INTERNATIONAL **CONSENSUS DOCUMENT**

USE OF WOUND ANTISEPTICS IN PRACTICE

MANAGING THE CHALLENGES AND RISKS OF INFECTION IN WOUND CARE

USE OF DIFFERENT ANTISEPTICS IN PRACTICE

WOUND CLEANSING AND TIPS FOR BEST PRACTICE

GUIDANCE AND PATHWAYS FOR ANTISEPTIC USE

THE IMPORTANCE OF AN ANTIMICROBIAL STEWARDSHIP-FOCUSED APPROACH

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FOREWORD

Prevention, detection, treatment and management of wound infection remains a paramount concern for clinicians worldwide. Wound infection is a complex manifestation in which microorganisms outcompete the host immune system (Haalboom et al, 2019), and it is considered to be one of the most common and serious challenges hindering the wound healing process (Mota et al, 2021). Chronically infected wounds are associated with significant physical, emotional and economic burdens, and these are increasing due to an ageing population and rising prevalence of comorbidities (Zhu et al, 2022). Therefore, clinicians need to take a proactive approach to ensure the effective and sustainable management of wound infection in clinical practice.

The use of antiseptics to prevent and treat wound infection is increasingly being explored, due to the rapid spread of antimicrobial resistance (AMR) and rising emergence of multidrug resistant bacteria, such as *Staphylococcus aureus* (Barrigah-Benissan et al, 2022). Early and judicious use of topical antimicrobial agents, such as antiseptics, may have an important role to play in limiting biofilm formation, including limiting regrowth and spread of infection (Schultz et al, 2017). Furthermore, advocating for the responsible use of antibiotics to preserve their effectiveness for generations to come is crucial.

To address these issues, an international group of experts convened for an online meeting in August 2023 to develop this international consensus document, focusing on the use of antiseptics in practice for the prevention and treatment of wound infection.

This consensus document aims to:

- Address the challenges and risks of infection in wound care
- Consider experiences and practice around the world
- Provide an overview of the different antiseptics used in practice
- Focus on cleansing alongside antisepsis
- Provide guidance on the use of antiseptics in practice
- Reaffirm the importance of an antimicrobial stewardship-focused approach.

The guidance in this document aims to shed light on the potential benefits of using antiseptics to prevent and treat wound infection, alongside practical guidance on how to use them safely and effectively in clinical practice. There needs to be an environment that fosters behavioural change with a focus on sharing best practice, to ensure that infection prevention practices are being followed and interdisciplinary working is embraced.

Harikrishna K. R. Nair (Chair)

Managing the challenges of wound infection

Identifying wound infection can be challenging, and this is especially the case in chronic wounds and in patients with dark skin tones, where infection may not present with the same clinical signs and symptoms as it does in acute wounds or light skin tones (Rutter, 2018). Chronic wound infection delays the healing process, and it has a significant burden on healthcare systems with implications for practice, including increased pain and reduced quality of life (Falcone et al, 2021). It is important to note that chronic wounds always have a bacterial burden which does not necessarily require action in order for the wound to heal. Regardless, early and accurate detection of wound infection is essential, so that appropriate treatment can be selected in a timely manner to prevent development of further complications. Likewise, an ability to correctly rule out infection prevents the unnecessary use of antibiotics (Lipsky et al, 2016; Haalboom et al, 2019), and clinician experience can play a major role in the detection of infection.

Defining wound infection and related terms

It is clear that properly defined terminology is essential, and definitions can provide guidance and help with communication. However, it is difficult to define wound infection, and existing literature reviews have shown that infection is not defined very well in general. In particular, there is some confusion regarding the difference between contamination, colonisation, a wound infected with a biofilm and an infected wound. According to the International Wound Infection Institute (IWII, 2022), wound infection is defined as 'the invasion of a wound by proliferating microorganisms to a level that invokes a local and/or systemic response in the host'. In contrast, biofilms are complex polymicrobial communities – attached either to each other or to a surface and become encased within an extracellular polymeric substance – that can increase the likelihood of a wound becoming infected and can prevent wound closure (Wolcott et al, 2016; Kadam et al, 2019). Once microbes reach a critical level, which depends on microbial consortium synergy as well as microbial numbers, there is potential for a biofilm-infiltrated wound to deteriorate to clinical infection (Alves et al, 2020). See **Box 1** for more information on the difference between the terms colonisation, contamination, local infection, spreading infection, systemic infection, debridement, disinfectant, antibiotics and antiseptics.

The IWII Wound Infection Continuum

The IWII Wound Infection Continuum (WIC) is a well-recognised educational tool that provides a framework to conceptualise the impact that microorganisms have on the host, the wound and on wound healing (IWII, 2022).

The IWII-WIC consists of five distinct stages:

- Contamination
- Colonisation
- Local infection (covert and overt stages)
- Spreading infection
- Systemic infection.

See **Figure 1** *(Page 6)* for more information on each stage and its associated signs and symptoms.

Diagnosis of wound infection using microbiology

Identification of wound infection is often the result of both clinical judgement and microbiological testing (Haalboom et al, 2019). However, subjectivity is a major challenge in the assessment of clinical signs and symptoms of wound infection, as they can manifest differently depending on the individual patient's wound type and underlying comorbidities. It has been revealed

BOX 1 | Key definitions related to wound infection (IWII, 2022)

Antibiotics: Antibiotics are the only antimicrobial compounds that can also be administered systemically. Antibiotics target specific sites within bacterial cells; however, overuse of topical administration may contribute to bacterial resistance.

Antiseptics: An antiseptic is a topical antimicrobial agent with broad-spectrum activity that inhibits multiplication of, and can kill microorganisms. Depending upon its concentration, an antiseptic may have a toxic effect on human cells; however, modern antiseptics show good tissue compatibility. Biocompatibility index may be a useful tool to evaluate antiseptic agents for use in clinical practice (Müller and Kramer, 2008). Antiseptics may be referred to as preservative agents, particularly in countries where these products are regulated as medical devices. Development of resistance to topical antiseptics is uncommon (Haesler et al, 2022).

Contamination: Contamination refers to the presence within the wound of microorganisms. No significant host reaction is evoked and no delay in wound healing is clinically observed (Haesler et al, 2022).

Colonisation: Colonisation refers to the presence of microorganisms within the wound that are undergoing limited proliferation. No significant host reaction is evoked and no delay in wound healing is clinically observed (Haesler et al, 2022).

Debridement: The removal of devitalised (non-viable) or viable tissue from, or adjacent to, a wound. Debridement also removes exudate and bacterial colonies (e.g. biofilm) from the wound bed and promotes a stimulatory environment. Methods of debridement include autolytic debridement (promotion of naturally occurring autolysis), surgical sharp debridement, conservative sharp debridement, enzymatic debridement, mechanical debridement (e.g. mesh pad), biological debridement (e.g. larval therapy) and low frequency ultrasonic debridement (Ayello et al, 2016; European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel, Pan Pacific Pressure Injury Alliance (EPUAP/NPIAP/PPPIA), 2019). In addition, new debridement technologies can include oxidative agents, which is referred to as oxidative debridement (Dissemond et al, 2020). Depending on their concentration, oxidative agents can help degrade, soften or eliminate necrotic tissue and/or slough. Oxidative debridement is distinct from autolytic debridement, which is caused by either hydration-related dissolution or dissolution via autologous proteases.

Disinfectant: Substances recommended by the manufacturer for application to a non-living object to kill microorganisms (IWII, 2022).

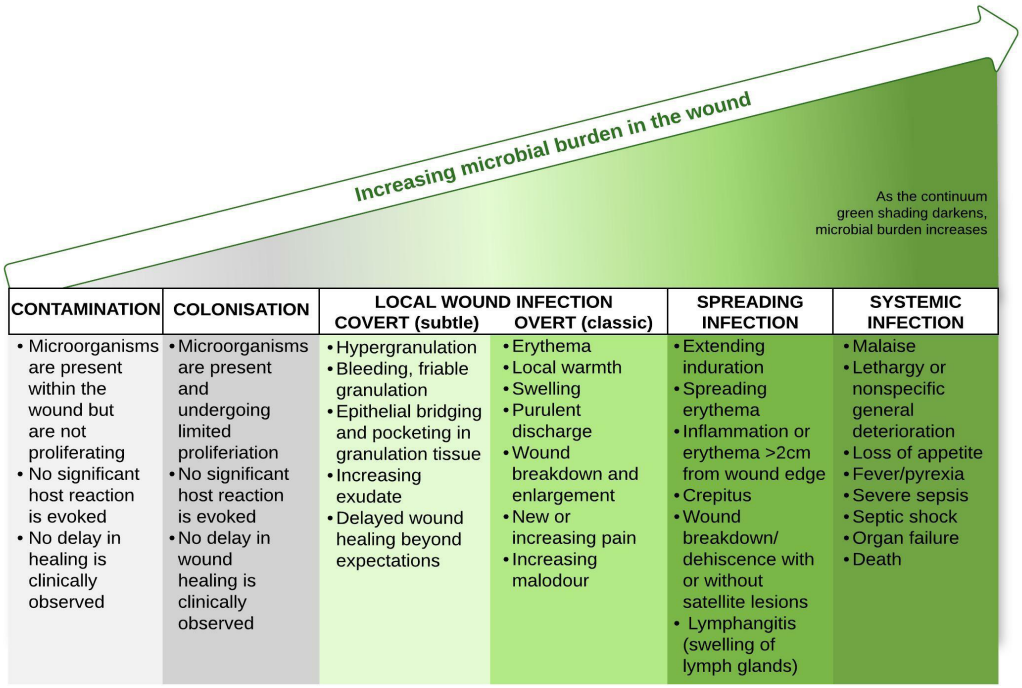
Local infection: Local infection refers to the presence and proliferation of microorganisms within the wound that evoke a response from the host immune system that often includes delayed wound healing. Local infection is contained within the wound and the immediate periwound region (less than 2cm). Local infection often presents as subtle (covert) signs that may develop into the classic (overt) signs of infection (Haesler et al, 2022).

Spreading infection: Spreading infection arising from a wound refers to microorganisms spreading from the wound into adjacent or regional tissues, evoking a host response in the structures in the anatomical area beyond the periwound region. Signs and symptoms of spreading infection include diffuse, acute inflammation and infection of skin or subcutaneous tissues (IWII, 2022).

Systemic infection: Systemic infection arising from a wound refers to microorganisms spreading throughout the body via the vascular or lymphatic systems, evoking a host response that affects the body as a whole. Signs of systemic infection include a systemic inflammatory response, sepsis and organ dysfunction (Haesler et al, 2022).

Managing the challenges of wound infection *(Continued)*

FIGURE 1 | The International Wound Infection Institute Continuum (IWII, 2022)



CONTAMINATION	COLONISATION	LOCAL WOUND INFECTION COVERT (subtle)	LOCAL WOUND INFECTION OVERT (classic)	SPREADING INFECTION	SYSTEMIC INFECTION
• Microorganisms are present within the wound but are not proliferating • No significant host reaction is evoked • No delay in healing is clinically observed	• Microorganisms are present and undergoing limited proliferiation • No significant host reaction is evoked • No delay in wound healing is clinically observed	• Hypergranulation • Bleeding, friable granulation • Epithelial bridging and pocketing in granulation tissue • Increasing exudate • Delayed wound healing beyond expectations	• Erythema • Local warmth • Swelling • Purulent discharge • Wound breakdown and enlargement • New or increasing pain • Increasing malodour	• Extending induration • Spreading erythema • Inflammation or erythema >2cm from wound edge • Crepitus • Wound breakdown/ dehiscence with or without satellite lesions • Lymphangitis (swelling of lymph glands)	• Malaise • Lethargy or nonspecific general deterioration • Loss of appetite • Fever/pyrexia • Severe sepsis • Septic shock • Organ failure • Death

that most patients receive initial antibiotic treatment based on clinical assessment and without the diagnostic confirmation of a microbiological test (World Health Organization [WHO], 2019). Therefore, there is a growing need for more rapid and reliable laboratory testing, which may also prove to be an important cornerstone of antimicrobial stewardship (AMS; Bogers et al, 2019).

Although accurate diagnosis of wound infection should involve clinical microbiology and immunological testing, inappropriate/inadequate microbiological testing is a widely recognised problem (Bogers et al, 2019). There was a consensus from the expert panel that there is a global decline in the utilisation and correct use of clinical microbiological tests and diagnostic tools, which can have a negative effect on patient outcomes (WHO, 2016). Additionally, in some countries, barriers and constraints may impede the uptake of microbiological diagnostics, including availability of experts, costs, and issues with reimbursement and regulations. Not all healthcare facilities have access to a microbiology laboratory (WHO, 2019), and research have shown that the potential of microbiology testing may not be fully utilised due to prolonged turnaround times (Skodvin et al, 2019), lack of adequate diagnostic capabilities and distrust in results from the laboratory (Rolfe et al, 2021). Despite these challenges, effective and improved microbiological testing has the potential to positively influence patient outcomes and reduce the inappropriate use of antibiotics (Skodvin et al, 2019). However, clinicians need to bear in mind that a positive swab result is not necessarily an indication for administration of antibiotics.

Wound swabs versus tissue biopsies

It is evident that more research and clarity is needed on whether wound swabs are sufficient to diagnose infection, or if tissue biopsies are needed. Wound swabs are unable to reveal the true microbiology of biofilms within the wound, which is generally the source of infection. It is also important to note that biofilm community is a structure that constantly varies in form, due to

external and internal processes (Laverty et al, 2014), and this can cause challenges when taking swabs/biopsies. Although tissue biopsy has historically been considered the gold standard for wound culture, they are invasive, painful and expensive, and often require specialist training to carry out (Atkin et al, 2019; Høiby et al, 2015). It was revealed during the discussion with the expert panel that wound swabs are often taken, instead of tissue biopsies, due to cost and time constraints. The need for joined-up working and effective communication, between tissue viability teams and microbiologists/infection prevention teams, was emphasised.

While there are studies claiming that biopsies yield the most accurate and reliable culture results (Brock et al, 2022), some studies show that non-invasive wound swabbing techniques can provide similar results to tissue biopsies (Esposito et al, 2017; Haalboom et al, 2018; 2019). Furthermore, the few available investigations that compare different yielding techniques do not sufficiently describe the transport and specimen pre-processing procedures. Currently, there is no evidence to suggest that either technique is better at diagnosing infection. As well as being non-invasive, wound swabs are relatively easy to perform and pose a lower burden on the patient – e.g. they may reduce fear and pain (Haalboom et al, 2019). However, when the presence of resistant bacteria or a systemic infection is suspected, tissue biopsies may be required.

Taking a whole-person approach to wound infection

It has been shown that clinical signs and symptoms of wound infection are often missing in patients with arterial, or venous, insufficiency and diabetes neuropathy (Glaudemans et al, 2015; Leaper et al, 2015; Lipsky et al, 2016). Therefore, clinicians should take a whole-person approach and consider the patient's disease status to decide which treatment option is most appropriate. In addition, any underlying disease/comorbidity needs to be controlled; for example, glycaemic control is necessary if the patient has diabetes. Moreover, evidence exists to suggest that socioeconomic status plays an important role in the development of wound healing complications (Sharma, 2018). Therefore, the impact of socioeconomic status, as well as individual patient comorbidities, needs to be considered when managing wound infection.

Biomarkers and other indicators of wound infection

Clinicians usually rely on assessing clinical signs and symptoms to identify wound infection in practice (e.g. pain, erythema, oedema, heat and pus). However, these signs are not always indicative of infection (Haalboom et al, 2019). Although there are specific markers to diagnose infection, such as biomarkers, the use of these markers depends on the type of microbe present. No single marker currently exists to detect whether a wound is infected or not. Some biomarkers have been described as indicators of both bone and soft tissue infection, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and procalcitonin (PCT). However, there is a difference between bone infection and soft tissue infection; they are treated differently and their reactions to intervention differ. Research has shown that enzymatic biomarkers related to wound infection may be useful for the early detection of wound infection (Mota et al, 2021). Other indicators that have been studied as potential biomarkers to help identify infection include bacteria, proteins and metabolites.

Local temperature of wounds is often considered a predictor of infection (Tegl et al, 2015; Power et al, 2017). Zhang et al (2021) found differences in temperature among wounds infected with different pathogens. Another study by Power et al (2017) found that temperature measurements are highest in acute, non-healing or worsening wounds, and that as wounds progress towards healing, temperature reduces. However, there are few available methods to monitor infection and healing progression in wounds using temperature as an indicator. Moreover, it may be challenging to use high temperature as an indicator of infection in some conditions such as peripheral arterial disease, which can present with cold legs.

Managing the challenges of wound infection *(Continued)*

The pH of a wound may also be a possible early indicator of infection, so wound pH monitoring can be a useful tool for determining the presence or absence of infection (Kordestani et al, 2023). As well as temperature and pH, other microenvironmental parameters and local indicators that could help predict infection include uric acid, lactic acid, glucose and exudate composition (Zhang et al, 2021). Although these factors are relevant to research, monitoring and measuring these indicators in practice can be challenging for clinicians.

Antiseptics for wound infection

A culture of overprescribing antibiotics exists, especially for patients with chronic wounds. It is widely acknowledged that clinicians can find it challenging to distinguish when to use antibiotics prophylactically and when to use them to treat infection. However, there is a consensus that an infected wound should be treated antiseptically and application of antibiotics for locally colonised wound infections needs to be avoided (Kramer et al, 2018), due to the rising emergence of multidrug resistant bacteria and spread of AMR. It is important to bear in mind that antiseptics should never be the sole treatment to prevent or treat infection; they are an adjunct in a similar way to antibiotics. Other treatment modalities such as debridement are just as important and may be necessary depending on the patient's wound – e.g. sharp or mechanical debridement **[Box 2]**.

Experiences and practices around the world

In many parts of the world, antiseptic agents are non-indicated in chronic wound care (Barrigah-Benissan et al, 2022). In some countries, tap water or saline are the only recommended substances for the purpose of wound cleansing, and antisepsis is considered a controversial cleansing method. Although saline is the most widely used product for chronic wound cleansing in clinical practice, methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* can grow and survive in saline (Dong et al, 2020), and studies have shown the benefits of using antiseptic agents (Kramer et al, 2018; Schultz et al, 2021).

It was agreed by the expert panel that variations exist in practice between hospitals, as clinicians often have their own criteria to diagnose wound infection. In addition, some clinicians use antiseptics prophylactically while others use them solely as adjuncts. The risk of wound infection is influenced by characteristics of the individual (host), their wound and the environment, as well as the influence of caregivers (IWII, 2022); therefore, consideration needs to be given to all these factors.

Addressing the challenges of antisepsis

There are various challenges that can be presented when using antiseptics for the prevention and treatment of wound infection, including issues with tolerability, inactivation by organic matter and the spread of AMR/cross-resistance (Punjataewakupt et al, 2019; Barreto et al, 2020). It was shared by the expert panel that in the United States (US), use of antiseptics and antimicrobials is based on five key considerations: activity, tolerability, safety, availability and cost. Clinicians need to consider efficacy; however, a view was raised that in Spain, many clinicians are unaware of the mode of action of the antibiotics, antiseptics and antimicrobials they prescribe, which is best for individual clinical scenarios and what their benefits of use are. Therefore, guidance is needed on when the most appropriate time to apply antiseptics is – e.g. when the wound is at risk of infection or when the wound is already infected.

Availability can play a significant role in decisions concerning treatment of wound infection, as some clinicians treat patients with antibiotics without taking a wound swab first (WHO, 2019). Use of antiseptics can largely be driven by availability, what is on patients' insurance plans and what is available in clinics/facilities. Additionally, first-line treatment is not always delivered by someone with sufficient training in wound care.

BOX 2 | Treatment modalities that need to be considered alongside antiseptics

- Compression therapy for venous leg ulcers (Patton et al, 2023)
- Offloading and pressure redistribution for pressure ulcers (Bowers and Franco, 2020)
- Restoration of arterial inflow for ischemic ulcers (Schultz et al, 2017)
- Offloading and glycaemic control for diabetic foot ulcers (Vouillarmet et al, 2016; Schaper et al, 2020)
- Skin assessment and care
- Debridement of wound bed and wound edges
- Management of other systemic diseases.

Differences in prescribing

A view was raised by the expert panel that in the United Kingdom (UK), tissue viability teams generally manage wounds at first point of contact, and that tissue viability nurses are allowed to prescribe antiseptics in addition to doctors. When patients are transferred into the community and may have to pay prescription costs for certain antibiotics or antimicrobials, patients may refuse or use them inappropriately. Unlike in the UK, prescribing is restricted to doctors in some countries such as Germany – although it was suggested that many nurses have greater knowledge about caring for chronic wounds than doctors.

There are also reimbursement considerations, especially across many countries in Europe, and in low and middle-income countries. In Germany and Austria, all antibiotics are reimbursed; however, antiseptics are not. As a result, German doctors tend to use antibiotics more than antiseptics to prevent infection from spreading, because otherwise they may find themselves in a position where they have to persuade patients to buy antimicrobials and antiseptics themselves. In addition, these patients often ask for antibiotics instead as they don't have to pay for them. It was also discussed that in Spain, there can be issues with litigation, which may cause clinicians to feel pressure when using antiseptics prophylactically. There was a consensus from the expert panel that although the guidance discourages clinicians from using antibiotics on chronic wounds, when they are not needed, it was agreed that there needs to be more emphasis on the evidence that shows antimicrobials and antiseptics as being more effective for treating local wound infection than antibiotics. It needs to be clear that antibiotics are an exception, if not obsolete, in the treatment of chronic wounds, as the evidence shows that antiseptics can be more effective and are associated with little to no resistance.

Prevention is better than cure

It is widely acknowledged that there needs to be a greater emphasis on prevention of infection, rather than treatment. In Austria, healthcare providers are only allowed to spend a specific amount for the treatment of existing illnesses. As a result, there is a lack of spending on prevention. A similar view was raised that in Brazil, budgets do not tend to cover spending on prevention; therefore, there are cost implications of using antiseptics in clinical practice. The expert panel agreed that globally, there is a need to change mindsets to move away from a reactive healthcare model to a proactive approach. This involves focusing less on treatment in isolation and increasing investment in preventative measures.

More evidence is needed

There was a consensus from the expert panel that although the theoretical foundation for using antiseptics is strong, indirect evidence dominates the literature. There are difficulties in obtaining concrete evidence for the use of antiseptics to prevent infection, as comparable patients are needed, and this is challenging in the field of chronic wounds. Most research on antiseptics is *in vitro* and/or using animal models (Schwarzer et al, 2020). Alongside a lack of standardised methodology, there is also ongoing debate about the transferability of this research to clinical practice (IWII, 2022). Although there is a lack of clinical evidence, judicious use of topical antiseptics has a role to play in preventing and managing wound infection (Schultz et al, 2017).

Antiseptic use in practice

Due to the growing emergence of multidrug resistant bacteria, alarming spread of AMR, development of new-generation antiseptic agents and improved formulation of existing antiseptics with fewer side effects, wound antisepsis is increasingly being considered as a vital asset for the prevention, treatment and management of wound infection (Barrigah-Benissan et al, 2022). There is a culture of overprescribing and misusing antibiotics in wound care – especially for chronic wounds – and according to the literature and expert opinion, antiseptics are more effective and most do not pose a risk for the development of bacterial resistance or cross-resistance (Hessam et al, 2016; Kramer et al, 2018; Dissemond et al, 2020). However, there are a limited number of studies that investigate the efficacy of antiseptic agents in the healing of chronic wounds (Barrigah-Benissan et al, 2022).

Antiseptics versus antibiotics

IWII (2022) has defined an antiseptic as a 'topical agent with broad-spectrum activity that inhibits multiplication of, or sometimes kills, microorganisms'. Antiseptics are generally applied to skin, mucous membranes and surface wounds, as well as other living tissues, with the aim of inhibiting microbial growth without necessarily killing microbes (Babalska et al, 2021). Due to the emergence of new technologies, such as the introduction of oxidative cleansers, antiseptics can act beyond bacterial killing and without cytotoxicity (IWII, 2022). For example, some cleansers contain oxidative agents (e.g. hypochlorous acid [HOCl]), and these cleansers may play a role in removing microbes as well as softening and removing slough and necrotic tissue via oxidative processes, depending on concentration (Olszowski et al, 2003; Pattison et al, 2003).

While antiseptics are unspecific/multitarget – which means they possess a broad spectrum of antimicrobial activity with a disruptive or biocidal effect on bacteria, fungi, parasites and viruses – antibiotics kill bacteria (biocidal effect) or inhibit their growth (static effect) only (Babalska et al, 2021; IWI, 2022; Malanovic et al, 2022). In addition, microorganisms can develop resistance to antibiotics, although resistance is not usually observed in antiseptic agents and various classes of cleansers (Kramer et al, 2018). However, research has shown that bacteria have developed resistance against silver and triclosan (Pareek et al, 2021). Moreover, while both antiseptics and antibiotics can be applied topically, only antibiotics can be administered systemically. To help reduce risk of further antibiotic resistance, antiseptics can help maintain efficacy and effectiveness of antibiotics, by preserving them for clinical scenarios that require appropriate systemic treatment (Roberts et al, 2017).

Differing modes of action

Antiseptics vary in terms of characteristics, features, efficacy and intention for use, and it has been suggested that differences in antimicrobial spectrum of activity between antiseptics is the result of varying mechanisms of action (Alves et al, 2020). Antiseptics are broadly classified as pharmacological drugs or medical devices, depending on their primary mode of action (Kramer et al, 2018). Pharmacological antiseptics act pharmacologically, metabolically and/or immunologically; for example, these antiseptics may bind to adhesion proteins, or their biochemical or immunological destruction can inhibit attachment of bacteria. On the other hand, some antiseptics that are classed as medical devices act primarily through physical interactions (e.g. rinsing, absorption and moisture regulation). It is important to bear in mind that in some countries, including the US and Canada, antiseptics that act pharmacologically are sometimes classed as medical devices Through interactions with various cellular and extracellular mechanisms involved with wound healing, antiseptics can play a key part in not only inhibiting a wide range of disease-causing microorganisms, but also in facilitating wound healing (Rothenberger et al, 2016).

All antiseptics can be used either prophylactically or therapeutically, depending on the tissue compatibility with human cells. Prophylactic antiseptics are applied once or a few times over a short period of time. This form tends to be strong and fast-acting. In contrast, therapeutic antiseptics are often referred to as slow-acting; they are used continuously and often for longer periods of time.

Using antiseptics agents against biofilm

A meta-analysis conducted by Malone et al (2017) found that biofilm is prevalent in up to 100% of all chronic wounds. Biofilms in chronic wounds can be highly tolerant to antibiotics and antiseptics (Alves et al, 2021), so debridement and dressing changes are key to remove most bacteria, biofilms, virulence factors, necrotic tissue and slough. However, some research suggests that debridement is insufficient on its own to reduce biofilm, so it is not recommended for use in isolation (Schultz et al, 2017). It has been suggested that following debridement, a 'window of opportunity' may exist that causes biofilm to become more susceptible than normal to topical antiseptics (Omar et al, 2017; Schultz et al, 2017; Alves et al, 2021). Therefore, antiseptics could help complement the debridement process by helping to delay biofilm reformation, and reduce infection risk and need for antibiotics. In particular, evidence shows that octenidine (OCT) and polyhexamethylene biguanide (PHMB) are effective at eroding the biofilm matrix and reducing microbial load (Rembe et al, 2020; Stuermer et al, 2021). Wound cleansing solutions containing PHMB and betaine surfactants can also be used as antiseptics, and it is suggested that their use can support wound bed preparation (WBP) and the removal of bacteria, debris and biofilm (Bellingeri et al, 2016). **Box 3** provides an overview of the numerous indications for antiseptics in the prevention and treatment of wound infection.

BOX 3 | Indications for antiseptics in preventing and treating wound infection (Kramer et al, 2018; IWII, 2022)

- Prevention of infection of acute wounds – e.g. traumatic, bite and gunshot wounds
- Prevention of postsurgical wound infections, such as surgical site infection (SSI), when there is a high risk of infection – e.g. traumatic and contaminated wounds
- Treatment of clinically manifested wound infections that show clinical signs and symptoms of local or spreading infection – e.g. critically colonised wounds
- Decolonisation of wounds colonised with multidrug resistant bacteria
- Preparation for – or in conjunction with – surgical, sharp or conservative-sharp debridement or wound cleansing of chronic wounds, as part of a biofilm-based treatment approach.

Properties of an ideal antiseptic product

One of the most essential properties of an ideal antiseptic agent is its ability to promote wound healing (Bigliardi et al, 2017). As well as promoting wound healing and reducing the microbial burden of a wound, an ideal antiseptic agent should exhibit good local tolerability (Bigliardi et al, 2017; Barreto et al, 2020). In order to kill a broad range of disease-causing microorganisms, antimicrobial activity of an antiseptic needs to be unspecific or multitarget (Malanovic et al, 2022). A list of the most important properties of an ideal antiseptic agent are listed in **Box 4**.

Use of antiseptics in practice

Topical antiseptics can come in various preparations, including liquids, gels, pastes or impregnated dressings, although their effects tend to differ depending on type and concentration of the preparation (IWII, 2022). Examples of antiseptics used in the care of chronic wounds are halogenated compounds (e.g. iodophor agents, such as povidone iodine [PVP-I] and cadexomer iodine, and chlorine-containing agents, such as hypochlorite and HOCl), biguanides (e.g.

Antiseptic use in practice *(Continued)*

BOX 4 | Properties of an ideal antiseptic agent (To et al, 2016; Kramer et al, 2018; Babalska et al, 2021)

- Possess antimicrobial activity at the site of action against a broad spectrum of microorganisms, including Gram-positive and Gram-negative bacteria, fungi and viruses
- Ability to penetrate biofilm
- Does not cause resistance or cross-resistance
- Is fast-acting in acute wounds
- Can handle excess wound exudate (if it is a dressing)
- Cost-effective
- Non-traumatic
- Easy and safe to use
- Does not cause allergic reactions or pain
- Is not toxic, carcinogenic or mutagenic
- Tolerability should be equal to Ringer solution, physiological saline or an inert hydrogel
- Suitable chemical and physical properties – e.g. in regard to colour (does not colour the skin), smell and consistency.

polyhexanide, also known as PHMB, and chlorhexidine) and OCT (Kramer et al, 2018; Babalska et al, 2021). Alternative antiseptic therapies include silver. Honey can also be used, which mainly acts by dehydrating bacterial biofilm and, therefore, it may affect locally infected wounds. It is vital to bear in mind that the same type of antiseptic can differ in terms of regulatory class (medicinal products/medical devices), concentration, formulation and purpose, which may sometimes be overlooked by clinicians in practice.

Through discussions with the expert panel, it was found that, other than traditional PVP-I, the antiseptic agents most commonly used in practice worldwide are biguanides, including PHMB, OCT and chlorinated agents, such as HOCl and Dakin's solution. It was shared that in Central Europe, OCT is predominantly used, while in North America and Australia, PHMB is the most available agent. In England, both chlorhexidine and OCT are widely used in practice. In the UK, chlorhexidine is often used for pre-operative skin antisepsis, but not during wound dressing changes. In the US, chlorhexidine is also used as a skin cleanser but it is not yet available as an antiseptic.

Octenidine

OCT is a commonly used antiseptic, in the form of a gel or liquid, that is widely used for a large range of clinical applications for both acute and chronic wounds. OCT has a high safety profile; therefore, it is often the agent of choice in neonates. OCT possesses an antimicrobial spectrum that covers a wide range of multidrug resistant Gram-positive bacteria (e.g. *Staphylococcus aureus*), Gram-negative bacteria (e.g. *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) and yeast/fungi (e.g. *Candida auris* and other *Candida* species; Alvarez-Marin et al, 2017; Nikolić et al, 2019; Ponnachan et al, 2019; Malanovic et al, 2020; Spettel et al, 2022). Some research shows that antiseptic properties can change under the influence of substances such as exudate, mucins, albumin or blood (Pitten et al, 2003; Kapalschinski et al, 2017). However, compared to other antiseptic agents, OCT has been shown to be effective within a short contact time at low concentrations, and in the presence of substances, including blood and mucin (Pitten et al, 2003; Assadian, 2016; Alvarez-Marin et al, 2017; Conceição et al, 2019). OCT possesses both anti-inflammatory and immunomodulatory properties to positively influence various aspects of wound healing (Seiser et al, 2021), and alcoholic preparations of OCT

are shown to have a sustained/remnant effect (Lutz et al, 2016). Furthermore, application of an OCT-containing wound gel has also been shown to improve scar quality, result in significantly fewer wound healing disorders, reduce frequency of hypertrophic scars and keloids, decrease transepidermal water loss and improve skin elasticity, in comparison to conventional wound care (Matiasek et al, 2018a).

Polyhexamethylene biguanide

PHMB is an antiseptic that is available in the form of solutions, gels, non-adherence bacterial barriers and bio-cellulose dressings (To et al, 2016). It possesses a high therapeutic index and broad-spectrum antimicrobial activity that kills Gram-positive and Gram-negative bacteria (including *Staphylococcus epidermidis* and *Escherichia coli*), fungi, parasites and certain viruses (Worsley et al, 2019; Rippon et al, 2023). PHMB has not been shown to cause development of resistance, is safe (non-cytotoxic) and does not cause damage to newly growing tissue (Rippon et al, 2023). There is evidence to show that topical PHMB may promote healing of chronic stalled wounds, reduce bacterial burden, eliminate MRSA and alleviate wound-related pain (To et al, 2016). Moreover, PHMB has a sustained/remnant effect and may result in fewer dressing changes, which has both time and cost benefits (Worsley et al, 2019). However, research has shown that higher concentrations of PHMB require a comparatively long exposure time of 15 minutes in order to reach full bactericidal efficacy (Radischat et al, 2020).

Povidone iodine

PVP-I is used in various forms, including liquids, ointments and powder, and is the go-to antiseptic for acute wounds, including gunshot wounds, stab wounds and bites (Sopata et al, 2020), as well as lacerations, bruises and deep wounds (Gmur and Karpinski, 2020). Its antimicrobial activity is broad, and PVP-I has been shown to kill a range of Gram-negative and Gram-positive bacterial strains, and both enveloped and non-enveloped viruses (Bigliardi et al, 2017; Eggers et al, 2018; Lepelletier et al, 2020). Additionally, PVP-I is noted for its ability to penetrate biofilm, lack of resistance, anti-inflammatory properties, good tolerability and absence of negative effects on wound healing (Bigliardi et al, 2017). Although it has been described to have a low cytotoxicity (Bigliardi et al, 2017), *in vitro* experiments have shown that PVP-I can be cytotoxic (Day et al, 2017; Ortega-Llamas et al, 2022). Research has also shown that exposure of the body to large amounts of iodine may result in both hyperthyroidism and hypothyroidism (Burchés-Feliciano et al, 2015).

Hypochlorous acid

HOCl is an oxidising agent with potent antimicrobial activity, and it is able to remove slough and necrotic tissue. A wide variety of chloride-containing solutions are associated with high efficacy against microorganisms (Severing et al, 2019). HOCl is also capable of inflicting damage to cellular components of microorganisms, depending on dose and concentration (Harriott et al, 2019). HOCl appears to possess biocidal and a broad spectrum of activity against both Gram-positive and Gram-negative bacteria (including *Staphylococcus aureus* and *Pseudomonas aeruginosa*), viruses, sores and fungi (Sakarya et al, 2014; Kiamco et al, 2019; Nair et al, 2019). As HOCl has both anti-inflammatory and immunomodulatory properties, and positively influences various aspects of wound healing (Del Rosso and Bhatia, 2018; Kramer et al, 2018; Nair er al, 2023), it is implicated in both acute and chronic wound infections (Centers for Disease Control and Prevention [CDC], 2021). There is some *in vitro* evidence that for some antiseptics, such as HOCl, an exposure time of 3–10 minutes is sufficient to penetrate and affect biofilms (Day et al, 2017; Harriott et al, 2019; Robson, 2020). However, as is often the case with *in vitro* data, it is possible that these clinical observations may not directly translate to practice, under all conditions, since problems associated

with biofilm in wounds have remained persistent despite the use of agents shown to be effective in *in vitro* situations. Nonetheless, HOCl meets the requirements for a topical antiseptic, as it is fast-acting, non-toxic for humans at concentrations of use, easy to apply, cost-effective, non-irritating and non-sensitising (CDC, 2021; Wounds International, 2023). There are also numerous different formulations available, with different concentrations and various additives. The lack of cytotoxicity of HOCl as an antiseptic is explained by evidence that discusses the clearance pathways (Winterbourn and Brennan, 1997; Kearns and Dawson, 2000; Li et al, 2004). Furthermore, there is a substantial body of published clinical and health economic evidence that shows the benefit of using HOCl as an oxidative antiseptic cleanser (Wang et al, 2007; Nair et al, 2019; 2023).

Chlorhexidine

Although primarily used for wound irrigation and cleansing (Norman et al, 2016), chlorhexidine is an antiseptic agent that is active against both Gram-positive and Gram-negative bacteria, fungi end enveloped viruses (Bednarek et al, 2020; Wei et al, 2021). For the purpose of pre-operative skin antisepsis and not wound treatment, chlorhexidine is widely used in clean surgeries (Wei et al, 2021), and is bacteriostatic at low concentrations and bactericidal at higher concentrations (Bednarek et al, 2020). There is evidence to suggest that chlorhexidine, for the purpose of pre-operative skin antisepsis may also protect against superficial SSI, bloodstream infection, nosocomial infections and pneumonia (Wei et al, 2021). However, recent evidence suggests that chlorhexidine gluconate is associated with levels of cytotoxicity (Cheong et al, 2022) and the rare, but serious, risk of anaphylactic reactions (Food and Drug Administration, 2022). Moreover, a recent study by Lescat et al (2021) showed that there was cross-resistance to chlorhexidine.

Biocompatibility or therapeutic index

Considering an antiseptic's biocompatibility index (BI), also known as therapeutic index, can help with selecting the most appropriate agent. It is generally referred to as a concept that measures the antibacterial activity of an antiseptic in practice compared to its cytotoxicity and, therefore, allows for comparison of different substances. A BI value of greater than 1 indicates that the antiseptic possesses a broad spectrum of activity against microorganisms and a low level of cytotoxicity against fibroblasts and keratinocytes – e.g. OCT and polyhexanide, which have a BI score of 1.7–2.1 and 1.4–1.5, respectively (Müller and Kramer, 2008; **Table 1**). In addition, considering the BI of an antiseptic can help with selecting a product based on both antimicrobial performance and cytotoxicity level. However, it is important to note that there is currently a lack of data on BI for HOCl.

Table 1. Biocompatibility index (BI) as a quotient of IC50 for L929 cells and the required minimal inhibitory concentration for a reduction factor of ≥3 log10 (Müller and Kramer, 2008; Kramer et al, 2018)

Antiseptic	$BI_{E.coli}$ (mg/L)	$BI_{S.aureus}$ (mg/L)
Chlorhexidine digluconate	0.83	0.98
Octenidine (OCT)	1.73	2.11
Hypochlorous acid (HOCl)/sodium hypochlorite (NaOCl)*	13.20	16.50
Polyhexamethylene biguanide (PHMB)	1.51	1.36
Povidone iodine (PVP-I)	0.68	0.68

* Previous research has found that the therapeutic index for HOCl is very high (Wang et al, 2007; Eriksson et al, 2022).

Considerations for product selection in practice

Use of an antiseptic or antimicrobial compound in isolation, and without anything else, is not considered best practice. An antiseptic should be used as an adjunct and should form part of a spectrum of treatment. Beyond antimicrobial action/performance, there is a need to consider and not lose sight of other benefits of antiseptics – e.g. oxidative debridement (associated with the presence of oxidative agents such as HOCl), matrix metalloproteinase (MMP) modulation, extracellular matrix degradation (ECM) and anti-inflammatory capabilities. For example, some antiseptics consist of oxidative substances that promote debridement such as HOCl. There was a consensus from the expert panel that sometimes clinicians do not have sufficient understanding of the different modes or chemistries of action, and why they are using a particular antiseptic or its indication. All antiseptics have slightly different modes of action, so they affect cellular components of disease-causing microorganisms, as well as any surrounding viable or non-viable tissues, differently. Some antiseptics can have a positive effect on the proliferation of fibroblasts or help control odour, so clinicians need to be aware of the modes of action of different antiseptics beyond their bacterial-killing properties. Additionally, some antiseptics may react with each other; for example, an oxidising agent such as HOCl may react with another oxidisable antiseptic agent. Clinicians also need to avoid mixing and matching products where considered inappropriate to do so.

Nomenclature can sometimes be confusing; for example, hypochlorite and hypochlorous sound similar but are different – although they both have potent antimicrobial activity, they possess different levels of cytotoxicity, with hypochlorite being more cytotoxic and possessing a lower therapeutic index than HOCl (Hidalgo et al, 2002; Barsoumian et al, 2013; Ortega-Peña et al, 2017; Mangum et al, 2018). It is also important to keep in mind that there is a difference between efficiency and duration of developing efficiency; for example, HOCl and OCT are both fast-acting in their efficacy, but HOCl has no residual effect while OCT has a long-lasting residual effect. Fast-acting and fast-degrading antiseptics are often designed to be used frequently; for example, due to its high therapeutic index, HOCl-based cleansers can be used frequently, and with negative pressure wound therapy (NPWT) with instillation (Kim et al, 2018; Alberto et al, 2020). Depending upon its concentration, an antiseptic may have a toxic effect on human cells – e.g. hypochlorite. However, development of resistance to topical antiseptics is uncommon.

Focus on cleansing

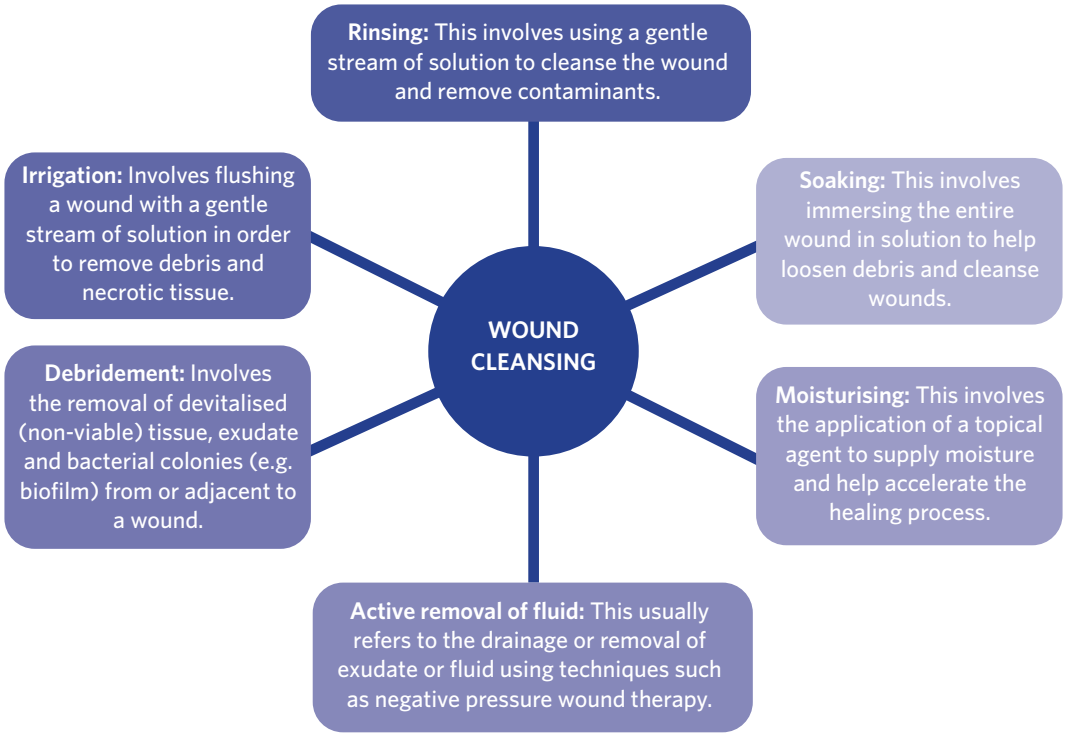
Wound cleansing is a key component of WBP and is defined as the 'active removal of surface contaminants, loose debris, non-attached non-viable tissue, microorganisms and/or remnants of previous dressings from the wound surface and its surrounding skin' (Alavi and Maibach, 2020; Haesler et al, 2022; IWII, 2022; Haesler and Carville, 2023). Chronic wounds with devitalised tissue or suspected biofilm often require vigorous cleansing to dislodge loose devitalised tissue, microorganisms and debris from the wound bed (EPUAP/NPIAP/PPPIA, 2019). Therefore, the process of wound cleansing may differ depending on the wound, and clinicians should refer to the standard protocol of care for their individual organisations.

Clinicians also need to be mindful of terminology; for example, 'cleaning' and 'cleansing' are often used interchangeably, but the latter is more commonly used in the context of wounds **[Box 5]**. Further clarification on terms that are commonly used in reference to wound cleansing is provided in **Figure 2**.

BOX 5 | Cleaning versus cleansing

In the context of wounds, 'cleansing' often refers to the removal of contaminants, debris and foreign material from the wound's surface. Often involving techniques such as rinsing, soaking and irrigation, the purpose of wound cleansing is to create an environment that is optimal for wound healing. In contrast, 'cleaning' often has a broader connotation than 'cleansing'. 'Cleaning' can refer to the use of disinfectants and other non-specific substances that are applied to an inanimate object, such as surfaces and instruments, to kill microorganisms. These products are often unsuitable for wounds and can even be cytotoxic to cells involved in wound repair (IWII, 2022).

FIGURE 2 | Terminology used in the field of wound cleansing



Wound bed preparation

Wound care of chronic wounds should be conducted alongside WBP. The purpose of WBP is to help create a moist environment that optimises conditions for debridement and wound healing, by producing a well-vascularised stable wound bed to reduce bacterial load, decrease exudate level and increase granulation tissue formation (Wounds UK, 2021; Barrigah-Benissan et al, 2022). WBP is a framework for the assessment, diagnosis and treatment of wounds that can be implemented in combination with wound hygiene (Sibbald et al, 2011; Murphy et al, 2021; Shamsian, 2021).

The dynamic and rapidly evolving concept of WBP was initially recognised by Schultz et al (2003), with Atkin et al (2019) developing the original TIME concept to TIMERS, comprising the six components that underpin WBP (Tissue, Inflammation/Infection, Moisture balance, Edge of wound/Epithelisation, Repair and regeneration, Social factors). The WBP model is reliant on effective, accurate and timely assessment to help clinicians identify patients with chronic wounds quickly, rather than failing to address problems and causing wounds to worsen for prolonged periods without treatment.

Tools for assessment

Additional tools that can be used in clinical practice to improve local wound assessment are the Triangle of Wound Assessment and the MOIST (Moisture balance, Oxygen balance, Infection control, Support strategies and Tissue management) concept. The Triangle of Wound Assessment is a holistic framework that extends the current concepts of WBP and TIMERS beyond the wound edge (Wounds International, 2015). It is designed to assess and manage several wound areas, including the wound bed, wound edge and periwound skin, and is a useful tool to guide clinicians when evaluating a wound, setting goals and selecting the most appropriate treatment (Gil, 2020). Moreover, MOIST is a wound healing concept that builds on the existing TIME concept and takes into consideration several novel therapeutic options that have become available since the TIME concept was first introduced (Dissemond et al, 2022). MOIST aims to improve the local treatment of wounds and address factors that can adversely affect desired clinical outcomes (Gray et al, 2013). Both the Triangle of Wound Assessment and MOIST can be applied as part of a holistic wound assessment.

Selection of an appropriate wound cleansing solution

Selection of a wound cleansing solution should reflect the goals of treatment as identified through an assessment of the patient and their wound. Choice should ultimately be influenced by the wound type, comorbidities and patient preferences. Although the ideal wound cleansing solution has not been established conclusively, important considerations are listed in **Box 6**.

Use of antiseptics during wound cleansing

Historically, physiological saline, Ringer's solution and tap water have been the mainstays of wound cleansing solutions. However, antiseptics are increasingly being explored for the cleansing of wounds and removal of biofilm (Sakarya et al, 2014), as well as removal of slough via oxidative mechanisms. A variety of topical antiseptics are commonly used in practice to cleanse and irrigate wounds, including chlorhexidine, OCT, hypochlorite, PHMB, PVP-I and HOCl (Snyder et al, 2017). Where wounds are cleansed with soap or an antimicrobial scrub, this should be performed carefully to avoid causing further trauma to the wound (Alves et al, 2021). Cleansing of the wound needs to be performed at every dressing change. If considered appropriate, debridement (e.g. mechanical [sharp or surgical], enzymatical or biosurgical [maggot therapy]) can help disrupt any remaining necrotic tissue and biofilm, and facilitate wound healing (Sun et al, 2016; Sibbald et al, 2021; De Francesco et al, 2022).

Focus on cleansing *(Continued)*

BOX 6 | Considerations for selection of a wound cleansing solution (Kramer, 2020; Kramer et al, 2018; IWII, 2022)

- Wound type, aetiology, anatomical location and visible structures
- Wound bed tissue type
- Risk of wound infection
- Any signs and symptoms of local wound infection or spreading infection
- Patient factors (e.g. comorbidities, allergies and level of pain)
- Compatibility with dressings
- Clinical efficacy and sensitivities of the solution
- Colonisation with multidrug resistant organisms
- Goals of treatment
- Cost-effectiveness
- Antiseptic presentation (e.g. gel, solution, spray, dressing, etc.)
- Local policies, resources and availability.

There is a consensus that antiseptics and antimicrobials should only be used once a wound has been cleaned and debrided to remove barriers, including slough, necrotic tissue, biofilm and debris. However, more evidence is needed, as some experts believe that pre-treatment with antiseptics, such as those containing oxidising agents, can help loosen tissues and make debridement and detachment of tissues easier. Conversely, if a wound is exuding heavily, the performance of an antiseptic may be diluted; therefore, debridement and de-sloughing can be useful before an antiseptic is employed. In addition, further research should help address disparities in practice concerning the temperature at which antiseptics are used, with some clinicians warming/cooling them and others using antiseptics at room temperature.

Contact time

There was a consensus from the expert panel that contact time (i.e. how long the wound is exposed to an antimicrobial) often depends on how much time the clinician has with the patient. *In vitro* studies and investigations using animal models dominate the literature (Schwarzer et al, 2020), but neither accurately reflect the use of antiseptics in real-world settings; for example, contact time in laboratory research is often 24 hours or longer while in clinic, antiseptics may only remain in contact with the wound for 10 to 15 minutes – e.g. during wound cleansing (Johani et al, 2018). If unsure, clinicians should always refer to a product's Instructions for Use (IFU).

Guidance and pathways for antiseptic use

Use of antiseptics needs to be tailored to the specific needs of the patient and their wound. As part of the decision-making process to determine whether an antiseptic agent is required, and what type, clinicians need to determine the wound's aetiology and underlying cause of infection. The wound also needs to be managed according to healing phase and type (Kramer et al, 2018). Selection of an antiseptic agent depends on the target of its action and presence of interfering substances (Babalska et al, 2021). Clinicians need to possess comprehensive knowledge on a product before using it. Moreover, appropriate choice of antiseptics is critical, as some agents may cause skin irritation and colouring of disinfected areas (Matiasek et al, 2018b). Guidance on using antiseptics for wounds in practice is listed in **Box 7**.

BOX 7 | Tips for using antiseptics in practice

- Assess needs and suitability by conducting a thorough assessment of the patient and their wound – e.g. health status, medical history, underlying conditions, age, ability to self-care, wound characteristics and infection risk
- Select an appropriate agent for the wound and infection type, making sure to consider the patient's preferences and goals of treatment
- Follow the product's instructions for guidance on dosage, application frequency and contact times
- Cleanse the wound, debride if necessary and, particularly with oxidative antiseptics, soak for 3–10 minutes
- Maintain aseptic technique, use sterile equipment and adhere to proper infection control practices
- Dress the wound appropriately with a dressing that is compatible with the antiseptic
- Monitor the wound by looking for signs of improvement or deterioration, and adjust the treatment plan as needed
- Educate the patient on caring for their wound
- Work as part of a wider multidisciplinary team and consult a specialist when required
- Keep up-to-date with the latest guidelines on antiseptics for the prevention and treatment of wound infection.

Considering different wound aetiologies

It is important to consider underlying pathophysiology when selecting an antiseptic agent. Some antiseptics may be better than others depending on the type of wound – e.g. pressure/venous/diabetic ulcers. A study found that topical HOCl can accelerate healing times in venous leg ulcers (Bongiovanni, 2014), and there is low level evidence for the adjunct use of HOCl to resolve infection and improve healing in venous leg ulcers (Armstrong et al, 2015). However, more research is needed, and the effects of topical antiseptics on pressure ulcers is also unclear. It is suggested that healing may be promoted in ulcers if the number of microorganisms is reduced with the help of antimicrobial agents (Norman et al, 2016). Moreover, guidelines from EPUAP/NPIAP/PPPIA (2019) currently recommend the use of HOCl-based cleansers on pressure ulcers.

Table 2 considers some dos and don'ts of using antiseptics in practice.

Table 2. Dos and don'ts of using antiseptics in practice

Do	Don't
✔ Do consider the patient's allergies and tolerance level when selecting an antiseptic	✘ Don't overuse antiseptics and only use them when clinically indicated
✔ Do wash your hands thoroughly and follow infection control procedures when applying antiseptics	✘ Don't ignore signs of adverse reactions to an antiseptic, and make sure to adjust treatment as necessary
✔ Do wear gloves, and use sterile equipment and aseptic technique	✘ Don't use antiseptics as a substitute for proper wound cleansing and debridement
✔ Do monitor the wound's progress and adjust treatment as necessary	✘ Don't mix different antiseptics as this can lead to adverse reactions or reduced effectiveness

Guidance and pathways for antiseptic use *(Continued)*

The two-week challenge

There is ongoing debate about what the most appropriate duration of antimicrobial treatment is, with longer duration being associated with a heightened risk of inducing AMR. A two-week challenge is often recommended, in which healthcare professionals should use a topical antiseptic for at least two weeks before evaluating its efficacy in managing wound infection. After two weeks, the healthcare professional should reevaluate and either (Ayello et al, 2012; IWII, 2022):

1. Discontinue if signs and symptoms of infection have resolved
2. Continue with the antimicrobial if the wound is still progressing but there are still signs and symptoms of infection (treatment may be required for up to four weeks to attain results)
3. Consider an alternative antimicrobial if there is no improvement and refer to a wound care specialist
4. Reassess the underlying disease.

Figure 3 presents a pathway that has been created to guide the use of antimicrobial treatment for patients with wounds, with or without infection risk (Wounds UK, 2021).

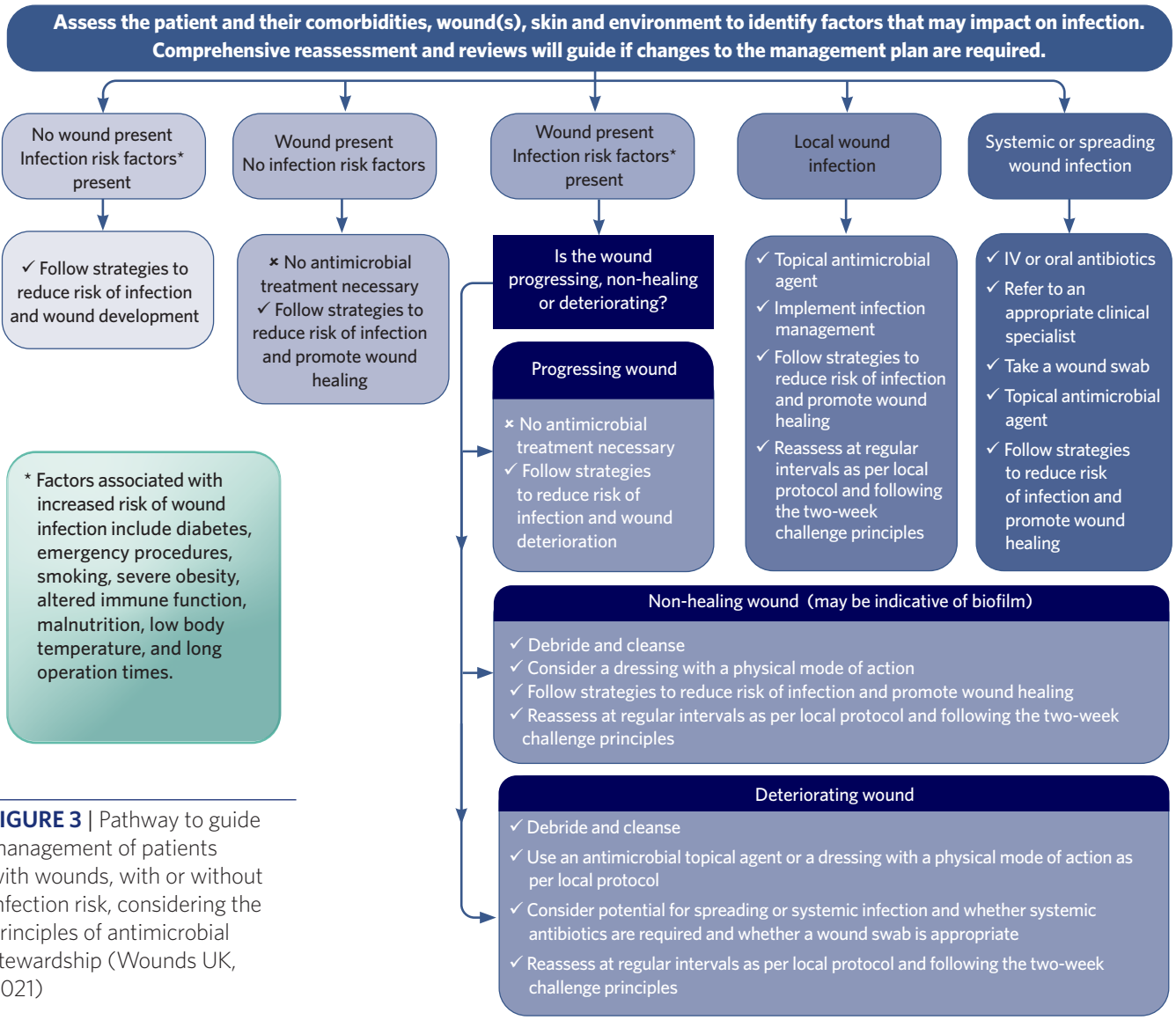


FIGURE 3 | Pathway to guide management of patients with wounds, with or without infection risk, considering the principles of antimicrobial stewardship (Wounds UK, 2021)

Antimicrobial stewardship (AMS)

AMR is a global public health emergency that is estimated to contribute to over 5 million deaths worldwide each year (WHO, 2022). Inappropriate use and overuse of antibiotics has led to an increase in AMR, so there is an urgent need to improve the quality of antibiotic prescribing worldwide. AMS refers to the 'organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness' (National Institute for Health and Care Excellence, 2023). Ultimately, an AMS-focused approach recognises the importance of safeguarding the effectiveness of antibiotics to improve patient outcomes and reduce the spread of infections caused by multidrug resistant microorganisms. Numerous global initiatives have been created to measure the effects of these programmes in tackling AMR **[Box 8]**, and key AMS strategies that have been identified include (Lipsky et al, 2016; Roberts et al, 2017; Stryja et al, 2020):

- Increasing efforts towards effective infection control methods, including hand hygiene/decontamination practices, using PPE as per local protocol, correct removal of PPE, good waste management, comprehensive documentation and management of the patient's environment
- Creating a consistent knowledge base and educational opportunities for clinicians on the effective use of antimicrobials, and to reduce variation in practice – thus reducing diagnostic uncertainty, clinical ignorance, ritualistic behaviour, clinical fear and patient demands
- Prescribing the appropriate antimicrobial treatment when therapy is indicated, and minimising the unnecessary use of antimicrobials, overly broad-spectrum treatment regimens and the use of antibiotics for non-infected wounds
- Prescribing the appropriate antimicrobial duration, at an optimal dose, administered through the most appropriate route for the indicated condition and patient status (the 'Five Rights'; **Box 9**)
- Using an agent that has the lowest risk of adverse effects.

BOX 8 | Initiatives that have been created around the globe to support AMS strategies (Ousey and Blackburn, 2020)

- The Transatlantic Taskforce on AMR Partnership
- The Global Antibiotic Resistance Partnership
- Global Health Security Agenda
- The Joint Programming Initiative on AMR
- The Global Action Plan on AMR, which has been endorsed by WHO, Food and Agriculture Organization and World Organization for Animal Health
- The 5-year national action plan for tackling AMR, developed by the Department of Health
- World antimicrobial awareness week coordinated annually by WHO.

BOX 9 | The 'Five Rights'

The 'Five Rights' of drug administration are a crucial component in medication safety, particularly antibiotics. Here, the 'Five Rights' have been adapted for the appropriate prescribing of topical antimicrobials in wound care:

1. Right diagnosis and care plan
2. Right antimicrobial and the right delivery system
3. Right time to initiate antimicrobial treatment
4. Right antimicrobial dose
5. Right duration of antimicrobial treatment.

Antimicrobial stewardship (AMS) *(Continued)*

Barriers to the implementation of antimicrobial stewardship (AMS) strategies

Studies have highlighted several key barriers to the implementation of AMS strategies (Rolfe et al, 2021; Limato et al, 2022; Wu et al, 2022). Importantly, improving the adoption, implementation and sustainability of AMS programmes requires a systemic change in behaviour through increased public awareness and education (Wounds UK, 2020). Major barriers to the implementation of AMS strategies include (Limato et al, 2022; WHO, 2022):

- Clinician knowledge deficits regarding optimal use of antibiotics
- Ineffective resourcing and limited infrastructure for AMS programmes
- Lack of communication and interprofessional relationships between healthcare providers
- Cost-prohibitive bacterial culture testing and thresholds of national health insurance coverage
- Limited access to antimicrobials, as well as concerns around cost
- Resistance to changing current practices regarding antimicrobial prescribing
- Limited access to reliable diagnostic or microbiological testing.

Guidance for AMS best practice

There needs to be an environment that fosters behavioural change with a focus on a back-to-basics approach to infection prevention, such as hand hygiene. The AWaRe (Access, Watch, Reserve) antibiotic book is a resource that was developed by WHO and contains guidelines for the management of common infections (WHO, 2022). It also helps with selecting the most appropriate intervention for each clinical setting. Most government organisations have published plans to tackle AMR, and these can be accessed online, so clinicians should always check and refer to their own country's guidelines, as well as local protocols where available.

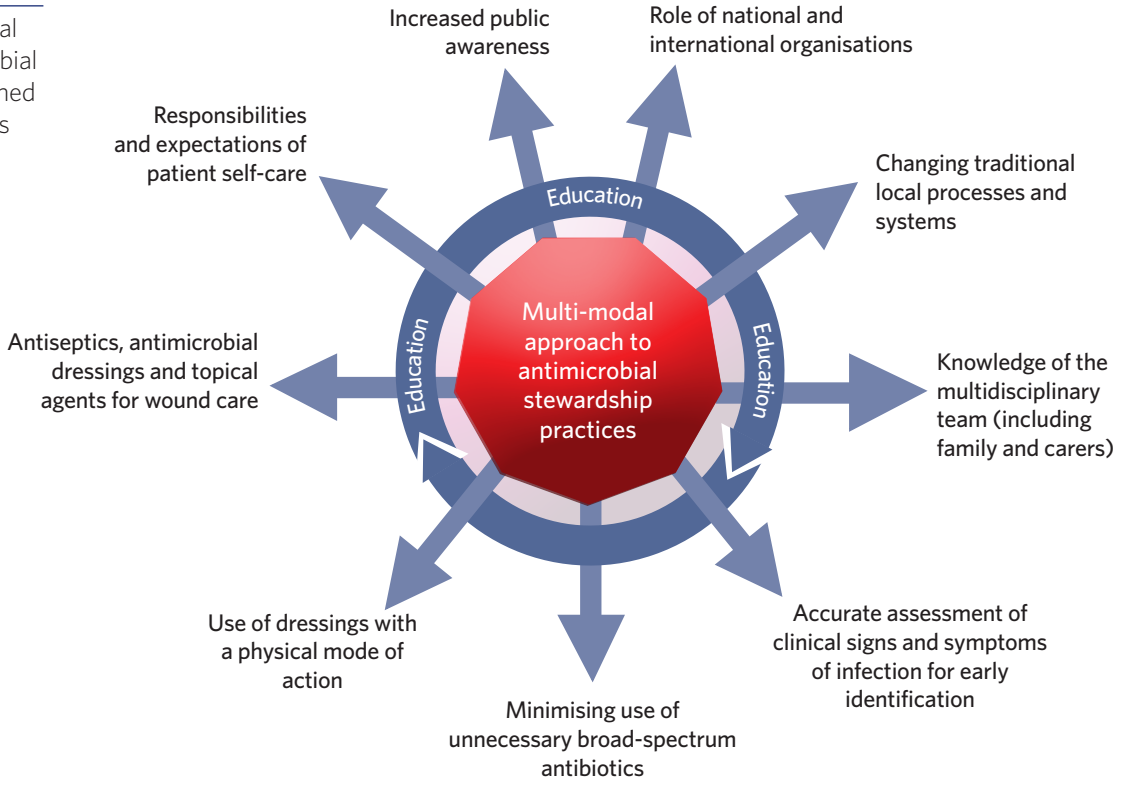
There is strong and growing evidence that antiseptics can be useful agents for reducing AMR, but they are under-used, particularly in the fields of wound care and surgical site management (Roberts et al, 2017). It is believed that using antiseptics, where considered appropriate, will help reduce the use of antibiotics. However, this does not imply that clinicians should prescribe antiseptics every time without indication. Antiseptics need to be used judiciously and clinicians should refer to a consultant, microbiologist or appropriate expert if unsure at any point.

For the optimal management of wound infection, working within a multidisciplinary team (MDT) of experts is essential – e.g. clinicians, surgeons, infectious disease experts, microbiologists, pharmacologists and geriatricians (Falcone et al, 2021). An MDT approach helps coordinate services as a team, to work together towards specific goals to optimise care and outcomes for the patient.

Clinician and patient/public education

Each member of the MDT is responsible for reducing the impact of AMR. Ongoing education is vital to optimise care for patients, and the clinician's responsibility is to educate themselves and the patient, so that members of the public are made aware of the importance of AMS programmes. Where patients are assessed as having the capacity and willingness to self-care, they should be supported to reduce their modifiable infection risk. Combating AMR requires a multi-modal approach led by education and better understanding of the infection continuum. **Figure 4** illustrates the multimodal approach to AMS practices underpinned by education. Early identification of infection will lead to faster and more effective treatment; therefore, creating opportunities for training and education to increase clinicians' confidence in recognising and identifying the signs of infection is essential (Wounds UK, 2020).

FIGURE 4 | Multimodal approach to antimicrobial stewardship underpinned by education (Wounds UK, 2020)



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