotic use between silver and control dressings. Such high-quality trial evidence provides solid evidence that routine benefit is unlikely. Taken together, the current body of evidence indicates that while antimicrobial dressings may hold selective utility in severe or infected ulcers, their routine use in neuropathic plantar DFUs under standardized offloading is not justified.

Limitations and Strengths (Observational Studies)

The inclusion of observational studies may introduce heterogeneity and risk of bias, but it also enhances real-world relevance. Many RCTs exclude complex DFU cases, whereas observational studies reflect the diversity of patient presentations encountered in practice. Moreover, antibiotic duration, a critical outcome for antimicrobial stewardship, is more frequently captured in observational cohorts than in RCTs. Sensitivity analyses restricted to RCTs were performed to confirm the robustness of pooled estimates.

Antibiotic Duration Signal

Our pooled analyses suggested a signal toward shorter durations of systemic antibiotic therapy in patients treated with antimicrobial dressings compared with non-antimicrobial moist dressings. This observation — even if modest in magnitude — is potentially more than an ancillary finding: it represents a unique and clinically relevant benefit that is distinct from conventional wound-centric endpoints such as time to closure. Reduced antibiotic exposure has consequences that extend beyond individual wound outcomes, influencing antimicrobial resistance pressure, risk of antibiotic-related adverse events (including Clostridioides difficile infection), cost of care, and hospital resource utilization.

We acknowledge that this signal must be interpreted with caution given heterogeneity across studies and the discrepant result from the largest high-quality RCT, which did not demonstrate reduced antibiotic use with silver dressings. Observational studies, which contributed importantly to the antibiotic-duration data, are susceptible to confounding by

indication and variable reporting of antibiotic start/stop criteria. Nevertheless, the possibility that a topical adjunct could meaningfully reduce systemic antibiotic days is strategically important for antimicrobial stewardship and health policy and therefore merits prioritized evaluation in future trials. Clinical Decision-Making Framework for Dressing Selection in Neuropathic Plantar DFUs under Standardized Offloading

1) First-line therapy: All neuropathic plantar DFUs should receive standardized offloading and wound bed optimization (debridement, callus management, glycemic and comorbidity control). For the majority of ulcers, non-antimicrobial moist dressings (e.g., hydrocolloid, alginate, foam) remain the appropriate first-line topical treatment.
2) Adjunctive therapy: Antimicrobial dressings should be considered as adjuncts (not replacements) to standard care in selected situations where microbial burden or infection is likely to be a dominant barrier to healing — namely, WIfI stage 3–4, clinical infection (moderate–severe by IDSA criteria), probe-to-bone positive or radiologic evidence of osteomyelitis, recurrent ulcers despite optimal care, or markedly heavy exudate with suspected biofilm. When used, antimicrobial dressings should be time-limited and their clinical effect objectively reassessed.
3) Implementation and stewardship: Use of an antimicrobial dressing must be integrated with definitive measures—surgical debridement, culture-guided systemic antibiotics when indicated, and vascular optimization—as applicable. Given mixed RCT evidence and cost considerations, routine prophylactic use of antimicrobial dressings is not recommended.
4) Decision thresholds and escalation: If an antimicrobial dressing is initiated, reassess clinically and by wound area at 2–4 weeks; lack of objective improvement (e.g., <50% area reduction at 4 weeks or persistent signs of infection) should prompt discontinuation of the topical agent and escalation to further diagnostic or therapeutic measures.
5) Summary: This framework balances the pooled "signal" of benefit from smaller and heterogeneous studies with the "solid evidence" from large, high-quality RCT(s) that did not demonstrate routine superiority. It prioritizes standardized offloading and targeted, time-limited adjunctive antimicrobial use in high-risk cases while embedding antibiotic stewardship and cost-awareness into clinical decisions.

Stepwise Clinical Algorithm for Clinicians

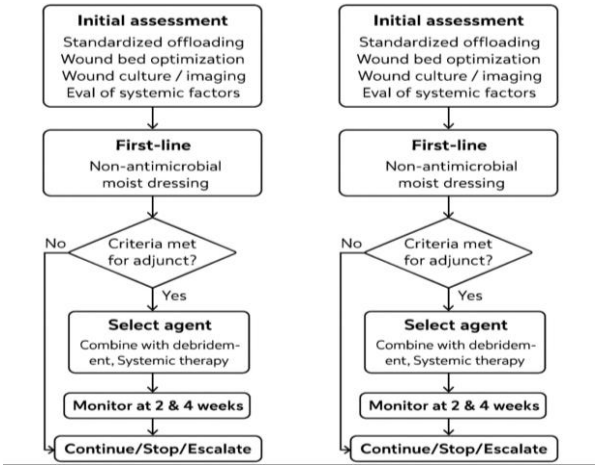


Figure 2. Stepwise clinical algorithm for topical dressing selection in neuropathic plantar diabetic foot ulcers under standardized offloading

Initial assessment includes standardized offloading, wound bed optimization, wound culture or imaging when indicated, and evaluation of systemic factors. First-line therapy is non-antimicrobial moist dressing. Antimicrobial dressings are considered only if criteria for adjunctive use are met, combined with debridement and systemic therapy when indicated. Monitoring at 2 and 4 weeks is recommended, with continuation, discontinuation, or escalation based on response.

1) Initial assessment: confirm neuropathic plantar DFU and institute standardized offloading; baseline measures (wound area, probe-to-bone, ABI, WIfI staging, cultures if infection suspected, X-ray/MRI if osteomyelitis suspected); optimize systemic factors.
2) First-line topical care: non-antimicrobial moist dressings.
3) Evaluate for adjunctive antimicrobial dressing if WIfI stage 3–4, moderate–severe infection, probe-to-bone or imaging suggestive of osteomyelitis, recurrent/stalled ulcer after ≥4 weeks, or heavy exudate with suspected biofilm.
4) Select antimicrobial dressing agent: silver, cadexomer iodine, PHMB, medical-grade honey — tailored to wound characteristics, cost, availability, and contraindications.
5) Adjunctive use and combination therapy: always combine with debridement and systemic antibiotics if indicated.
6) Monitoring and stopping rules: reassess at 2 and 4 weeks; stop or escalate if <50% area reduction or worsening infection.
7) Escalation: bone biopsy, targeted systemic antibiotics, surgery, vascular referral, advanced therapies as per protocols.

Practical Guidance for Clinicians

1) Indications: WIfI 3–4, moderate–severe infection, probe-to-bone positive, stalled/recurrent ulcer, heavy exudate with biofilm.
2) Contraindications/caution: Routine prophylactic use in uncomplicated neuropathic plantar DFU; allergy to dressing agent; iodine caution in thyroid disease or pregnancy.
3) Duration and stopping rules: Trial period 2–4 weeks, reassess at 2 and 4 weeks, discontinue if no improvement or adverse events.
4) Outcome metrics: Healing at 12 weeks, time to healing, wound area reduction at 4 weeks, antibiotic days, amputation rates, length of stay, adverse events, cost per healed ulcer, patient-reported outcomes.
5) Stewardship and cost note: Reserve antimicrobial dressings for cases where they may meaningfully alter systemic antibiotic need or where high bioburden impedes healing. Consider local cost-effectiveness before adoption.

Economic Implications and Cost-Effectiveness

The choice between antimicrobial dressings must be judged not only by clinical effect size but also by their economic impact. Silver-containing dressings are substantially more expensive than most non-antimicrobial moist dressings; PHMB products occupy an intermediate cost tier; honey-based dressings are variable but often less costly than branded silver foams. Given modest or inconsistent clinical effects, the incremental cost per additional healed ulcer may be large. Cost-effectiveness is context dependent: in high-income countries, small gains may justify costs if they reduce hospital stay; in low- and middle-income countries, priorities may be better directed to standardized offloading and

vascular care. Future trials should embed economic evaluation (cost-effectiveness, QALY, budget impact) to inform policy.

CONCLUSION

Antimicrobial dressings—most notably silver-based products—may improve healing outcomes in diabetic foot ulcers, as shown in several pooled analyses, but their superiority over non-antimicrobial moist dressings is not consistently demonstrated in high-quality randomized trials conducted under conditions of standardized offloading. The evidence therefore does not support routine use of antimicrobial dressings as first-line therapy for neuropathic plantar DFUs. Instead, they should be considered as adjuncts in selected cases, particularly in severe or infected ulcers, or in patients with high WIfI stage or osteomyelitis, where microbial burden is an important barrier to healing. Future multicenter RCTs with standardized offloading, detailed subgroup reporting, and long-term follow-up are urgently needed. Until such data become available, clinical decision-making should balance potential benefits against cost, patient context, and the overarching principles of antibiotic stewardship.

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