Non-medicated wound dressings in managing infected wounds and wounds with biofilms



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Antimicrobial resistance is a global issue that is present in wound care, in part, due to the inappropriate use or overuse of dressings containing antimicrobials. As a result, the World Union of Wound Healing Societies (WUWHS) and a group of experts in the field of wound care collaborated on a Position Document titled "The Role of Non-medicated Dressings for the Management of Wound Infection" (WUWHS, 2020). The Position Document highlights the impact that the misuse and overuse of topical and systemic antimicrobials have on antimicrobial resistance worldwide. Non-medicated wound dressings (NMWDs) are an alternative to dressings that containing active antimicrobials, and are suitable for wounds at risk of infection and where biofilm is suspected. A webinar supported by Hartmann AG was broadcast on September 15, 2020 at the WUWHS 2020 online conference to launch the Position Document. The session covered the practical aspects of treating infection, inflammation and biofilm within antimicrobial stewardship practices to reduce the burden of antimicrobial resistance. The symposium closed with practical guidance for when and how to use NMWDs in practice, including case examples.

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One of the biggest challenges facing clinicians today is non-healing, chronic wounds. Traditionally, treatment for wound infection and biofilm — and for managing the risk of infection — has included topical antimicrobials or systemic antibiotics.

A new WUWHS 2020 Position Document titled "The Role of Non-medicated Dressings for the Management of Wound Infection" raises awareness of the misuse and overuse of antimicrobials (including antibiotics and dressings containing antimicrobial substances). The Position Document comprises three articles, which aim to provide guidance on:

- The characteristics and role of non-medicated wound dressings (NMWDs), and how they can be used to help combat antimicrobial resistance (AMR)
- The role of NMWDs in the prevention and management of infected wounds
- Clinical evidence to support the use of NMWDs.

In the webinar, Prof. Karen Ousey, Prof. Dr. Tomasz Banasiewicz and Dr. Hans Smola described the rationale for developing the new Position Document and summarised the key outcomes of the Position Document.

Antimicrobial resistance in wounds

AMR is an umbrella term for the overuse of antibiotics, antiseptics and antimicrobials, including medicated wound dressings. Medicated dressings are defined as dressings that contain an antimicrobial, such as silver or iodine. Medicated dressings kill bacteria in a variety of direct antibiotic–bacteria interactions (e.g. inhibition of DNA replication, inhibition of cell wall synthesis). However, bacteria can become resistant to medicated dressings, and so they the dressings lose their efficacy (Bjarnsholt et al, 2007).

AMR is a severe, global concern, and there is a growing rise in number of bacterial pathogens resistant to available therapeutic antimicrobial agents. The World Health Organization (WHO, 2019) have identified that AMR is one of the 10 biggest threats to health. AMR is not a new concept; the past 10 years have seen the publication of many national and international documents that aim to identify the causes of

AMR and suggest ways to reduce the threat (e.g. WHO, 2019).

Prof. Karen Ousey set the scene by outlining the latest global facts and figures on AMR. If nothing is done to reduce the burden of AMR, by 2050 there could be 10 million deaths attributed directly to AMR, costing £66 trillion (O'Neill, 2014). This amount exceeds the cost of cancer treatment. There is currently no published guidance for prudent antimicrobial therapy in infected wounds, so how do we manage AMR in wound care?

Antimicrobial stewardship practices

Antimicrobial stewardship practices focus on infection prevention and control, accurate infection and biofilm diagnosis and the appropriate use of antimicrobial and antibiotic treatments to avoid treatments becoming ineffective (Bjarnsholt et al, 2007; Uchil et al, 2014; Phillips et al, 2015).

Everyone within the multidisciplinary wound care team plays a part in antimicrobial stewardship (i.e. nurses, family doctors, pharmacists, medical staff in acute settings, wound care specialists, infection and prevention control teams). Clinicians also have a responsibility to educate and encourage supported care and the role that patients and carers can play in antimicrobial stewardship (e.g. antibiotics or a medicated wound dressing are not always necessary and the importance of hygiene and effective regular hand washing).

Non-medicated wound dressings

NMWDs are currently defined as wound dressings that do not contain any active pharmaceutical component but reduce bioburden and bacterial load via alternative methods (WUWHS, 2020). NMWDs sequester and kill bacteria based on physical mechanisms and chemical interactions, without the need for topical antimicrobials or antibiotics.

Examples of NMWDs include hydrogels, hydrocolloids, super-absorbent polymers (SAPs) dressings, carboxymethylcellulose (CMC), dialkylcarbamoylchloride (DACC) and hydro-responsive wound dressings (HRWDs). NMWDs are important for the treatment of both acute and chronic wounds, as they remove and sequester bacteria from the wound bed to help manage infection and bioburden. The antimicrobial mode of action of NMWDs involves multiple steps taking place in a coordinated manner:

1. **Debridement:** disruption of devitalised tissue
2. **Absorption**: uptake of microorganisms
3. **Sequestration:** microorganisms drawn in and locked away
4. **Retention:** microorganisms held and immobilised within the wound dressing core
5. **Removal:** microorganisms are easily removed when the dressing is removed from the wound

Each of these mechanisms is individually able to reduce bacterial numbers *[Figure 1]*.

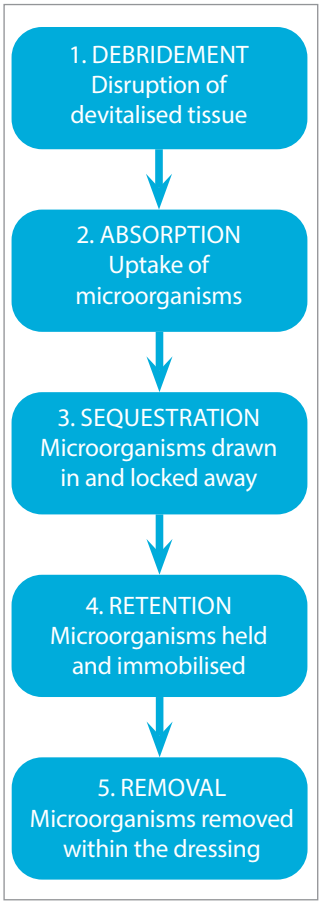

Figure 1. Mechanism of action of NMWDs for infection prevention and management (WUWHS, 2020).

Understanding the cause of wound chronicity

Patients with chronic wounds require a unique, multi-facted approach to manage their wounds, including management of the wound bed, surrounding tissue and optimisation of the patient's status (i.e. nutritional condition, management of other comorbidities and cause of the wound). Therefore, is impossible to create a 'one-size-fits-all' approach.

However, standardisation offers the opportunity to reduce variation in assessment and management. Algorithms such as T.I.M.E. (Tissue, Inflammation/Infection, Moisture, Edge/Epithelialisation) offer a treatment path to follow for wound bed assessment and preparation (Schultz et al, 2003; Moore et al, 2019).

Previous studies have shown that 78-100% of chronic wounds are likely to contain biofilm, so the existence of a biofilm should always be considered in a wound that is not healing (Hogsberg et al, 2011; Malone and Swanson, 2017; Schultz et al, 2017). However, it is very important to remain aware that bacteria are never the primary cause of a chronic non-healing wound. Patient factors, such as diabetes, peripheral vascular disease, peripheral neuropathy, trauma and increased plantar pressure may be the main cause of chronicity. Therefore, biofilms and wound chronicity cannot be managed by dressings alone; a standardised approach is necessary for consistency and to reduce variation in practice. Prof. Banasiewicz put forward an *aide memoire* to identify and manage chronicity using the T.I.M.E. acronym *[Box 1]*.

Effective use of systemic antibiotics

Systemic antibiotics are usually only indicated for clinical signs and symptoms of systemic infection or sepsis caused by planktonic bacteria. The overall picture suggests that high proportion of patients receive antibiotics for infection. In a review study of Canadian hospitals of over 4000 patients, a third received antimicrobials: 73.3% for therapeutic use, 14.2% for medical prophylaxis and 8.2% for surgical

Box 1. Identifying and managing chronicity using the T.I.M.E. acronym.

- **Think!** – Assess the primary reason of chronicity, then treat
- **Infection/inflammation recognition** – Local tools are available to identify the signs and symptoms of infection and inflammation
- **Microbiology** – Knowledge and understanding of the biofilm bacterial communities will guide appropriate care. Commonly used approaches to analysis DNA include 16S ribosomal RNA (rRNA) sequencing, whole genome (shotgun) sequencing and RNA transcriptomics.
- **Effective use of appropriate treatments and duration** – Consider NMWDs, and whether systemic antibiotics or medicated dressings are required.

prophylaxis (Frenette et al, 2020). Acute infections are relatively easy to treat compared to biofilm as most antibiotic agents act on metabolic pathways in active bacterial cells. When these therapies are employed against biofilm microorganisms that differ markedly in both physiology and activity, antibiotics typically fail to eradicate biofilm (Lebeaux et al, 2014).

Administration of a single antibiotic (even a broad-spectrum agent) will often not eradicate the biofilm microorganisms because:

- The antibiotic level at the site of infection is insufficient: biofilms have been found to withstand antimicrobial concentrations 100 to 1,000 times higher than that of planktonic microbes.
- Bacteria in the biofilm are slow growing or can be dormant.
- Bacteria in the biofilm are encapsulated in a protective matrix called extracellular polymeric substance (EPS), which helps biofilm resist antimicrobial treatments (WUWHS, 2020). The antibiotic is inactivated by accumulated enzymes in the biofilm matrix – produced by other resistant species growing alongside the pathogen (associated resistance) (Lebeaux et al, 2014).

This leads to a perceived notion that higher levels of antibiotics are required to actively combat the microorganisms within the biofilm, leading to frequently inappropriate treatment.

Instead of using antibiotics or antimicrobial agents, biofilms can be destroyed or removed by creating a hostile environment for the bacteria and removing the biofilm and the infected tissue. If a wound has excessive non-productive inflammation, infection or suspected biofilm, then NMWDs can be considered as an alternative to antimicrobial dressings. If necessary, NMWDs can be used in conjunction with other antimicrobial agents to aid in the overall management of the infection and contribute to reducing the level of bacterial bioburden.

Guidelines from the WUWHS (2020) Position Document exist on how to use NMWDs for the management of excessive inflammation, wound infection and biofilm *[see Figure 2]*.

How to use NMWDs for infected wounds or wounds at risk of infection

The clinical signs and symptoms of wound infection are well-established and are a guide for treatment (e.g. erythema, swelling, local and systemic hyperthermia, pain, odour). Treatment often includes debridement, plus antimicrobial treatment agents with or without topical agents. However, it can be challenging to decide when to initiate systemic antibiotics, and it can be a subjective decision based on the experience and speciality of the clinician (Olen and Forssell, 2013). Prof. Hans Smola described how understanding the mechanism of infection and inflammation makes the decision less subjective.

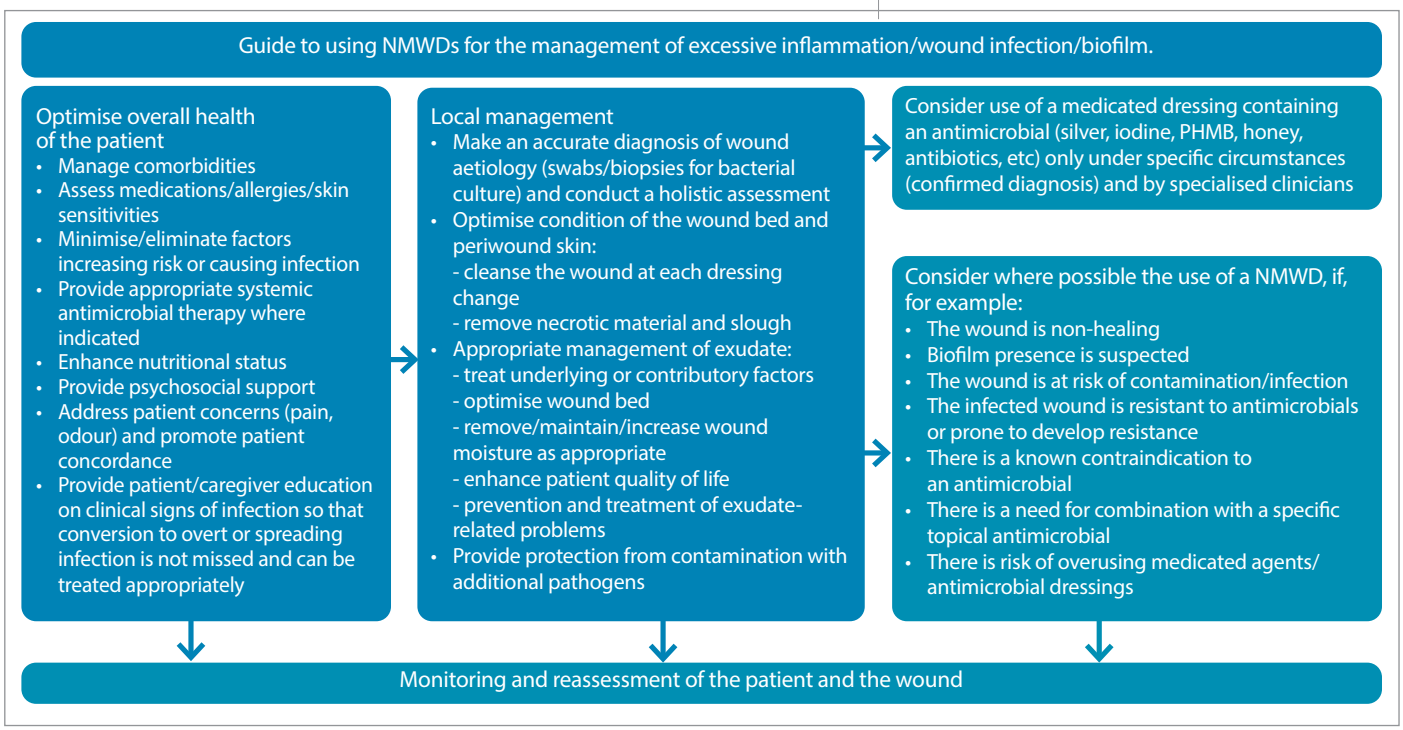

Figure 2. Factors to consider when using NMWD for the management of excessive inflammation, wound infection and biofilm (WUWHS, 2020)

Table 1. The cell signalling mediators and the impact of non-medicated wound dressings at each stage of wound healing.

Stages of healing:	Debridement	Wound bed preparation	Granulation tissue	Epithelialisation
	Necrosis / Autolytic debridement / Inflammation / Granulation tissue formation / Epithelialisation			
Associated cell signalling mediators	• DAMPs • PAMPs • Inflammatory mediators • Ischaemic mediators	• Inflammatory mediators • Infection/PAMPs	• Connective tissue synthesis • Cell proliferation and motility	• Cell motility and proliferation
Impact of NMWDs on the wound	Removal of wound healing inhibitors	Shift the local wound environment towards granulation tissue build-up	Prevent damage to the granulation tissue, provide optimal healing conditions	Protect the wound bed and prevent wound damage
Impact of NMWDs on wound progression	Move away from inflammation	Move towards a synthetic mesenchyme	Maintain a productive granulation tissue	Boost epithelialisation

Understanding the mechanism of infection and inflammation

Bacteria produce metabolites that stimulate inflammatory cells that produce mediators that initiate inflammation (Kawal et al, 2010). The clinical signs and symptoms observed are trigged by the host immune response and are not caused by the bacteria or their metabolites directly. Necrotic tissue also releases components that stimulate the immune reactions and can mimic an infection, can make identification of infection and inflammation difficult. *Figure 3* illustrates the cascade of inflammation, which can be initiated by bacteria or necrotic tissue.

Pathogen-associated molecular patterns (PAMPs) kill bacteria, and damage-associated molecular patterns (DAMPs) degrade tissue.

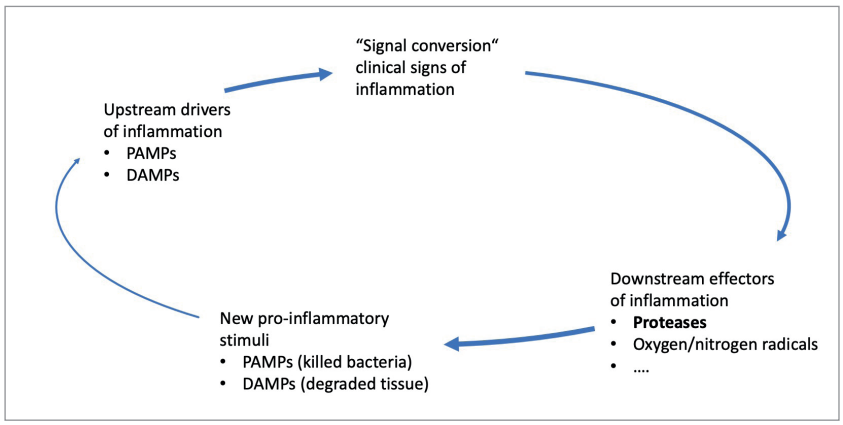

Figure 3. Cascade of inflammation.

PAMPs and DAMPs are upstream drivers of inflammation and trigger the immune response into producing the clinical signs of inflammation. A cascade of downstream-standardised effects of inflammation is triggered by the breakdown tissue via proteases and reactive oxygen or nitrogen species. The metabolised tissue releases the pro-inflammatory stimuli (DAMPS and PAMPs) and the cycle continues with the potential for relapse of chronic inflammation.

Table 1 shows the cell signalling mediators and the impact of non-medicated wound dressings at each stage of wound healing. Understanding the mechanism of inflammation can identify how to move the wound to healing and stop the inflammation cycle. The body mounts its own autolytic debridement to remove drivers of the inflammatory response, but this can be assisted with surgical debridement and the use of dressings. NMWDs can support wound bed preparation and prevent damage at the granulation tissue and epithelisation stage.

Role of NMWDs in infected or at-risk wounds

NMWDs such as HRWDs (e.g. HydroClean®, Hartmann AG) do not contain any active antimicrobial agent, instead Ringer's solution is released by the dressing to help soften devitalised tissues and cleanse the wound. HRWDs support autolytic debridement,

stimulate normalisation of wound environment and inactivate excess matrix metalloproteases (MMPs), inducing the progression to granulation. This occurs through the "rinsing motion" of the wound dressing itself. Bacteria-containing exudate is absorbed and bound into the absorbent core of the dressing and is retained by the dressing. The wound bioburden is reduced by removal of the bound bacteria at each dressing change. They are ideal for patients with infected wounds or wound that are at-risk of infection as they effectively eradicate bacteria with a physical mode of action, while not inducing microbial resistance.

NMWDs such as super-absorbent polymer (SAP) dressings (e.g. Zetuvit Plus Silicone/Border®, Hartmann AG) also do not contain any active antimicrobial agent. SAPs have been shown to inhibit MMP activity in chronic wounds by binding and locking the protein within the particles and blocking associated co-factors, such as calcium, magnesium and zinc (Eming et al, 2008). SAPs are small granules that absorb and bind bacteria and MMPs, thus contributing to undisturbed wound healing. Chronic wounds treated with SAP-containing dressings had a 36% increase in granulation tissue after 14 days compared to wounds treated with amorphous hydrogel, which had a 14.5% increase in granulation tissue (p=0.0005; Humbert et al, 2014).

SAP-containing dressings are ideal for exuding wounds at-risk of infection as they effectively absorb and retain the exudate containing wound healing inhibitors and bacteria by a physical mode of action, while not inducing bacterial resistance.

Using NMWDs in practice - Case studies

Two cases presented by Prof. Banasiewicz illustrated that there are many approaches to treating the patient and wound depending on the individual characteristics. Cases studies included in this article illustrate the combined approach of NMWDs, medicated wound dressings, antiseptics, negative pressure wound therapy (NPWT) to encourage wound healing.

Case 1. Septic and necrotic venous leg ulcer

This patient had a venous leg ulcer that had been present for 4 month, which had become septic and necrotic. Systemic antibiotics had been ineffective, likely due to the ischaemic tissue in the lower limb, which was suggestive of biofilm. The aim of treatment was to create a hostile environment so the biofilm communities could not thrive. The wound was extensively debrided in surgery *[Figure 3]*. NPWT with instillation using an antiseptic solution was combined with NWMDs for 2 weeks; the dressing was changed twice a week *[Figure 4]*. Zetuvit Plus Silicone® was used while there were high levels of exudate. Once the wound began to develop granulation tissue, the dressing was changed to a HRWD (HydroClean®). A skin graft was performed. The dressing regimen included Zetuvit Plus Silicone®. *Figure 5* shows the wound after 3 weeks. The patient was discharged 5 weeks after the skin graft. The total length of treatment was 12 weeks from the first surgical intervention.

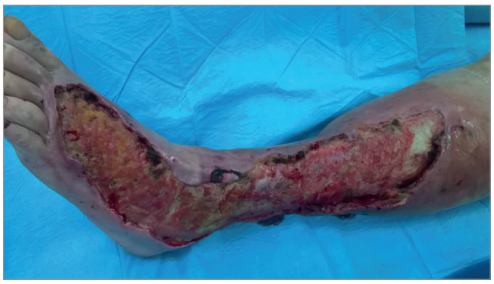

Figure 3. After extensive surgical debridement.

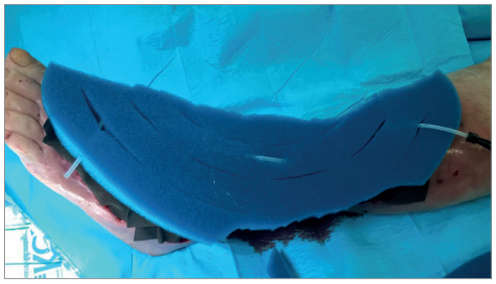

Figure 4. Application of NPWT.

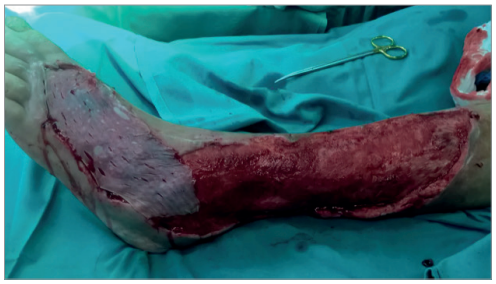

Figure 5. 3 weeks after skin graft was performed.

Case 2: Ambulatory patient with a chronic leg ulcer

The patient had a chronic leg ulcer and was ambulatory, so it was important to not limit their mobility during treatment *[Figure 6]*. The aim was to clean the wound, remove exudate, and absorb and sequestrate the bacteria. Following thorough physical debridement, a HRWD (HydroClean®) was used for 2 weeks to cleanse, debride, deslough the wound bed *[Figure 7]*. Then a SAP dressing (Zetuvit Plus Silicone®/Border) in combination with

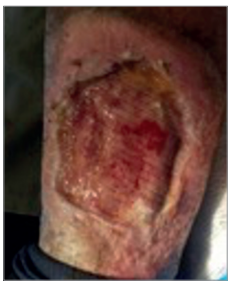

Figure 6. Leg ulcer at day 0.

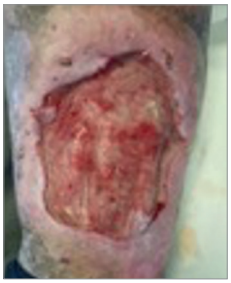

Figure 7. Leg ulcer at day 7.

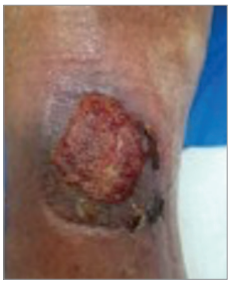

Figure 8. Leg ulcer at week 3.

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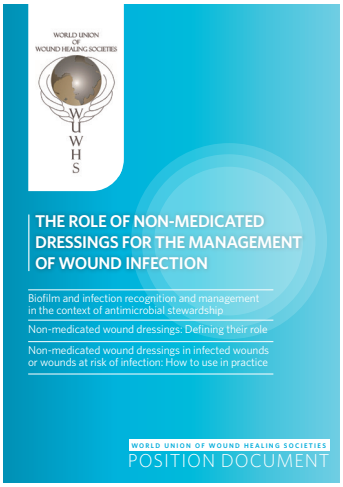
Octenillin® gel (Schülke) were used to provide a moist wound healing environment *[Figure 8]*. The patient's wound healed fully after 2 months.

Summary

Diagnosing wound infection can be challenging for many clinicians. There is evidence to suggest that systemic antibiotics and antimicrobial dressings are prescribed unnecessarily. NMWDs, such as HydroClean® and Zetuvit Plus Silicone®/ Border, offer a treatment option that does not impact on microbial resistance.

Many patients and healthcare systems could benefit from a more tailored individualistic approach, reserving antimicrobial therapy for correctly diagnosed local infection. The new WUWHS Position Document offers innovative perspectives and new clarity on the role of NMWDs, and how they can be used to help combat AMR in wounds. Deployment of more frequent wound debridement/cleansing and using dressings without an active ingredient, such as NMWDs, offer an ideal option in the drive to promote antimicrobial stewardship. WINT



Download the Position Document at: https://www.woundsinternational.com/resources/details/the-role-of-non-medicated-dressings-for-the-management-of-wound-infection

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