

# A research roundup of recent papers relevant to wound care


This section brings together information found online and published in other journals about wound healing research. The aim of this roundup is to provide an overview, rather than a detailed summary and critique of the papers selected.

## QUALITY RANDOMISED CLINICAL TRIALS OF TOPICAL DIABETIC FOOT ULCER HEALING AGENTS

Bolton LL (2014) *Advances in Wound Care*. doi:10.1089/wound.2014.0571

Diabetic foot ulcers (DFU) significantly add to global economic, social, and clinical burdens. Healing a DFU fast and well limits complications that can lead to lower extremity amputation, morbidity, and mortality. Many promising topical DFU healing agents have been studied in randomised clinical trials (RCT) but few have led to significant changes in practice or agreement in relation to topical product use. This critical review of DFU topical healing RCTs summarises methodological flaws identified in their design and conduct, highlighting ways to improve study quality so researchers can increase the likelihood of RCT success in propelling effective topical DFU healing agents toward clinical use. The authors summarise that the key issues include inadequate sample size, risk of bias, irrelevant or unreported inclusion criteria, substandard outcome measures, unmatched group characteristics that predict non-healing at baseline, unequal or uncontrolled concurrent interventions or standard of care, heterogeneous subject or DFU samples, unblinded allocation, treatment, or outcome measures, or inadequate follow-up for clinical relevance. These can add bias or unexplained variability to RCT outcomes, limiting clinical or statistical significance and accuracy of results.

### *Implications for Practice*


This critical review summarises ways to overcome these deficiencies to optimise DFU clinical trial design and conduct. It provides a blueprint for future excellence in RCTs testing safety and efficacy of topical DFU healing agents and smoothing the path to their clinical use. 

## BIOFILMS AND WOUNDS: AN IDENTIFICATION ALGORITHM AND POTENTIAL TREATMENT OPTIONS

Percival SL, Vuotto C, Donelli G, Lipsky BA (2014) *Advances in Wound Care*. doi:10.1089/wound.2014.0574

The presence of pathogenic or virulent biofilms as a fundamental risk factor that prevents a chronic wound from healing and increases the risk of the wound becoming clinically infected is undisputed. Presently there is no unequivocal gold standard method available for clinicians to confirm the presence of biofilms in a wound. In the absence of specific biomarkers to demonstrate microscopic wound biofilms, the article suggests present focus on biofilm research should be placed on changing clinical practice. It aims to help support clinical practice, recommending an algorithm intended to demonstrate evidence of the presence of a biofilm in a wound to assist with wound management. The authors suggest that this is best achieved by utilising an anti-biofilm toolbox approach, rather than speculating on unscientific approaches to identifying biofilms. They suggest that the best approach to controlling biofilm should include initial wound cleansing, periodic debridement, followed by the application of appropriate antimicrobial wound dressings.

### *Implications for Practice*

Reliance on microscopic techniques to visualise biofilms alone is flawed. They are entities that are patchy and dispersed rather than confluent, particularly on biotic surfaces. Consequently, detection of biofilms by microscopic techniques alone can lead to frequent false-negative results. Furthermore, visual identification using the naked eye of a pathogenic biofilm on a macroscopic level on the wound is not possible. The suggested approach is reported as the most effective method in removing pathogenic biofilms. However, further research is needed in relation to the efficacy of specific products, frequency of application and frequency of debridement in order to obtain optimum results. 

JEANETTE MILNE  
Tissue Viability Nurse  
Specialist, South Tyneside  
Foundation Trust

**A MOLECULAR MECHANOTRANSDUCTION PATHWAY REGULATES COLLECTIVE MIGRATION OF EPITHELIAL CELLS**

Das T, Safferling K, Rausch S, Grabe N, Boehm H, Spatz JP (2015) *Nature Cell Biology* DOI: 10.1038/ncb3115

For wounds to close, cells need to move collectively. The central molecular mechanism that allows cells to coordinate these movements over larger distances has been unclear; the authors identify the key molecule, Merlin, that controls collective migration of epithelial cells. Intercellular mechanical forces are linked to collective cell movements and demonstrate how local interactions give rise to collective dynamics at the multicellular level. Within a wound, these two processes are linked via signal transduction pathways. There is a lead cell in the collective, mechanically connected to its follower cells by cell-to-cell contacts. The forward motion of the lead cell puts mechanical tension on the follower cells. The Merlin protein senses this tension and initiates spatially-polarised following movement. The follower cells respond by forming ‘leg-like’ protrusions directed at the lead cell in order to move forward.

*Implications for Practice*

This study shows how the Merlin protein converts cellular forces to collective cell motions by acting as a mechanochemical transducer. Merlin is the only protein in the signal network that conveys this property to cellular collectives. If Merlin fails, the cells lose their ability to move collectively and trigger the relevant pathophysiological responses. Human merlin is coded by the gene NF2 in Chromosome 22 and links actin filaments to cell membrane or membrane glycoproteins. Merlin is also a tumour suppressor and regulator of the Hippo pathway, which controls cell proliferation and organ size. Further studies are needed to clarify its role in relation to chronic wounds that fail to epithelialise, and to identify if Merlin is responsible for other complications such as over granulation. Future research will also focus on identifying corrective treatments to diagnose and treat deficiencies in order to expedite healing. **WUK**

**WOUND DRESSINGS AND COMPARATIVE EFFECTIVENESS DATA**

Sood A, Granick MS, Tomaselli NL (2014) *Advances in Wound Care* 3(8): 511–29

Wound healing is a complex and intricate process. Acute wounds have the potential to become chronic wounds, requiring the physician to have a thorough understanding of outside interventions to bring these wounds back into the healing cascade. The development of effective interventions in wound care remains an area of intense research. Some of these, such as negative pressure wound therapy, have undoubtedly changed wound care practice. Over recent years, topical growth factors, biologic dressings, skin substitutes, and regenerative materials have helped to advance the wound-healing process. There is an overwhelming amount of wound dressings available in the market. The point of using advanced dressings is to improve specific wound characteristics. It is only after properly assessing the wound characteristics and available products that the “ideal” dressing may be chosen.

*Implications for Practice*

The future of wound-healing remains unknown. Few high-quality, randomised controlled trials evaluating wound dressings exist. In the absence of this, we risk the continued increase in the number of products, with a resultant increase to the existing confusion in relation to product choice. Unfortunately, patients are also often given conflicting advice as a result of the lack of irrefutable evidence. Until further data emerges, the use of best practice statements/consensus documents, and education on the available products, must prevail. As knowledge of wound-healing evolves, as does the complexity of the products. In turn, the cost per application is increasing. It is imperative that clinicians working in the wound care community are educated, to enable critique of the supporting evidence in order that they can make informed clinical choices in relation to comparative efficacy and health economics. **WUK**