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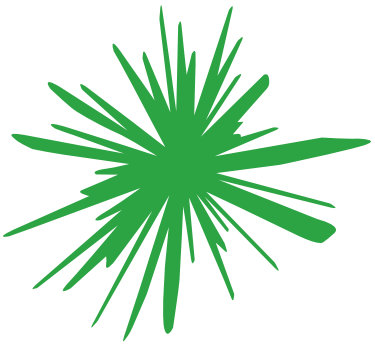

International Wound Infection Institute

WOUND INFECTION IN CLINICAL PRACTICE

Principles of best practice

2022

Third Edition

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01 Foreword

Wound infection continues to be challenging for people with a wound, their families and health professionals. Wound infection can lead to protracted wound healing, multiple health service visits and increased hospital admission duration. This comes at significant economic cost and negatively impacts quality of life outcomes for the person with a wound and their family. Accurate and timely identification of the signs and symptoms of wound infection are critical to achieving effective management of wound infection.

This edition of *Wound Infection in Clinical Practice*, authored by the International Wound Infection Institute (IWII) Committee, is an update from our previous consensus document published in 2016. Advances in research and clinical practice relating to the wound environment, risk factors for infection, biofilm, antimicrobial resistance, and new technologies for identification and management of wound infection have been incorporated into this update. Our intention is to provide practical information based on the latest understanding of the science and clinical applications regarding wound infection.

We have expanded some chapters and added new chapters, discussed some recent controversies in the field, and provided new definitions relating to the topic that arose from a recent consensus process conducted by the IWII. In updating the document, rigorous methodology was implemented, including a systematic literature review, a Delphi process (to refine definitions), critical appraisal of the evidence on clinical efficacy of topical antimicrobials, and peer review from global key interdisciplinary opinion leaders.

Integral to this document is an updated version of the IWII Wound Infection Continuum (IWII-WIC) for use by health professionals in their clinical practice and by educators and researchers. To facilitate its use, the IWII-WIC is presented as a removable poster. Other versions of the IWII-WIC are available from the IWII website, including simplified versions for patient and/or student teaching.

The IWII is a volunteer organisation that has been promoting prevention, identification and management of wound infection since 2006. The IWII provides this consensus document free to download via Wounds International (www.woundsinternational.com), and from www.woundinfection-institute.com, and the document is available in multiple languages. The IWII also provides additional information and resources to support the implementation of practice guidance outlined in this document, including Made Easy and Top Ten Tips resources focused on aspects of wound infection prevention and management. These text, graphic and multimedia resources will be updated regularly as a part of the IWII implementation plan for this 2022 edition of *Wound Infection in Clinical Practice*. Membership and access to the IWII is free.

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02 Supporting Best Practice in Wound Infection

This update provides an opportunity to explore contemporary advances in wound infection knowledge and practice. Scientific and clinical understanding of chronic wound infection has developed rapidly since the last edition of this document. Awareness of the presence and impact of wound biofilms has continued to advance enormously; and the major influence of biofilms on chronic wound healing is well recognised,[1-4] but not yet fully understood.[5-8]

The primary determinants of the pathological process through which presence of bacteria and other microorganisms results in wound infection and harmful effects on an individual with, or at risk of, a wound can be briefly outlined as:

- The ability of the individual's immune system to combat potential opportunistic pathogens,[9-12] which is influenced by a range of potential factors discussed throughout this document.
- The number of microbes in the wound; a greater number of microbes can more successfully overwhelm host defences.[9, 11, 12]
- The species of microorganism present; some microbes have greater capacity to produce a detrimental effect (virulence) and some microorganisms can form and reform biofilms more rapidly.[11, 13, 14]
- The combination of microflora in the wound; some microorganisms appear to synergistically overwhelm the individual's immune system more rapidly, through either collaborative or competitive processes that require more research to elucidate more fully.[15, 16]

A holistic and collaborative approach is fundamental to the delivery of best practice in prevention, diagnosis, assessment and management of wound infection. This is of particular importance in the context of increasing antibiotic resistance and the significance of ensuring antimicrobial stewardship. These concepts, and current best practice in wound infection are highlighted throughout this document.

WOUND INFECTION TERMINOLOGY

An important aspect that underpins delivery of best clinical practice in wound infection is the language used by clinicians. Accurate use of terminology is important for conveying information and meaning within and between the multidisciplinary team, other health professionals involved in a person's general health care, the person with a wound and their family caregivers.[17] Consistent use of terms and language is important for accurate and consistent understanding in both written (e.g. clinical documentation) and verbal communication (e.g. clinical case discussion) and influences the quality and consistency of care. It is also important for conveying research outcomes and commercial information associated with wound infection and its management, and in educating both clinicians and people with wounds.

The International Wound Infection Institute (IWII) has continued to advance the work it undertook for the last edition of this document in 2016, which focused on advancing consensus on wound infection frameworks and related terminology.[12, 18, 19] At that time, consensus was reached that the concept of critical colonisation, which suggests a specific moment when microbial burden reaches a critical level (above 10^5 cfu/ml of exudate or per gram of tissue), was not representative of the science. Consensus was reached that the term local wound infection more accurately represented the phase of infection in which covert (subtle) local clinical indicators of infection (e.g. pocketing, epithelial bridging and hypergranulation) can be identified by expert wound clinicians. These clinical indicators are primarily observed in the hard-to-heal wound or before the wound exhibits overt (classic) signs and symptoms of erythema, warmth, swelling, purulent discharge, delayed wound healing beyond expectations, new or increasing pain, and increasing malodour. The term local wound infection is now well accepted as describing a phase within the IWII-WIC.[12, 18, 19]

To accompany this 2022 edition of the document, the IWII undertook another consensus process that included experts nominated by international wound organisations, with a goal of addressing lack of agreement and standardised use of terms associated with wound infection.[20] The resultant consensus definitions are used throughout this document and glossary and have been published for use in other wound guidelines and consensus documents. Notably, the experts participating in this process agreed on a consensus definition for biofilm that varies substantially from the definition on which IWII experts reached agreement in 2016. This change reflects advances in our understanding regarding what is and is not, known about wound biofilms, which is discussed in more detail in *06 Wound Biofilms*.

03 Wounds at Risk of Infection

All open wounds are contaminated or colonised with microorganisms; however, not all contaminated wounds become infected. The symbiotic relationship between the host and the colonising microorganism becomes pathogenic when the host's immune system becomes compromised by the virulence of organisms present within a wound,[21] and wound infection occurs.[22] The host's immune system may become compromised through several potential mechanisms, such as increase in production of toxins by microorganisms,[21] and the ways in which microorganisms might interact metabolically with the host and other microorganisms (social microbiology). Biofilms also contribute to delayed wound healing and increase the risk of wound infection.[23-25]

FACTORS ASSOCIATED WITH RISK OF WOUND INFECTION

The risk of wound infection is influenced by characteristics of the individual (host), their wound, and the environment. Host factors that influence the development of wound infection are systemic, multifactorial and encompass many variables. The type of wound (i.e. aetiology) also contributes to the risk of infection, with acute wounds having a range of different risk factors for infection as compared to chronic wounds. For example, the risk of infection in a surgical wound is influenced by the type of surgery (level of contamination risk), duration of surgery and several host and environmental factors.[26-28] Table 1 outlines individual, wound and environmental risk factors associated with wound infection.

Table 1: Factors associated with increased risk of wound infection

Individual (host) risk factors[23, 26, 29-44]

- Poorly controlled diabetes (i.e. hyperglycaemia)
- Peripheral neuropathy (sensory, motor and autonomic)
- Neuroarthropathy
- Radiation therapy or chemotherapy
- Conditions associated with hypoxia and/or poor tissue perfusion (e.g. anaemia, cardiac disease, respiratory disease, peripheral arterial disease, renal impairment or rheumatoid arthritis)
- Immune system disorders (e.g. acquired immune deficiency syndrome)
- Connective tissue disorders (e.g. Ehlers-Danlos syndrome)
- Corticosteroid use
- Malnutrition or obesity
- Alcohol, smoking or illicit drug use
- Poor compliance with treatment plan

Wound risk factors[27, 31, 35, 37, 44-46]

Acute wounds	Chronic wounds	Acute and chronic wounds
■ Contaminated or dirty wounds ■ Traumatic injuries ■ Operation is classified as contaminated or dirty ■ Inappropriate hair removal ■ Operative factors (e.g. prolonged surgery, blood transfusion or hypothermia)	■ Duration of wound ■ Large wounds ■ Anatomically located near a site of potential contamination (e.g. perineum or sacrum)	■ Foreign body presence (e.g. drains, sutures or wound dressing fragments) ■ Haematoma ■ Necrotic or sloughy wound tissue ■ Impaired tissue perfusion ■ Increased exudate and oedema that is not adequately managed ■ Wounds over bony prominences or probing to bone ■ Involvement of tissue deeper than skin and subcutaneous tissues (e.g. tendon, muscle, joint or bone)

Environmental risk factors[31, 34, 44]

- Unhygienic environment (e.g. dust, unclean surfaces, or presence of mould/mildew)
- Hospitalisation (due to increased risk of exposure to antibiotic resistant microorganisms)
- Inadequate hand hygiene and aseptic technique
- Inadequate management of moisture (e.g. due to exudate, incontinence or perspiration)
- Interface pressure that is inadequately off-loaded

Some formal tools are available for assessing risk of developing wound assessment. Work on formal wound infection risk assessment tools has primarily focused on risk of acute wound infection following surgery, generally with a focus on specific types of surgery (see Table 2). Risk variables included on these tools include sub-sets of the risk factors outlined in Table 1, but none of the tools below includes a comprehensive assessment of the patient, the wound and the environment. They could be used in conjunction with clinical judgement and to inform a comprehensive assessment.

Table 2: Sample of tools available to assess the risk of wound infection

Risk assessment tool	Wound type	Risk variables	Predictive power
Australian Clinical Risk Index (ACRI)[47]	Surgical site infection following cardiac surgery	Includes diabetes and BMI as risk variables	Low predictive ability in all types of cardiac patient (AUC = 0.64, 95% CI, 0.5 to 0.7)[48]
Brompton and Harefield Infection (BHIS) Score[49]	Surgical site infection following cardiac surgery	Includes gender, diabetes, BMI, cardiac function and emergency vs elective surgery status	Moderate predictive ability (area of receiver operating characteristic (aROC) curve=0.727)[49]
Malunion of the Sternum (MUST) score[50]	Surgical site infection following cardiac surgery	Includes age, gender, BMI, previous surgery and diabetes as risk variables	Moderate predictive ability (area under curve [AUC] = 0.76, 95% confidence interval [CI] 0.72 to 0.79)[50]
National Nosocomial Infections Surveillance Risk Index[51]	Surgical site infection following cardiac surgery	Includes surgical contamination status, pre-anaesthetic score and surgery duration	Low predictive ability in cardiac surgery patients (AUC = 0.62 (95% CI 0.5 to 0.7)[48]
Perth Surgical Wound Dehiscence Risk Assessment Tool (PSWDHRAT)[52]	Wound dehiscence in surgical wounds	Includes comorbidities, smoking, previous surgery, age and BMI as risk variables	Moderate predictive power (71%)[52]
Wounds At Risk (WAR) Score[53, 54]	All wounds	Comorbidities, medications, wound contamination, age, wound duration, wound aetiology, wound dimensions, wound anatomical location	Correlation shown between WAR score of and confirmed presence of *Pseudomonas aeruginosa* (p=0.0001)[54]
Wound Infection Calculator[55]	Post operative wound infection following spinal surgery	Includes gender, BMI, smoking, physical status score, level of surgical invasiveness	High predictive ability (AUC = 0.81)[55]
Wound Infection Risk Assessment and Evaluation tool (WIRE)[56]	Community-based wounds	Comorbidities, immune status, smoking, medications, nutrition, antibiotic therapy	Psychometric testing is planned[56]

PREVENTING WOUND INFECTION

Prevention of wound infection is focused on implementing strategies to reduce the patient's individual risk factors. Establishing clinical goals, working with the patient and their family, and suggested general strategies to reduce wound infection risk are discussed in more detail in *07 Holistic Assessment and Management*. In addition to an individualised approach to addressing clinical and environmental wound infection risk factors, topical antimicrobials might have a role for preventing wound infection in very high risk wounds[57] (see *09 Topical Antimicrobial Therapy*). The clinical benefits should be weighed against the risks and the principles of antimicrobial stewardship (see *11 Antimicrobial Resistance and Stewardship*).

04 Identifying and Assessing Infection in a Wound

Wound infection is the invasion of a wound by proliferating microorganisms to a level that invokes a local, spreading and/or systemic response in the host. Microorganisms multiply within the wound, developing a range of virulence factors to overcome the host defences leading to local tissue damage and impeding wound healing.[11, 58]

Host defences generally destroy microbes, unless the immune system of the host is compromised[59] or circumvented by microbes through an array of measures. Excessive and prolonged inflammatory response, delayed synthesis of collagen and epithelialisation and tissue damage is manifested by wound infection.[24] Intervention may therefore be required to assist host defences in removing or destroying the invading microorganisms.[21]

THE IWII WOUND INFECTION CONTINUUM

The IWII-WIC (see Figure 1 and back of document) is a well acknowledged educational tool that provides a framework to conceptualise the impact that microorganisms have on the host, the wound and on wound healing. The IWII-WIC, based on expert consensus, is a way to conceptualise the microbiological process, informed by clinical presentation of wounds. As the science progresses, the IWII-WIC framework may require review. The IWII-WIC represents the various stages of microbial presence in a wound that increase in severity, from contamination to colonisation, local infection (covert and overt) extending to spreading and systemic infection.[19, 60, 61] As a resource for use at the bedside, and cognisant of antimicrobial stewardship and biofilm-based wound care,[62] clinical wound infection management has been included with the IWII-WIC in this document.

STAGES OF THE IWII WOUND INFECTION CONTINUUM

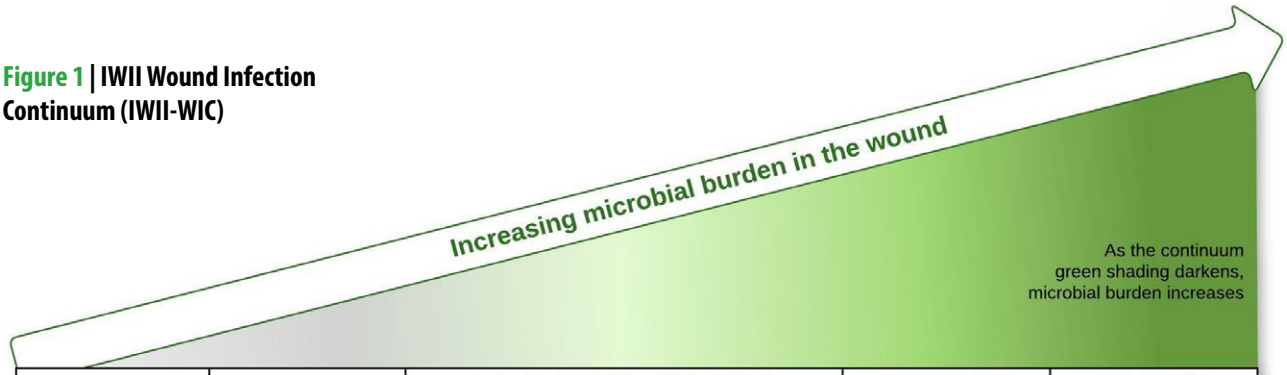
The IWII-WIC has evolved over time as our understanding of wound infection advances. The most recent major evolutions to the IWII-WIC were agreed by wound infection experts in 2016 using a consensus process,[12, 19] and included removal of the term "critical colonisation" that had previously been used to refer to the specific point at which microbial burden overwhelms host defences. It is now understood that microbial burden evolves on a continuum and identifying a specific point when wound infection becomes 'critical' is not possible.[12, 63] Conceptually, the concept of covert (subtle) local wound infection is now used to describe the clinical indicators primarily observed in the chronic wound before the wound exhibits overt (classic) signs and symptoms of local wound infection.

The IWII-WIC includes five conceptual stages:

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

It details the signs and symptoms commonly exhibited by the individual and the wound as infection develops. Definitions for these five stages were recently agreed on in an international consensus process.[20]

Figure 1 | IWII Wound Infection Continuum (IWII-WIC)



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 • Lymphangitis • Crepitus • Wound breakdown/ dehiscence with or without satellite lesions • Inflammation, swelling of lymph glands	• Malaise • Lethargy or nonspecific general deterioration • Loss of appetite • Fever/pyrexia • Severe sepsis • Septic shock • Organ failure • Death

Contamination is used to refer to a stage in which there is presence within the wound of microorganisms that are presumed not to be proliferating. No significant host reaction is evoked and no delay in wound healing is clinically observed.[20] In a contaminated wound, the host defences destroy microorganisms through a process called phagocytosis.[64, 65]

Colonisation is used to refer to a stage in which the presence of microorganisms within the wound that are presumed to be undergoing limited proliferation. In a colonised wound, no significant host reaction is evoked, and no delay in wound healing is clinically observed.[20] Due to the protective function of the skin microbiome, all open wounds are colonised with microorganisms at the time of skin breakdown,[66] but at this stage the virulence appears to be low. Microorganisms that colonise a wound may also arise from exogenous sources or as a result of environmental exposure.

Local infection is used to refer to a stage of infection in which there is presence and proliferation of microorganisms within the wound that evoke a response from the host, often including a delay in wound healing. Local infection is contained within the wound and the immediate periwound region (less than 2cm). Local infection often presents as covert (subtle) signs and symptoms[12, 19] that may not be immediately recognised as a sign of infection.

Covert (subtle) signs and symptoms of wound infection include:[62, 67-70]

- Hypergranulation
- Bleeding, friable granulation
- Epithelial bridging and pocketing in granulation tissue
- Increasing exudate
- Delayed wound healing beyond expectations.

As local wound infection progresses, classic cardinal (overt) signs and symptoms that are traditionally associated with local infections generally become evident and are more recognisable

as an indicator of wound infection. However, these symptoms may be masked in people with compromised immune systems and/or poor vascular perfusion.

Overt (classic) signs and symptoms of wound infection may include:[62, 67-69, 71]

- Erythema (which may present differently depending on the individual's skin tone)
- Local warmth
- Swelling
- Purulent discharge
- Wound breakdown and enlargement
- New or increasing pain
- Increasing malodour.

Spreading infection (also referred to as cellulitis) describes the stage of infection in which there is invasion of the surrounding tissue by infective microorganisms that have spread from a wound. Microorganisms proliferate and spread to a degree that signs and symptoms extend beyond the wound border.[9, 72] Spreading infection may involve deep tissue, muscle, fascia, organs or body cavities.

Spreading infection signs and symptoms may include:[62, 67]

- Extending induration
- Lymphangitis (swelling of lymph glands)
- Crepitus
- Wound breakdown/dehiscence with or without satellite lesions
- Spreading inflammation or erythema greater than 2cm from the wound edge.

Systemic infection refers to the stage of infection in which microorganisms spread throughout the body via the vascular or lymphatic systems, evoking a host response that affects the body as a whole. In the context of wound infection, microorganisms spread from a locally infected wound. Systemic inflammatory response can also be triggered by a local wound infection through other pathways, for example release of toxins or a dysregulated immune system.

Systemic signs and symptoms of infection may include:[67, 69]

- Malaise
- Lethargy or nonspecific general deterioration
- Loss of appetite
- Fever/pyrexia
- Severe sepsis
- Septic shock
- Organ failure
- Death.

CLINICAL ASSESSMENT OF WOUND INFECTION

Continuous, accurate, holistic assessment of the individual and their wound are essential for effective wound treatment.[73, 74] Early identification and subsequent treatment to reduce or eliminate infection is clinically and economically beneficial, and essential to facilitate wound healing[75-78] and to reduce the impact on the individual, their family caregivers and on healthcare systems.[79] Undertaking holistic assessment of wound infection risk, including evaluation of host factors, and the wound history is discussed under *07 Holistic Assessment and Management*. This holistic assessment should also include a clinical assessment of the wound. Clinical assessment of wound infection includes evaluation of anatomical location and presentation of the wound bed and the periwound region.[80]

Microbial burden is not always associated with signs and symptoms of infection.[61] Clinical signs and symptoms have been reported to be inaccurate and unreliable.[81-83] However, cultures, molecular techniques and other diagnostic results take time, and are sometimes inaccessible and costly.[45] Clinicians regularly apply their knowledge and skills to make a clinical assessment through identification of the signs and symptoms described in the IWII-WIC.[79]

A wound infection assessment tool can aid the evaluation of a wound. Scoring systems and diagnostic criteria have been developed to assist in the identification and assessment of infection in specific types of wounds (e.g. the Centre for Disease Prevention and Control's criteria for surgical site infection[84]). Although various assessment tools and classification systems exist, most have not been developed or psychometrically tested specifically for assessing wound infection. Table 3 outlines commonly used clinical wound infection assessment tools, together with their psychometric properties. As no single sign or symptom reliably confirms the presence or absence of wound

Table 3: Wound infection assessment tools

Assessment tool	Wound type	Description	Psychometric testing
ASEPSIS[85]	Developed for cardiac surgery but may be applied to other types of surgical wounds	■ A method of assessing wound healing that defines characteristics that are awarded points ■ Includes objective assessment criteria ■ Points are given for:[85, 86] - **A**dditional treatment - **S**erous discharge - **E**rythema - **P**urulent exudate - **S**eparation of the deep tissues - **I**solation of bacteria - **S**tay duration (time spent as an inpatient)	■ Sensitivity and specificity of a range of total ASEPSIS scores (score >10 to score >40) in predicting hospitalisation, antibiotic therapy and surgery are reported[86] ■ Good inter-rater reliability[87]
Clinical Signs and Symptoms Checklist (CSSC)[83]	Variety of wound types	■ Includes 12 clinical signs and symptoms of infection ■ Includes five classic signs/symptoms of wound infection ■ Includes seven secondary signs and symptoms of wound infection	■ Sensitivity and specificity of individual signs and symptoms reported in different populations[83, 88] (range sensitivity 0.18 to 0.81; specificity 0.56 to 1.00)[83] ■ Positive and negative predictive values of individual signs and symptoms reported in different populations[83, 88]
Infection Management Pathway[78]	All wound types	■ Standardises the assessment and diagnosis of causes of delayed healing related to local infection and biofilm ■ Provides a treatment plan based on which signs/symptoms of infection are present ■ Pathway is commercially positioned	■ Feasibility and psychometric testing is planned[78]
IWGDF/IDSA System[89]	Diabetic foot ulcers	■ Developed as a part of PEDIS classification[89, 90] ■ Defines the presence and severity of foot infection in a person with diabetes on four levels of severity ■ Requires clinical examination and standard blood and imaging tests ■ Stratification aligns with therapeutic decisions	■ Moderately reliable as a predictor of hospitalisation[89] ■ Valid as an indicator of risk of amputation[90, 91] ■ Low inter-rater reliability[90]
IWII Wound Infection Continuum (IWII-WIC)[61]	All wound types	■ Presents clinical signs/symptoms as indicators of different wound infection stages[12] ■ Conceptual model and teaching tool[19]	■ Includes clinical signs and symptoms validated in other assessment tools
NERDS and STONES[92]	Chronic wounds	■ Mnemonics for signs and symptoms of superficial (NERDS) and deep (STONES) infection ■ Diagnose superficial infection in the presence of at least 3 of 5 clinical signs/symptoms of superficial infection (NERDS)[92] ■ Diagnose deep infection in the presence of at least 3 of 5 clinical signs/symptoms of superficial infection (NERDS) plus presence of signs/symptoms of deep infection (STONES)[92]	■ Sensitivity and specificity of individual signs and symptoms of superficial infection (NERDS) reported (range sensitivity 0.32 to 0.70; specificity 0.47 to 0.86)[93] ■ Sensitivity and specificity of individual signs and symptoms of deep infection (STONES) reported (range sensitivity 0.37 to 0.87; specificity 0.44 to 0.89)[93] ■ Sensitivity and specificity of 2-4 signs/symptoms from NERDS or STONES reported[93]
Therapeutic Index for Local Infections (TILI) score[94]	Acute and hard-to-heal wounds	■ Six indirect criteria for local wound infection, presence of all criteria indicates antimicrobial treatment should be commenced ■ Three direct indications; presence of 1 or more criterion indicates antimicrobial treatment should be commenced ■ Available in multiple languages	■ Psychometric testing is planned[94]
Wound Infection Risk Assessment and Evaluation tool (WIRE)[74]	Community-based wounds	■ Assesses risk of infection ■ Detects early wound infection ■ Identifies systemic infection based on clinical presentation	■ Psychometric testing is planned[74]

Suspect wound infection in the presence of multiple indicative signs and symptoms rather than the presence of any single sign or symptom.

infection,[78] these assessment tools generally present checklists for signs and symptoms, most of which are included in the IWII-WIC. Some of these tools and checklists also include scoring or a ranking system.

Infection in acute wounds (e.g. surgical or trauma-related wounds and burns) in healthy individuals should be recognisable to most clinicians.[79] However, recognition and interpretation of infection in individuals with chronic wounds can be a challenge that requires specific education and experience,[79] because it relies on the identification of covert (subtle) signs of local wound infection that may be masked in immunocompromised individuals (e.g. older adults or people with diabetes)[61, 77, 78] or in the presence of poor vascular perfusion. Wound clinicians require skills to promptly differentiate between local and systemic infection to:

- Establish appropriate management goals
- Select and rapidly implement the most suitable treatments to reduce inflammation and microbial burden[95]
- Prevent the serious complications of systemic infection[74]
- Make appropriate referrals.

USING THE IWII WOUND INFECTION CONTINUUM AND MANAGEMENT GUIDE

The IWII-WIC and Management Guide (see back of document) identifies holistic assessment and management of the individual, their wound and the physical environment. The management guide includes:

- Identification of wound infection based on signs and symptoms of the individual and the wound (remaining cognisant that immunocompromised people may not display the classic and overt signs of infection)
- Recognition of clinical indicators of potential biofilm
- Appropriate selection of a cleansing solution
- Debridement of the wound and post debridement care
- Choice of wound dressing
- Biofilm-based wound care (step-down/step-up approach[70]).

The IWII-WIC and Management Guide can be utilised at the bedside, with consideration to antimicrobial stewardship. When available, diagnosis of infection and/or selection of the most appropriate antimicrobial agent can be augmented through the use of microbiology diagnostic tools, and/or in combination with point-of-care diagnostics.[77]

CONSIDERATIONS IN ASSESSING WOUND INFECTION IN SPECIFIC WOUND TYPES

Wound aetiology should be considered when evaluating both the risk for wound infection and the way infection may present. Both the aetiology of a wound and the risk factors for a specific type of wound can be closely associated with the risk of that wound becoming infected. Additionally, and as discussed above, wound infection may present in more subtle ways in older or immunocompromised people, which may hinder the rapid identification and treatment of wound infection. These cumulative factors can lead to treatment delay and progressive infection.

Table 4: Wound infection assessment in specific wound types	
Type of wound	**Specific considerations**
Surgical site infection	■ Daily visual wound assessment (where possible depending on the type of wound dressing applied following surgery) and vital sign assessment[96] ■ Early indicators of wound infection: -Increased wound-edge distance (lack of approximation) -Increased wound exudate[96] -Increased heart rate[96] -Increased morning tympanic temperature[96] -Increasing pain ■ Wound edge colour (e.g. redness) and induration are not reliable indicators of wound infection and may present differently depending on the individual's skin tone[96]
Pressure ulcer/injury	■ Associated with spreading infection (e.g. cellulitis) and increased markers for infection[97, 98] ■ Full thickness pressure ulcers/injuries (i.e. Category/Stage 3 or 4 pressure ulcers/injuries) are more likely to exhibit any signs of infection, but particularly erythema and purulent exudate[97, 98] ■ Observe for indirect indicators of systemic infection (e.g. anorexia, delirium and/or confusion)[97, 98]
Diabetic foot ulcer	■ Sepsis is uncommonly reported[45] ■ Probing to the bone with a sterile metal probe or instrument to diagnose diabetic foot osteomyelitis is inexpensive, accessible and relatively safe[45] ■ Probing to the bone combined with plain X-rays and biomarkers of infection (e.g. ESR, CRP and/or PCT) can be used to diagnose osteomyelitis in the diabetic foot[45] ■ An increase in temperature in one area of the diabetic foot identified using infrared or digital thermometry (if accessible) combined with photographic assessment may be of value in the initial assessment of infection when performed via telemedicine[45]
Chronic leg ulcers	■ Wound observations that are independent predictors of infection:[99] -Ulcer area of 10cm^2 or larger[99] -Presence of wound bed slough[99] -Heavy wound exudate (however, consider exudate level in the context of whether leg volume reduction through compression has been achieved)[99] ■ Depression, chronic pulmonary disease and anticoagulant use are predictors of wound infection[99]
Skin tears	■ Distinguish trauma-related inflammation from infection[100] ■ Early indicators of infection include: -Increased wound-edge distance (lack of approximation) -Increased wound exudate -Increasing pain -Skin flap failure ■ Mechanism of injury should be considered (tetanus vaccination/booster may be required)[100]

The influence of diabetes on both the risk of experiencing a wound and the risk of that wound becoming infected is significant, and should not be underestimated when conducting an holistic assessment. Diabetic foot ulcers are known to harbour deep infection that may not be readily identified without invasive procedures (e.g. deep probing or surgery).[45] Table 4 includes considerations when assessing different types of wounds for infection.

05 Diagnosis of Wound Infection

Diagnosis of wound infection is a clinical decision based on the presence of signs and symptoms of infection,[46] including the classic cardinal signs of heat, pain, swelling, suppuration, erythema and fever. Microbiological results are used to provide information on the presence or absence of microorganisms and to identify the organisms and their sensitivities. Antimicrobial treatment can be selected based on susceptibilities of the specific pathogen(s). Elevated inflammatory markers and positive blood cultures also quantify the presence of infection.[101] Because all wounds are contaminated with microorganisms (i.e. not all microorganism contamination is associated with adverse effects), a wound should only be cultured to guide the selection of treatment after making a clinical diagnosis of wound infection based on signs and symptoms, or when there remains a high clinical suspicion of wound infection.

A comprehensive wound assessment facilitates early detection and timely treatment of infection. Therefore, it is imperative that clinicians understand the risk factors associated with wound infection.

Only collect a wound sample in the presence of clinical signs and symptoms of wound infection.

INVESTIGATIONS TO DIAGNOSE WOUND INFECTION

Clinical diagnosis of wound infection can be confirmed with haematological, radiological and microbiological investigations (see Table 5). The purpose of undertaking diagnostic investigations is to:

- Identify systemic effects of infection
- Assess for the presence of osteomyelitis, or deeper collections
- Identify any potential complications
- Identify the causative organism(s)
- Select antibiotic therapy or ensure empirical antibiotic therapy is appropriate to the resistant microorganism(s)[22, 45]
- Guide management approaches.

Microbiological analysis of a specimen from the wound (known as a wound culture) is performed to identify causative microorganisms and to guide antimicrobial therapy selection after a clinical diagnosis of wound infection has been made.[45, 103-105] Because all wounds are contaminated or colonised with microorganisms, a wound should only be cultured in specific clinical situations. Indications for requesting a wound culture are provided in Box 1.

TYPES OF WOUND SPECIMEN

The following methods can be used to collect a sample from the wound for microbiological analysis:

- Tissue biopsy or curettage
- Wound fluid aspirate (i.e. pus collection)
- Debrided viable tissue from the ulcer base via sharp debridement
- Wound swab.

Table 5: Potential diagnostic investigations	
Diagnostic investigations	**Purpose**
Haematological markers	
White blood cell (WBC) counts (e.g. granulocytes, lymphocytes, monocytes)	■ Detect presence of infection in the body; WBCs indicate an immune response
C-reactive protein (CRP)	■ Detect inflammation related to infection
Erythrocyte sedimentation rate (ESR)	■ Detect inflammation related to infection
Blood cultures	■ Performed to detect an infection in the blood and identify the causative organism(s). A positive blood culture indicates bacteraemia
Microbiology[22, 45]	
Wound culture	■ Identify causative organism(s) of infection ■ Construct antibiogram based on sensitivity testing
Radiological investigations[45]	
Plain x-rays	■ Identify presence of osteomyelitis or abscess
White cell/bone scan	
Magnetic resonance imaging (MRI)	
Computerised tomography (CT)	
Fluorodeoxyglucose positron emission tomography (PET)	
Leukocyte scintigraphy (with or without CT)	
Ultrasound[26, 102]	
Ultrasound	■ Identify extent of abscess, fluid collection or haematoma

Box 1: Indications for initiating microbiological analysis of a wound specimen[9, 106]

- Acute or chronic wounds with signs of spreading or systemic* infection‡
- Infected wounds that have failed to respond to antimicrobial intervention, or are deteriorating despite appropriate antimicrobial treatment
- In compliance with local protocols for the surveillance of drug-resistant microbial species
- Wounds where the presence of certain species would negate a surgical procedure (e.g. beta haemolytic streptococci in wounds prior to skin grafting)

* *In individuals showing signs of sepsis, blood cultures are also indicated, and other likely sites of infection should be considered as potential sources of infection. Other samples should be collected for microbiological analysis as relevant (e.g. specimens of urine, sputum or swab of the tip of a central venous line catheter)*

‡ *In immunocompromised patients (e.g. those taking immunosuppressants or corticosteroids, or with diabetes mellitus or peripheral arterial disease), also consider sampling chronic wounds with signs of local wound infection and/or delayed healing*

Where pus is present, it can be aspirated using a sterile syringe and needle and transferred to an appropriate specimen collection jar.[107]

Tissue biopsy is the preferred sampling method. It provides both quantitative and qualitative information. A tissue biopsy enables both the identification of the organism(s) present in the wound and the virulence.[21] However, tissue biopsy is costly, can potentially cause further tissue damage and requires a skilled operator; therefore, it is not routinely performed in most clinical settings.

In most clinical settings, wound swabbing is the most frequently used method for collecting a wound sample. This method of sample collection is simple, non-invasive and relatively inexpensive.[105, 108] Although definitive studies on the optimum method of wound sample collection are lacking, several studies suggest that the Levine technique is a more effective swabbing technique than the Z-swab technique.[105, 109, 110] This method is recommended for use, as outlined in Figure 2. After cleansing the wound using an inert (chemically inactive) wound cleanser, two

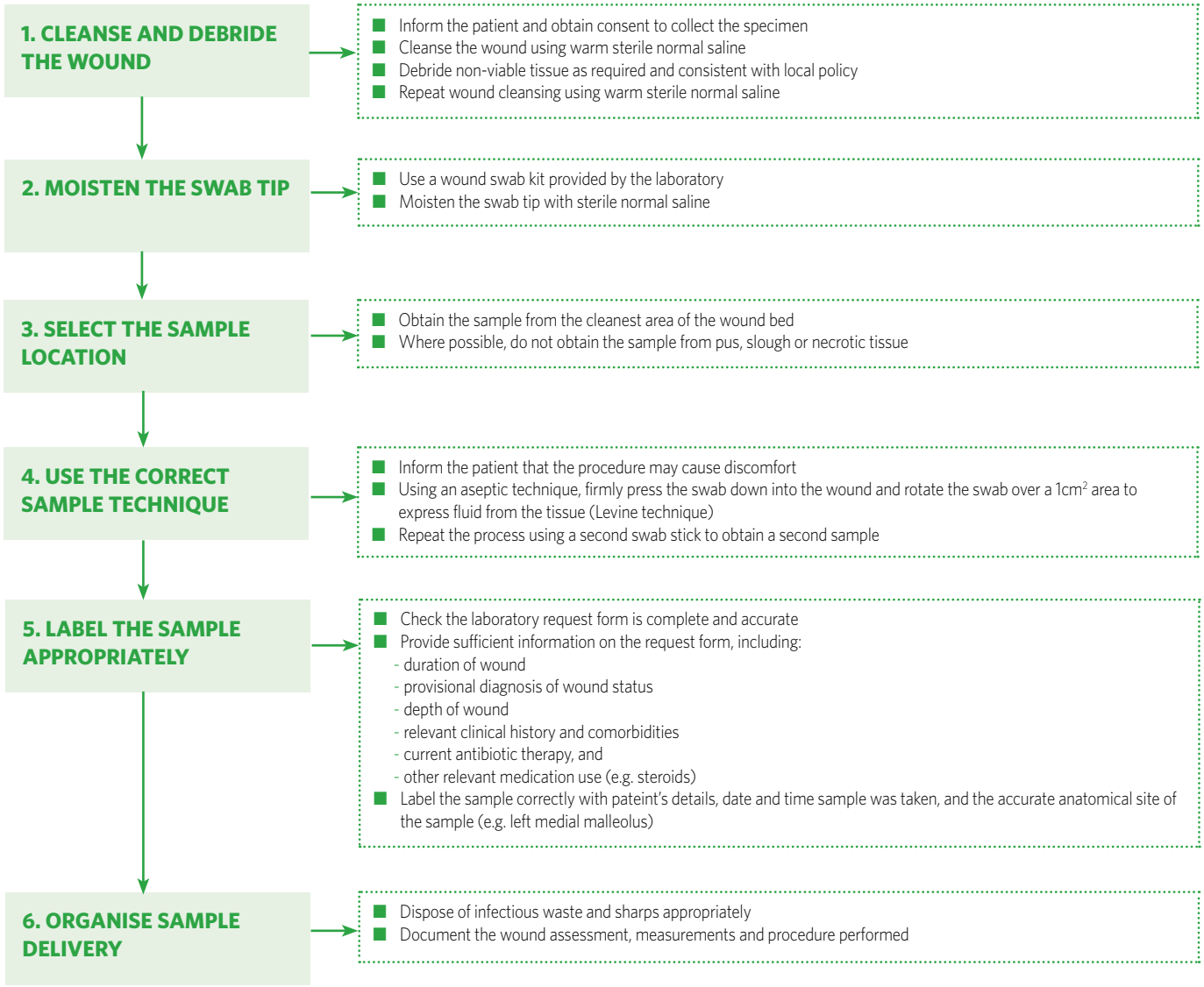
PRACTICE POINT

Use an inert wound cleanser and debride the wound (if required) prior to collecting a wound specimen to avoid false positive results.

PRACTICE POINT

Tissue biopsy is the preferred wound specimen for obtaining accurate cultures. When this is not an option, use the Levine technique to collect a wound swab. This will express microbes from below the wound tissue.

Figure 2 | Taking a wound swab for culture



wound swabs should be collected. In the laboratory, the first sample is used for a Gram stain to determine if the bacteria are Gram-positive (e.g. *Staphylococcus aureus* and *Streptococcus epidermidis*) or Gram-negative (e.g. *Escherichia coli* and *Pseudomonas aeruginosa*). These results are usually available from the laboratory within hours. A second wound swab should be placed in transport medium and is used to identify the species of bacteria.

Despite being the most widely used wound specimen collection method, microbiological analysis of a wound swab can only identify microorganisms on the surface of a wound and not the organism(s) beneath the surface of the wound.[111] Additionally, not all microorganisms collected on a wound swab will survive during transportation to the laboratory, influencing the accuracy of wound swab results.

Different types of microscopy, not all of which are readily available in all clinical settings, are outlined in Table 6. Direct microscopy examination (Gram stain) can be performed quickly by the laboratory to assess the number and type of microorganisms present in the wound sample. This allows the clinician to commence antibiotics without delay while waiting for the culture results (identification of the specific species), which can take 24 to 48 hours.[107]

Table 6: Types of microbiological examination[107, 112-114]

Type of microscopy	Mechanism	Resolution limit (maximum magnification)	Type of causative microorganism		Considerations for use
			Planktonic	Biofilm	
Light microscopy	Visible light	0.2 µm (1500x)	✓	✓	■ Primarily used on isolated cultures or sections of tissue ■ Gram stain used to establish presumptive species identification ■ Impossible to obtain definitive identification of microbial species ■ Low-cost and readily available
Fluorescence microscopy (FISH)	Ultraviolet light	0.1 µm (2000x)	✓	✓	■ Species can be identified and their relative locations mapped with fluorescent dyes/labels ■ Only fluorescent structures can be observed ■ Use is limited to microbial cell suspensions and thin tissue sections ■ Cost of dyes and probes is a limitation
Confocal laser scanning microscopy (CLSM)	Laser beam coupled to a light microscope	0.1 µm (2000x)	✓	✓	■ Species can be identified and their relative locations mapped with fluorescent dyes/labels ■ Tissue blocks can be examined and images obtained at regular depths can be reconstructed to generate 2D or 3D structure of whole specimen ■ Only fluorescent structures are observed ■ Fluorescence decays relatively quickly ■ Cost of equipment, dyes, probes, and technical support is a limitation
Scanning electron microscopy (SEM)	Electrons beamed onto specimen from an angle and deflected electrons collected	10 µm (500,000x)	✓	✓	■ Cannot examine living material ■ Minimal time required for sample preparation ■ Images of the surface layers of specimens provide insight into 3D structure ■ Dehydration of samples may cause changes ■ Cost of equipment and technical support is a limitation
Transmission electron microscopy (TEM)	Electrons beamed through a thin section of specimen	0.2 µm (5,000,000x)	✓	✓	■ Images provide detailed information on internal cellular structures or organisms ■ Cannot examine living material ■ Specimen preparation is lengthy, and may introduce artefacts ■ Cost of equipment and technical support is a limitation
Polymerase chain reaction (PCR)	Amplifies specific regions of DNA	0.1 and 10 kilobase pairs	✓		■ Can confirm genes of interest from bacteria, toxins, viruses and other microorganisms ■ Rapid and highly specific ■ Identifies non-cultivatable or slow growing micro-organisms such as mycobacteria, anaerobes, or viruses

Clinicians should be wary of interpreting a microbiology report in isolation. If sensitivities are provided in the laboratory report, less experienced clinicians may feel the need to commence antibiotics without considering the clinical indications. Consider the report in the context of the individual, their wound and your clinical judgement. If appropriate, consult a microbiologist or an infectious disease expert.

ADVANCED DIAGNOSTIC TECHNIQUES

Standard clinical microbiology laboratory results may only provide information about a small subset of the total bacterial species that are present, particularly in chronic wounds.[22] If infection with fungi, mycobacteria or anaerobic bacteria is suspected, for example following environmental contamination of a wound, this should be specifically requested or discussed with a microbiologist as these organisms require additional investigations and processing.

Since many microorganisms are difficult to culture by standard techniques, strategies to characterise genetic markers of microbial species using molecular techniques have been developed in specialist facilities.[115-117] In addition, DNA sequencing techniques are rapidly advancing. DNA sequencing techniques can more precisely identify microbial species in a wound specimen, including microbes not identified by culture-based techniques. DNA is extracted from the wound and amplified using polymerase chain reaction (PCR), a technique that creates multiple copies of the organism's DNA sequence.[118] These DNA samples are analysed and compared with a database of existing DNA sequences to identify all the microbial species involved in wound infection,[118] informing the selection of strategies to manage biofilm.[119] In the future, DNA sequencing will likely continue to have a greater role in diagnostics.[120-122]

Additional emerging and evolving diagnostic techniques are discussed in *12 Future Directions in Wound Infection Science and Practice*.

06 Wound Biofilms

Early research has provided evidence regarding biofilms in general and the concept of disease progression.[123, 124]The seminal work of three studies published in 2008 confirmed that biofilms develop in wounds.[1, 2, 125] Since then, a rapidly expanding body of scientific literature has attempted to describe the impact of biofilm on wound progression and healing. In a 2008 prospective study, use of scanning electron microscopy established that 60% of chronic wounds contained biofilm, compared to 6% of acute wounds.[2] More recently, a prevalence study confirmed almost 80% of chronic wounds contained biofilms, leading the authors to conclude that biofilms are ubiquitous in a chronic wound.[126] Despite the widespread clinical problem of wound biofilms, current understanding of their development and actions within a wound remains limited.[127]

The exact role that microorganisms in general, and biofilms specifically, play in impairing the wound healing process is still not fully understood. There has been an evolving understanding and acceptance of the association between biofilms, delayed wound healing and the risk of wound infection. It is evident that microorganisms are not easily eradicated from a wound, particularly in established wound infection.[5] This could be due to the observed increased tolerance that biofilms develop towards antibiotics, antiseptics and the host's defences. This understanding has led to the concept of the chronic, hard-to-heal wound that seeks to explain the potential presence of wound biofilm and strategies for its management.[44, 128]

BENCH RESEARCH ON BIOFILMS AND ITS APPLICATION TO THE CLINICAL WOUND ENVIRONMENT

Because so little is known about the role of biofilms in wounds and wound healing, theoretical constructs of wound biofilm to date have primarily focused on extrapolating that which is known from *in vitro* studies of biofilms to the chronic wound clinical environment.

It is relatively easy to grow microorganisms and biofilms in the laboratory using advanced models that replicate a clinical wound.[129] However, it is also extremely important to acknowledge the differences between a laboratory microenvironment in which an *in vitro* biofilm is grown and studied, and the environment of an acute or chronic wound (*in vivo*) that experiences biofilm. The differences in microenvironments are evident when studying both gene expression and antibiotic susceptibility, even when biofilms used in bench science models are cultured from a human wound.[5-8] Research has established that, in the *in vivo* setting, an infectious microenvironment develops, with low oxygen (hypoxic conditions),[2] pH changes and slow-growing microbial cells.[130] These physiochemical properties of the wound microenvironment are different from *in vitro* model systems and are important to understanding the potential inaccuracies that arise in extrapolating *in vitro* research directly to the clinical environment.

Ongoing evolution of the wound infection continuum highlights the importance of interactions between basic research and clinical observation with respect to understanding wound infection and managing wounds and their microorganisms and/or biofilms.

WHAT IS KNOWN (AND UNKNOWN) ABOUT WOUND BIOFILMS?

As described in the literature, *in vitro* biofilms are initiated by planktonic microorganisms and follow a defined developmental cycle. The *in vitro* hallmark of biofilms is the presence of a self-produced matrix of extracellular material composed of polysaccharides, proteins, extracellular DNA and supporting cross-linking metal ions such as calcium, magnesium and iron.

However, this knowledge may not directly translate to biofilm behaviour within a wound. How biofilms develop in chronic and acute wounds is still unknown, although observations have

confirmed the presence of both aggregates and single cell microorganisms within a wound.[1] Often there will be multiple different microorganism species present.[16] Understanding of the interplay between co-existing microbial species in chronic wounds and potential mechanisms that explain the increased tolerance of biofilm to the host and traditional antimicrobial treatment continues to be explored.[15]

Wound biofilms can be embedded in slough, debris, necrotic and other tissues, and the wound dressing itself. In contrast to the self-produced extracellular matrix observed *in vitro*, it remains unknown which *in vivo* matrix components the microorganisms self-produce, if any at all, and which are derived from the host.[24] Apart from being present both in aggregates and as single cells, microorganisms are present on both the wound surface and embedded beneath the surface of the wound bed within the extracellular matrix.[24] This has implications for how a wound is sampled for microorganisms, particular anaerobic bacteria, because a wound swab will only collect surface microbes and a biopsy (which is not always possible) will only represent a small area of the wound. These issues are discussed in *05 Diagnosis of Wound Infection*.

It is also unknown whether coaggregation as biofilm occurs before or after microorganisms enter the wound environment.[129] Some studies have identified bacterial aggregates on both healthy skin and acute epidermal wounds,[131-133] suggesting that in at least some clinical situations, biofilm may be established prior to its introduction to a wound. More research is required to confirm and fully understand this mechanism.

Additionally, it is important to acknowledge that neither planktonic microorganisms nor biofilm cause a wound to initially occur. Underlying environmental factors and/or disease factors that contribute to chronic wound development influence the ways in which microorganisms in any form act within the host and the wound. Their eradication is not the sole consideration to achieving wound healing. However, it is fair to assume that the presence of microorganisms and a biofilm do contribute to stalled healing and their removal could subsequently lead to improved wound healing, as applied in the concept of a hard-to-heal wound.[44, 128]

IDENTIFYING BIOFILMS IN A WOUND

Although earlier theories[4, 134, 135] proposed that macroscopic visual appearance of the wound (e.g. observation of a fibrin, necrosis and/or a slimy surface substance) could identify the presence of biofilm, current science has demonstrated that biofilms cannot be observed by the naked eye in biological systems such as a chronic wound without the assistance of diagnostic techniques,[136] some of which are discussed in *12 Future Directions in Wound Infection Science and Practice*. As noted above, biofilms can form deep in wound tissue where it is impossible to identify their presence visually.[3, 136, 137]

Research on wound samples shows that, while biofilm may be the underlying cause of the appearance of some wounds,[1, 126] visible changes that may be observed in the wound are not conclusive indicators of biofilm presence. Further, many wounds that appear to be healthy to the naked eye are shown via laboratory investigation to contain biofilm.[138] Currently there is no gold standard for wound sampling to identify biofilm or the presence of microorganisms, and in many cases it may not be necessary to identify whether a wound contains biofilms or not. However, the species of microorganisms present in the wound might be of clinical interest and inform treatment strategies.

Suspect the presence of biofilm in wounds that exhibit signs and symptoms of chronic inflammation and fail to heal at the expected rate with optimal care.

Box 2: Criteria indicative of potential biofilm in a wound[12, 19]

- Failure of appropriate antibiotic treatment
- Recalcitrance to appropriate antimicrobial treatment
- Recurrence of delayed healing on cessation of antibiotic treatment
- Delayed healing despite optimal wound management and health support
- Increased exudate/moisture
- Low-level chronic inflammation
- Low-level erythema
- Poor granulation/friable hypergranulation
- Secondary signs of infection

If a wound is hard-to-heal and is not responding to standard protocols of care (e.g. antimicrobial intervention), it should be assumed that tolerant microorganisms, within a biofilm, are present. In the absence of laboratory-confirmed diagnosis, best practice suggests that presence of biofilm be presumed in wounds displaying signs and symptoms of chronic inflammation. Criteria that are indicative of possible wound biofilm that have been established through expert consensus[12, 19] are listed in Box 2.

WHAT DOES THIS MEAN FOR TREATING WOUNDS?

Biofilms have increased tolerance to antimicrobial treatments. There is a growing body of evidence and agreement amongst wound clinicians and scientists that debridement represents a necessary process in reducing the presence of a biofilm within a wound. The evidence that biofilms can reside deep within the extracellular matrix of slough, debris, necrotic and other tissues provides a rationale for the practice of removing non-viable tissue via rapid debridement methods to reduce biofilms.[72, 136, 139-141] The principles of biofilm-based care, and strategies to increase its effectiveness in controlling biofilms is discussed in *08 Wound Bed Preparation: Cleansing and Debridement*.

07 Holistic Assessment and Management

Wound infections prolong the inflammatory response and stall or reverse the healing process,[11, 58, 59, 79] impacting individuals, care providers, healthcare systems and society. Immune defenses of the person with a wound are the primary factor influencing whether wound contamination progresses to clinical wound infection. People with infected wounds can experience limitations to their physical, social, and psychological functioning that can impact their quality of life.[142, 143] Therefore, promoting the person's health, immunity and wellbeing is an imperative in preventing or treating wound infection. A person-centred assessment of the individual, their wound and the wound care environment is critical to achieving positive outcomes.

The goal of holistic care in a person with wound infection is to readjust the interaction between the individual and the infecting pathogen in favour of the individual by:

- Identifying factors that may contribute to development of, or prolong, infection
- Establishing feasible goals of care and treatment options that are acceptable to the person and their family caregiver
- Developing a comprehensive wound infection prevention and management plan that is consistent with the person's preferences and goals of care.

HOLISTIC ASSESSMENT OF THE PERSON WITH OR AT RISK OF WOUND INFECTION

In addition to undertaking comprehensive clinical assessment of the wound (see *04 Identifying and Assessing Infection in a Wound*), factors that contribute to the person's experience of wound infection should be comprehensively assessed. These factors are often the same factors that contributed to the development of the initial wound and include:

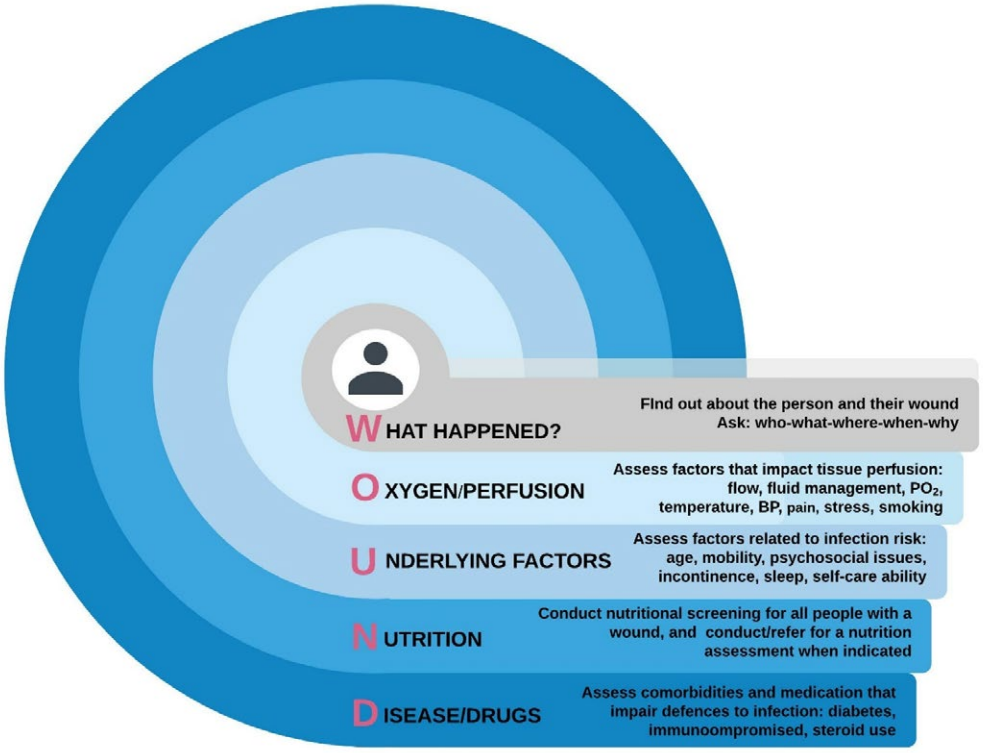
- The history of the person and their wound
- Comorbidities and their management
- Nutritional status
- Factors that influence the inflammatory and immune response
- Factors that influence local tissue healing
- Psychosocial factors and wellbeing.

Understanding the impact of each of these domains facilitates identification of factors of significance to the individual person and their wound.[144] Figure 3 provides a mnemonic and framework for holistic assessment of a person with or at risk of a wound infection.

Formal tools (e.g. nutrition screening and assessment tools) and pathways can assist the clinician in attaining a comprehensive, holistic assessment. Some options are outlined in Table 7.

Ask questions and listen to the person to learn about how the wound and its signs and symptoms are impacting their quality of life and wellbeing.

Figure 3 | Whole person wound infection assessment[145] Adapted from: Waters, N (2011) Using the WOUND mnemonic for whole patient assessment. *World Council of Enterostomal Therapists Journal* 31(1): 41-3



ENHANCING PATIENT ENGAGEMENT

A fundamental principle to holistic assessment and management is engagement of the person and their family caregiver in the process in order to understand their priorities, care goals and ability to be involved in managing the wound.[146, 147] Multidisciplinary teams are optimal, and a key player in the team is the patient themselves.[144]

Empowering patients using clear communication and providing education tailored to the person can offset anxiety about wound infection, enhance self-care skills and improve clinical outcomes.[148] For example, in one innovative nurse-led 'photos at discharge' initiative, providing people with wounds and their care providers with enhanced wound care information in photo format successfully addressed the risk of surgical site infections.[149]

PRACTICE POINT

Collaborate with the person and their family caregiver in care decisions to reduce the physical and psychosocial impact of wound infection.

Table 7: Person-centred wound assessment and management models		
Care model	**Model aims**	**Key model features**
Wounds UK Best Practice Statement on improving holistic assessment[148]	To encourage wide-ranging assessment that considers the impact of all aspects of the person's health and wellbeing on the healing process	Each best practice statement is emphasised by an accompanying 'Patient Expectation' that indicates what people with wounds can expect in their care
The Infection Management Pathway[78] incorporating the T.I.M.E. Clinical Decision Support Tool[150]	■ To promote comprehensive assessment and care continuity ■ To facilitate clinical decision making and best practice among non-wound care specialists ■ To support antimicrobial stewardship	Uses the mnemonic A-B-C-D-E: ■ **A**ssess the person, and their wound ■ **B**ring in a multi-disciplinary team ■ **C**ontrol underlying barriers to healing ■ **D**ecide appropriate treatment ■ **E**valuate outcomes and reassess goals
The Adult Burns Patient Concerns Inventory[151]	To improve wound clinician-patient-family communication and empower people to identify their concerns, facilitating delivery of a targeted patient-centred clinical encounter	■ A 58-item, holistic assessment tool for outpatient use ■ Domains include physical and functional wellbeing; psychological, emotional and spiritual wellbeing; social care and social wellbeing; and treatment-related concerns
Wound Healing Strategies to Improve Palliation[152]	To provide a palliative approach to assessment and care re-evaluation that meets the needs of a person with a chronic wound	When complete healing is not feasible, use the mnemonic S-P-E-C-I-A-L: ■ **S**tabilising the wound ■ **P**reventing new wounds ■ **E**liminate odour ■ **C**ontrol pain ■ **I**nfection prophylaxis ■ **A**dvanced, absorbent wound dressings ■ **L**essen dressing change
Universal Model for the Team Approach to Wound Care[153]	To promote patient advocacy that facilitates delivery of a management and care plan that encompasses the person's perceived needs, goals of care and appropriate healthcare services	■ Includes essential elements for an interdisciplinary wound care service ■ The person with a wound forms the focus but relies on the expertise of a wound navigator to organise wound care via established referral mechanisms ■ The wound navigator and multidisciplinary team explore beneficial healthcare system options to meet the needs of the person with a wound
TIMERS: expanding wound care beyond the focus of the wound[154]	Outlines a 10-step pathway for managing a wound, including treatment of palliative wounds in a maintenance fashion	■ Tissue (nonviable or deficient) ■ Infection/inflammation ■ Moisture imbalance ■ Edge of wound (non-advancing or undermined) ■ Regeneration/repair of tissue ■ Social factors affecting wound healing trajectory
Wound Bed Preparation 2021[155]	To facilitate a person-centered wound assessment that establishes goals of wound care as healing, maintenance, or palliation	■ Treatment of the cause ■ Patient-centered concerns ■ Assess ability to heal regularly ■ Local wound care, including debridement as appropriate and with pain control ■ Assess and treat wound infection ■ Moisture management ■ Evaluate the rate of healing ■ Edge effect ■ Organisational support

Numerous models are available to guide a whole-person assessment and development of a management plan for wounds at any stage in the IWII-WIC. The models summarised in Table 7 provide frameworks for person-centred wound infection practice.

HOLISTIC PREVENTION AND MANAGEMENT OF WOUND INFECTION

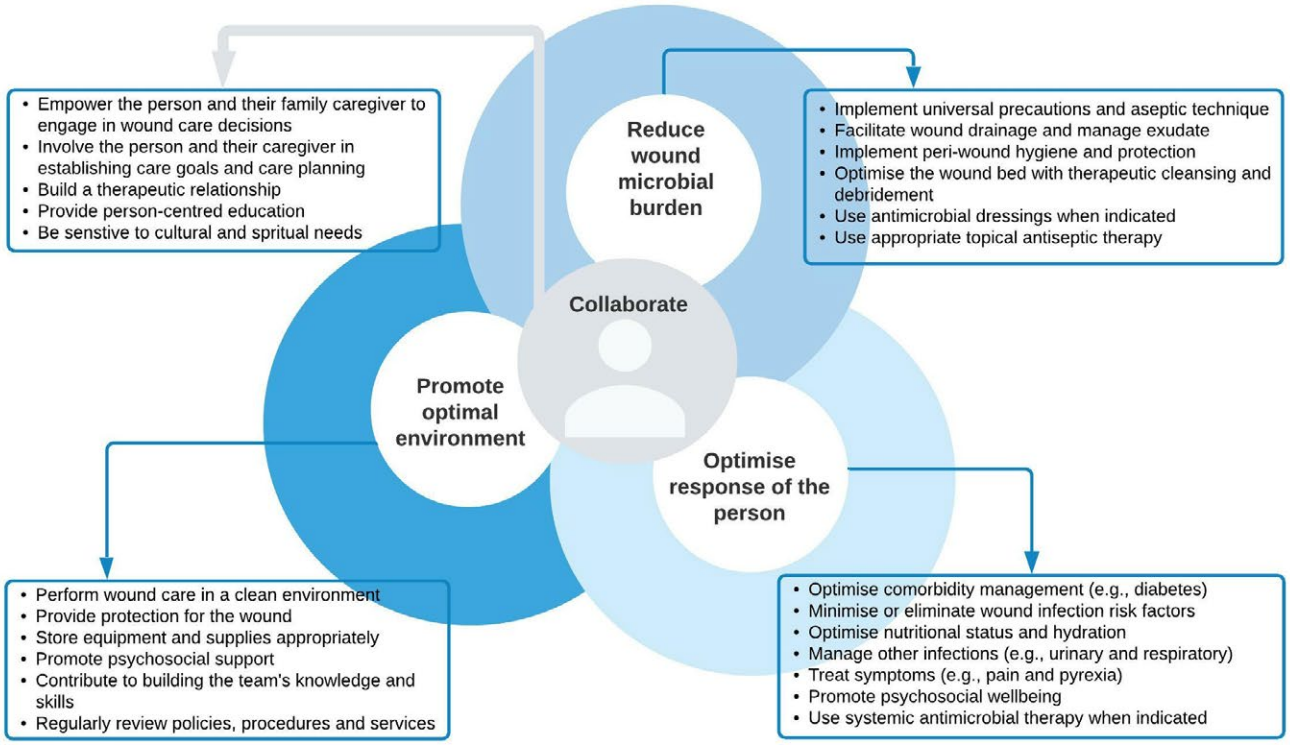
Early recognition and address of factors that could contribute to a person developing a wound infection and implementation of a care plan that extends beyond wound-level interventions is fundamental to wound infection prevention and management. Effective management with consideration to the person's psychosocial and financial status, comorbidities, and capacity to heal requires an interdisciplinary team approach.[144, 153, 155, 156]

A comprehensive wound infection prevention and management plan should arise from assessment outcomes and seek to achieve the person's goals of care. Holistic management addresses:

- Optimising the individual host response[9]
- Reducing local microbial burden[9]
- Promoting a positive environment for wound healing.[9, 156]

A collaborative and multidisciplinary approach is required to address these factors, including working with health professionals involved in other aspects of the person's clinical care (e.g. management of comorbidities). Strategies to address these domains are summarised in Figure 4.

Figure 4 | Holistic wound infection prevention and management



08 Wound Bed Preparation: Cleansing and Debridement

Wound bed preparation is defined as 'the management of the wound to accelerate endogenous healing or to facilitate the effectiveness of other therapeutic measures'.[31] The principles of wound bed preparation that will be discussed in this section are the entrenched concepts of TIME (Tissue; Infection/Inflammation; Moisture; Edge)[72, 157] and biofilm-based wound care (BBWC)[158] that guide best practice in wound assessment and management. Application of these principles promotes maintenance of a healthy wound bed and involves therapeutic wound cleansing and debridement, which aims to disrupt biofilm, prevent its reformation, and facilitate removal of necrotic, non-viable or infected tissue.

THERAPEUTIC WOUND CLEANSING

Wound cleansing is a fundamental component of wound bed preparation.[159, 160] Wound cleansing is defined as actively removing surface contaminants, loose debris, non-attached non-viable tissue, microorganisms and/or remnants of previous dressings from the wound surface and its surrounding skin.[20] Therapeutic cleansing is rigorous cleansing of chronic or hard-to-heal wounds and is performed:

- To remove excessive wound exudate or debris from the wound bed in order to optimise visualisation and reliable assessment
- Prior to collection of a wound sample (swab or biopsy)
- To assist in hydrating a desiccated wound bed.[155, 161]

Wound hygiene technique was referred to in the 2016 edition of this document and has been expanded by an expert panel as a term to remind clinicians that wound hygiene practices should be 'repetitive, regular, frequent and necessary'.[162] Wound hygiene involves cleansing, debridement of the wound bed and edge, and prevention of biofilm reformation.[162]

There is no consensus on wound cleansing techniques (e.g. passive soaking, swabbing, irrigation or showering/washing), inconsistencies in procedural aseptic techniques (i.e. sterile/surgical versus clean/standard), and antiseptic solutions abound in clinical practice.[163-166] Some experts consider that there is no rationale for routine cleansing of surgical wounds healing by primary intention,[167] and wounds healing in an orderly and timely manner require only minimal, gentle cleansing in order to avoid disrupting granulation and reepithelialisation. Conversely, chronic or hard-to-heal wounds with devitalised tissue or suspected biofilm require vigorous therapeutic cleansing to dislodge loose devitalised tissue, microorganisms or detritus from the wound bed.[97] Vigorous wound cleansing is a form of mechanical debridement.

Passive soaking or swabbing of the wound bed with wet gauze may not adequately cleanse the wound. Mechanical irrigation applied at a force of 4–15 pounds per square inch (PSI) is recommended.[161, 163, 168] Table 8 outlines the syringe size and needle gauges associated with different PSI pressures. Therapeutic cleansing with surfactant or antimicrobial cleansers may be of added benefit in removing tenacious devitalised tissue or suspected biofilm in chronic wounds.[162, 165, 168] Therapeutic wound cleansing exhibits the following characteristics:

- A sterile or non-sterile irrigation solution is selected based on an assessment of the wound, the individual and the healing environment[97]
- Pain is prevented and treated prior to undertaking wound cleansing[159, 169]
- An adequate volume of solution is used (50 to 100ml per centimetre of wound length)[169]

- Irrigation is performed at an appropriate pound per square inch pressure (PSI) of between 4 and 15 PSI[159, 161, 165]
- Irrigation or wound swabbing is performed with a solution of appropriate temperature (room temperature or slightly warmer)[161, 166, 169]
- An aseptic technique and appropriate personal protective equipment (PPE) is used when the patient, their wound or healing environment is compromised or to prevent cross-contamination[161, 169]
- The periwound skin (either the full area covered by the wound dressing, or 10–20cm from the wound edge[162]) is cleansed to remove exudate, effluent, debris, scale and/or to control skin flora
- The technique utilised avoids maceration of the periwound skin.[155]

Table 8: Achieving various irrigation pressures[97, 161, 170]

Syringe size (mls)	Needle/angio gauge (G)	Pressure (PSI)
35	25	4
35	21	6
35	19	8
20	18	12
12	22	13
12	19	20
6	19	20

Perform therapeutic wound cleansing for all wounds exhibiting signs and symptoms of local wound infection and/or containing slough, debris or contaminated matter.

SELECTING AND USING WOUND CLEANSING SOLUTIONS

The ideal wound cleansing solution has not been established conclusively. Selection of a solution is based on:[171, 172]

- Assessment of the wound (e.g. aetiology, anatomical location and visible structures)
- The person's risk of wound infection
- Signs and symptoms indicative of local wound infection or spreading infection
- Colonisation with multi-drug-resistant organisms
- Efficacy and organism sensitivities of solution
- Goals of care
- Local policies and resources.

Wound cleansing solution options are outlined in Table 9. Inert substances are appropriate for cleansing most non-infected wounds.[159, 161] Sterile normal saline or sterile water are inert solutions that are used in clinical situations requiring a sterile solution. Evidence from systematic reviews[163, 173-176] and randomised controlled trials[177-179] has demonstrated that potable water[178] is a safe alternative to other wound cleansing solutions for both chronic and acute wounds. Potable water might be chosen in low-resource settings, community settings or for wounds with high levels of exudate or fistula effluent.[166]

There is a role for judicious wound irrigation with an antiseptic solution, for example:

- To prevent surgical site infection when there is a high risk of infection (e.g. traumatic and contaminated wounds)

- In the presence of clinical signs and symptoms of local or spreading wound infection
- In conjunction with surgical, sharp or conservative-sharp debridement as a component of biofilm-based wound care.[166, 171]

Surfactants (surface active agents) are cleansing agents that contain a substance that lowers the surface tension between the wound bed and the fluid or between two liquids. The lowered surface tension facilitates the spread of the fluid across the wound bed. Surfactants assist separation of loose, non-viable tissue[72, 168, 180] by breaking bonds between non-viable tissue/debris and the wound bed.[161] These products might be chosen for cleansing wounds that require greater mechanical action when cleansing: for example, wounds with suspected biofilm.[180] Some topical antiseptic agents are manufactured in combination with a surfactant to capitalise on these properties and increase penetration of the antimicrobial agents across the wound bed.[72]

The manufacturers' instructions for wound cleansing surfactants and antiseptic agents should be adhered to in regard to efficacy, recommended duration of each application and duration of consecutive treatments.[172]

Table 9: Wound cleansing solution options

Fluid type	Safety profile	Comments	Key model features
Potable tap water	Hypotonic	■ No cytotoxicity ■ Not sterile	■ Generally inert solution that varies in content[169] ■ Effect achieved through mechanical detachment of contaminants[181] ■ Safe alternative when sterile solutions are not available or feasible (e.g. low resource settings or community settings)[177] ■ In low resource settings with non-potable water, boiled and cooled water is an alternative[165] ■ When using potable tap water, run the tap to remove contaminates before using the water[166]
Sterile normal 0.9% saline	Isotonic	No cytotoxicity	■ Inert, isotonic solution with no antimicrobial properties[169] ■ Effect achieved through mechanical detachment of contaminants[181] ■ Once opened, product is no longer sterile[182]
Sterile water	Hypotonic	No cytotoxicity	■ Inert, hypotonic solution with no antimicrobial properties[169] ■ Effect achieved through mechanical detachment of contaminants[181] ■ Once opened, product is no longer sterile[182]
Surfactant wound cleansers (e.g. Poloxamer 407, undecylenamido-propyl betaine and macrogolum)	Surfactant	Low cytotoxicity to fibroblasts and keratinocytes *in vitro*[180]	■ Categorised based on type of chemical charge[168] ■ Commonly combined with antimicrobial /antimicrobially-preserved agents including octenidine dihydrochloride (OCT) or polyhexamethylene biguanide (PHMB) ■ Removes bacteria without damage to healing wound tissues[180]
Super-oxidised solutions (hypochlorous acid and sodium hypochlorite are present as antimicrobial preservatives)	Hypotonic	Varies (see Table 11)	■ Contain naturally occurring hypotonic, oxidising agents[183] ■ Antimicrobial and antibiofilm action varies (see Table 11)
Povidone iodine	■ Antiseptic ■ Iodophor	Dose dependent cytotoxic effect on osteoblasts, myoblasts and fibroblasts[184, 185]	■ Antiseptic solution ■ Broad spectrum antimicrobial[185-189] and antibiofilm[185-187] action (see Table 11)
Other agents containing antimicrobials and/or active preservatives	Varies	Varies (see Table 11)	■ Range of antimicrobial/antimicrobially-preserved agents solutions, less commonly used solely as a cleansing agent (see Table 11)

DEBRIDEMENT

Necrotic, non-viable tissue provides a focus for infection, exacerbates the inflammatory response and impedes wound healing.[13, 170] This includes the presence of foreign material (e.g. wound dressing remnants, sutures, biofilm or slough, exudate and debris) on the wound bed. Debridement provides a window of opportunity in which the biofilm defences are temporarily interrupted, allowing for increased efficacy of topical and systemic management strategies.[14] However, the impact of the different types of debridement on biofilm may be dependent upon its stage in the biofilm development cycle.

A comprehensive assessment of the individual and their wound determines the goal of care and precedes the decision to debride and selection of the debridement method to employ.[190] However, caution should be taken, or debridement avoided, in the following situations:

- The non-infected ischaemic foot ulcer covered with dry eschar in the presence of inadequate tissue oxygenation to support infection control and wound healing[97, 190]
- In individuals when palliative management is the goal of care and necrosis covers vulnerable vascular structures
- In wounds with underlying, uncontrolled inflammatory causes (e.g. pyoderma gangrenosum)[191]
- When there is an increased risk of bleeding (e.g. during anti-coagulation or anti-platelet therapy)
- The level of pain management required to accomplish appropriate debridement necessitates anaesthetic.

The various methods of debridement are outlined in Table 10. Clinical evidence currently does not support any one debridement method as more effective than another,[192-195] and the optimal frequency of debridement is yet to be established. As noted in Table 10, some debridement methods (e.g. surgical debridement) will remove microorganisms from the wound bed rapidly. Selection of a debridement method should be based on clinical context, goals of care, the clinician's expertise and local resources.[196] When performing wound debridement, clinicians should always work within their scope of practice, and local policy and procedures.

BIOFILM-BASED WOUND CARE

Biofilm is particularly tenacious in chronic or hard-to-heal wounds and may delay healing; therefore its removal is of clinical importance.[204] It usually requires a multi-faceted approach, including physical removal through targeted wound hygiene, to eradicate. Debridement strategies, together with therapeutic cleansing with topical surfactant and antiseptic solutions and use of antimicrobial wound dressings, are recommended.[70, 136, 162, 212] Holistic management of the factors that influence wound infection (see Figure 4) is also required.

The goals of therapeutic cleaning and debridement in biofilm-based wound care (BBWC) are to:[70, 136, 162]

- Physically remove the most tolerant microorganisms from the wound bed
- Create an environment that prevents or delays biofilm reformation.

Because biofilms are located both superficial and deep within the wound bed tissue,[70, 136] the most effective debridement methods are those that rapidly, aggressively and comprehensively remove non-viable tissue, microorganisms and debris from the wound. This includes surgical, sharp, conservative-sharp and mechanical methods (e.g. monofilament/monofibre/foam pads and ultrasonic debridement).[204, 212-214] Post-debridement, the wound edge should be refashioned, by removing necrotic or over-hanging edges in which bacteria could harbour and re-aligning edges to facilitate advancement of the epithelium.[162] Cleansing should be re-performed to remove remnants from debridement and topical antimicrobials should be applied in order to prevent (or at least delay) reformation of biofilm colonies. Some research indicates that shorter exposure duration (e.g. less than 15 minutes) of the wound bed to antimicrobial solutions may be inadequate;[214] however, optimal cleansing time has not been ascertained. Surfactant-containing antimicrobial cleansers or antimicrobial preservative-containing cleansers may be useful to facilitate the agent's dispersal throughout the wound.[215] Multiple sessions of therapy may be required to attain management of biofilm and to observe improvement in the wound condition.[70, 136] Ongoing evaluation of the

Table 10: Types of debridement			
Method	**Description**	**Advantages**	**Considerations**
Surgical	Performed in the operating room or specialised clinic by qualified and competent practitioners using sterile scalpel, scissors or a hydrosurgical device[97, 160, 170, 195]	■ Fast and efficient ■ Maximises asepsis[190] ■ Disrupts biofilm and removes foci of infection[197] ■ If adequate tissue is removed, deeper biofilm can be disrupted[170]	■ Non-selective ■ Requires a general or local anaesthetic ■ Will result in bleeding ■ Expensive
Sharp	Performed by qualified and competent practitioners (e.g. medical practitioner, podiatrist, advanced practice nurse) using sterile scalpel, scissors or curette[97, 160, 170]	■ Fast and efficient ■ Disrupts biofilm and removes foci of infection[197] ■ If all non-viable tissue is removed, deeper biofilm can be disrupted[170]	■ May require a local anaesthetic ■ May result in bleeding ■ Limited selectivity, can reduce effectiveness if foci is not disrupted[198]
Conservative-sharp	Performed by qualified and competent practitioners using aseptic technique with sterile curette, scalpel and scissors[97, 170]	■ Removes and disrupts superficial biofilm[170]	Limited selectivity as aims to remove loose avascular or infected tissue without pain or bleeding[190, 199]
Autolytic	Autolytic debridement occurs naturally and can be aided by using topical agents and contemporary wound dressings that promote autolysis.[97, 170, 200, 201, 413] Examples include: ■ Cadexomer iodine ■ Fibre gelling wound dressings (e.g. alginates, hydrofiber, polyabsorbent fibres) ■ Honey ■ Moisture-balancing wound dressings (e.g. hydro-responsive wound dressings) ■ Surfactant and antiseptic solutions/gels	■ Highly selective ■ Inexpensive ■ Varying effectiveness in controlling biofilm ■ Pain free, no bleeding ■ Antimicrobial autolytic agents aid infection control ■ Polyabsorbent fibres have a continuous cleaning action[201]	■ Slow ■ May cause maceration or irritation of surrounding skin
Mechanical	Debridement performed using:[160, 170, 202-205] ■ Wet-to-dry dressings ■ Therapeutic irrigation ■ Monofilament /microfibre/foam debridement pads ■ Low-frequency ultrasound ■ Moistened gauze with aggressive circular contact	■ Evidence of disruption and removal of biofilm[170, 205] ■ Wet-to-dry dressings and irrigation is inexpensive ■ Debridement pads may improve patient comfort[161]	■ Non-selective ■ Wet to dry dressings are painful and can lead to wound bed trauma ■ Some mechanical debridement options are expensive
Enzymatic	Application of exogenous enzymes to the wound surface[170, 206]	■ Selective ■ Potentially some level of biofilm disruption/ removal[170]	■ Slower than instrument or other mechanical methods ■ May cause maceration or irritation of surrounding skin ■ Not widely available ■ Can be used as an adjunct to surgical debridement[206]
Chemical/ mechanical/ surfactant	Use of high or low concentration surfactant wound cleaners and gels that disrupt non-viable tissue, debris and microbials[181] in combination with mechanical activity	■ Selective ■ Inexpensive ■ Some level of biofilm disruption/removal[170] ■ May augment mechanical removal of debris when combined with negative pressure wound therapy[207]	■ Slower than other debridement methods ■ Some contain antimicrobial agents or active preservatives ■ May cause maceration of the periwound and surrounding skin (consider use of barrier products)
Biosurgical/ larval therapy	Medical grade fly larvae (e.g. *Lucilia sericata sp* and *Lucilia cuprina*) produce proteolytic enzymes that liquify devitalised tissue, which is then ingested by the larvae[97, 160, 208, 209]	■ Selective ■ Fast and efficient ■ Lysis of organisms ■ Evidence of removal of biofilm *in vitro* and in clinical studies[210, 211]	■ Slight pyrexia may occur because of lysis of organisms by larvae ■ Skin irritation may occur if enzymes contact surrounding skin ■ May be unacceptable to the patient[190]

effectiveness of BBWC through assessment of the inflammation and healing status of the wound should be undertaken. As the wound improves, BBWC strategies can be de-escalated.[70] However, for many chronic wounds complete response may take four weeks or longer.[70] This management strategy, referred to as the step-down/step-up approach, is summarised on the IWII-WIC.

09 Topical Antimicrobial Therapy

The term 'antimicrobial' is an umbrella term and refers to disinfectants, antiseptics (sometimes referred to as skin disinfectants), antivirals, antifungals, antiparasitics and antibiotics.[11, 216] The term refers to substances that are used to inhibit the growth of and/or kill microorganisms.[216] Antimicrobial agents may inhibit microorganism growth through either chemical or non-chemical, mechanical effects.

In general, most wounds that are healing do not require the use of antimicrobial therapy. However, there are some clinical situations in which judicious use of antimicrobial therapy is pragmatic and appropriate. Ensuring the selection and use of an appropriate topical antimicrobial is important to achieving desired outcomes for the wound and patient, preventing adverse events and to upholding the principles of antimicrobial stewardship.

Disinfectants are non-specific substances recommended by the manufacturer for application to an inanimate object (e.g. surfaces and instruments) to kill microorganisms. These products are not suitable for use on wounds, and many are cytotoxic to cells involved in wound repair.[188, 217] In contrast, antiseptics are suitable for managing wound infection, and their properties and use are discussed below. Both topical and systemic antibiotics, which are natural or synthetic molecules that have the capacity to destroy or inhibit bacterial growth,[188] also have a role in managing wound infection. However, their use must be limited to when they are necessary due to the rising concern regarding microbial resistance.

TOPICAL ANTISEPTIC THERAPY

Antiseptics are substances that have been prepared for use on living tissue, including open wounds.[188, 216] Antiseptics have a disruptive or biocidal effect on bacteria, fungi, parasites and/or viruses, depending on the type and concentration of the preparation. Antiseptics have multiple sites of antimicrobial action on target cells and therefore have a low risk of bacterial resistance. Thus, antiseptics have the potential to play an important role in controlling microbial burden in wounds while limiting exposure to antibiotics and reducing the risk of further antibiotic resistance.[217]

Topical preparations include liquids, gels, pastes or impregnated dressings. The properties of a topical antiseptic may depend on the vehicle by which it is delivered. Antiseptics are generally marketed as medical devices. The exact claims for the action of an antiseptic may depend on the regulations of the jurisdiction in which they are marketed. Drugs in general are disease modifying agents. Killing microorganisms in the wound bed may be considered as disease modifying. Thus, antiseptics are sometimes marketed as antimicrobial barriers within a dressing or as a preservative in a liquid, gel or paste formulation.

Topical antiseptics are non-selective and may be cytotoxic. This means they may kill skin and tissue cells involved in wound repair (e.g. neutrophils, macrophages, keratinocytes, and fibroblasts), thereby impairing the healing process. Cytotoxicity can be dose (concentration) and/or time (duration of exposure) dependent.[218] Newer-generation antiseptics are generally low or non-cytotoxic. Many older antiseptics, including hydrogen peroxide, traditional sodium hypochlorite (e.g. EUSOL and Dakin's solution), and chlorhexidine[219-221] are no longer recommended for use in open wounds due to the risk of tissue damage associated with their use.[218, 222] The exception for use of some older antiseptics might be for managing wounds in under-resourced geographic settings where contemporary antiseptics are not always available. In this case, the lowest concentrations of solution should be used, ceasing use as soon as the wound responds. Some antiseptics (e.g. sodium hypochlorite) have been re-developed as contemporary preparations with lower concentrations and more acceptable safety profiles.[217] It is essential to use products with a sustained release of antimicrobial agent at

concentrations sufficiently low to minimise toxicity but still able to destroy or inhibit microorganism growth. Table 11 summarises the properties of selected wound antiseptics in common use that have been observed in bench research (*in vitro* and animal models). Note that the table is not a complete list of antiseptics that are available and used across the world.

Table 11: Antiseptics (medicated and non-medicated) commonly used in wound treatment

Solution	*In vitro*/bench	Uses in wound treatment			Comments
		Cleanse / irrigate	Topical	BBWC	
Alginogel	■ Broad spectrum activity against Gram-negative and Gram-positive bacteria[223] ■ Prevents biofilm formation at ≤0.5% concentration[224] ■ Inhibits established biofilm growth at concentrations >0.5%[224]		✓		■ Alginate gel with two enzymes: lactoperoxidase and glucose oxidase[225] ■ Available in 3% and 5% concentration, selection based on wound exudate levels[224, 225] ■ Not toxic to keratinocytes or fibroblasts[223]
Concentrated surfactant gels (e.g. PMM surfactant)	■ Active against *P. aeruginosa, Enterococcus spp., S. epidermidis, S. aureus* and methicillin-resistant *S. aureus* (MRSA) biofilms[226]	✓	✓	✓	■ Poloxamer-based surfactant that forms a gel when it warms on tissue[226]
Copper (Metallic copper, cupric oxide and cuprous oxide nanoparticles)	■ Activity against Gram-negative and Gram-positive bacteria including *S. aureus, P. aeruginosa, E. coli.* and MRSA in *in vitro* models[227-229]		✓		■ Available as a surfactant and impregnated in dressings[227, 229] ■ Toxic to human cells, although toxicity is lower with nanoparticle preparations[227, 229]
Dialkyl carbamoyl chloride (DACC)	■ Capacity to bind with a range of bacteria including *S. aureus* and MRSA,[230] without further bacterial replication[231] ■ Capacity to bind with *P. aeruginosa*, *S. aureus, S. epidermidis* and MRSA biofilms[231, 232]		✓	✓	■ A dressing with fibres covered in a hydrophobic derivative of fatty acids; bacteria bind to the dressing and are removed with dressing change[232-235] ■ Antimicrobial effect is achieved by mechanical characteristics[232-234]
Honey (Medical grade)	■ Effective against Gram-positive and Gram-negative bacteria including *E. coli, P. aeruginosa, S. aureus, Acinetobacter, Stenotrophomonas*, MRSA and vancomycin-resistant enterococci (VRE)[236-239] ■ Inhibits biofilm activity, including *Pseudomonas* biofilms[240-243]	✓	✓	✓	■ Acidic, hyperosmolar sugar solution available as paste or dressings (e.g. hydrocolloids, alginates, tulle)[72, 236] ■ Antimicrobial effect relates to production of hydrogen peroxide by an enzyme within honey[236] ■ Promotes autolytic debridement[72, 244] ■ Select products that have been gamma irradiated[243]
Iodophors (Povidone iodine)	■ Broad spectrum activity against Gram-negative and Gram-positive bacteria, fungi, spores, protozoa and viruses[185-189] ■ Penetrate and disrupt biofilms, including *P. aeruginosa* and *S. aureus* biofilms at 1% concentration[185, 186] ■ Eradicates *S aureus, K. pneumoniae, P. aeruginosa* and *C. albicans* biofilms at 0.25% concentration[186, 187]	✓	✓	✓	■ Halogen antimicrobial[185] available as ointment, gel, liquid, surfactant and wound dressing[188] ■ Has additional anti-inflammatory effects[185, 186, 245] ■ No reports of bacterial or cross resistance[185-187] ■ Dose-dependent cytotoxic effect on osteoblasts, myoblasts and fibroblasts[184, 185] ■ Rapid release formulas may require 2–3 daily applications for optimal effect[185] ■ Contraindicated in neonates, iodine sensitivity, thyroid or renal disorders and large burns[185, 188]
Iodophors (Cadexomer iodine)	■ Broad spectrum activity against Gram-negative and Gram-positive bacteria, fungi, spores, protozoa and viruses[185] ■ Reduces microbial burden complicated by biofilm at 0.9% concentration[246]		✓	✓	■ Halogen antimicrobial[185] available as powder, paste, solution and wound dressings[247] ■ Dose-dependent cytotoxic effect on keratocytes and fibroblasts[185] ■ Contraindicated in children below 12 years, iodine sensitivity, thyroid or renal disorders and extensive burns[185]

Table 11: Antiseptics (medicated and non-medicated) commonly used in wound treatment *(Continued)*

Solution	*In vitro*/bench	Uses in wound treatment			Comments
		Cleanse / irrigate	Topical	BBWC	
Iodophors (Poly-vinyl alcohol [PVA]-based foam)	■ Broad spectrum activity against Gram-negative and Gram-positive bacteria, fungi, spores, protozoa and viruses[185] ■ Active against *P. aeruginosa* and *S. aureus* biofilms[185]		✓	✓	■ Halogen antimicrobial[185] available as dressing ■ Low level of cytotoxicity for most products[185, 248] ■ Dose-dependent toxicity has been observed with iodine-impregnated foam dressing[249]
Octenidine dihydro-chloride (OCT)	■ Broad spectrum action against Gram-positive and Gram-negative bacteria, MRSA and fungi[250-257] ■ Eradicates bacterial biofilm[258, 259] for up to 72 hours[250]	✓	✓	✓	■ Available in gel, irrigation and surfactant preparations[260] ■ Does not promote bacterial resistance ■ Good tissue tolerability has been demonstrated;[261, 262] not shown to disrupt healing[260] ■ Anaphylaxis and allergic response rarely observed[263, 264]
Polyhexa-methylene biguanide (PHMB)	■ Efficacious against Gram-positive bacteria, Gram-negative bacteria, fungi and viruses[186, 187, 247, 258, 265] ■ Effective against *P. aeruginosa, S. aureus*, MRSA and mixed species biofilms[186, 247, 258, 265-268]	✓	✓	✓	■ Available in gel, irrigation and surfactant preparations ■ Does not promote bacterial resistance[72, 186, 187] ■ Low cytotoxicity *in vitro*[265] ■ Eczema or anaphylaxis rarely observed[265]
Silver (Salts and compounds, including sulph-adiazine, oxides, phosphate, sulphates and chlorides	■ Concentration dependent effect in eradicating mature *P. aeruginosa* and *S. aureus* biofilm[186, 269] ■ Reduce bacterial loads complicated by biofilm[247] ■ Silver dressings/slow-release ions have broad-spectrum activity,[270] including against MRSA and VRE[188]		✓		■ Available as ointment, gel and wound dressing ■ Dose- and time-dependent cytotoxic effects on human fibroblasts, keratinocytes and endothelial cells,[186] may delay epithelialisation[188] ■ Microbial resistance appears uncommon[188, 270] but has been reported for some isolates[233, 271]
Silver (Elemental [metal and nano-crystalline])	■ Broad-spectrum activity against Gram-negative and Gram-positive bacteria,[272, 273] including *P. aeruginosa, E. coli* and *S. aureus*[273] ■ Inhibit biofilm formation[272]		✓		■ Available as wound dressings ■ No[273] or mild[274] concentration-dependent cytotoxic effect on fibroblasts
Silver with anti-biofilm mechanisms	■ Broad-spectrum antimicrobial action[275] ■ Prevents biofilm formation[275, 276]		✓	✓	■ Available as 1.2% ionic silver-impregnated dressing enhanced with EDTA (a chelating agent with its own broad-spectrum antimicrobial and antibiofilm activity[277]) and benzethonium chloride (BEC; a surfactant)[275, 276, 278]
Super-oxidised solutions (Sodium hypochlorite [NaOCl] antimicrobial preservative)	■ Eradicates *P. aeruginosa* and MRSA,[266] but has a time-dependent response[279]	✓	✓		■ Naturally occurring oxidising antiseptic,[183] sometimes available as a blend with hypochlorous acid (HOCl)[280] ■ Dose- and time-dependent cytotoxicity to keratinocytes and fibroblasts;[279] older preparations (e.g. traditional 0.4–0.5% Dakin's solution) have high tissue cytotoxicity[280]
Super-oxidised solutions (Hypochlorous acid [HOCl] antimicrobial preservative)	■ Broad-spectrum action against bacteria, virus and fungi, including MRSA[183, 266] ■ Eradicates bacterial and fungal biofilms[266, 281]	✓	✓	✓	■ Sometimes available as a blend with NaOCl[280] ■ Has an anti-inflammatory effect through reducing activity of histamines, matrix metalloproteinases, mast cell and cytokine activity[183] ■ Dose-dependent cytotoxicity, but non-cytotoxic at concentrations that achieve antimicrobial action[280]

CLINICAL EFFICACY OF TOPICAL ANTIMICROBIAL TREATMENTS

We conducted a systematic review of the clinical evidence available for topical antimicrobial treatments (see *14 Methodology*). Our literature search identified a paucity of high-level research on the efficacy of the more commonly used topical antimicrobial treatments in achieving the following clinical outcomes:

- Complete wound healing (within 8–12 weeks)
- Improvement in wound bed tissue type (using accepted scales/tools)
- Reduction in clinical signs and symptoms of local wound infection
- Reduction in laboratory-confirmed microorganisms or biofilm.

Most research on antiseptics explores in *vitro* and/or animal wound models (see Table 11).[247] However, there is no standardisation of methodology to allow direct comparison of study results and there is ongoing debate regarding the transferability of this research to the clinical setting. As discussed in *06 Wound Biofilms*, it has become evident that some observable features of *in vitro* biofilm may not accurately reflect the characteristics and behaviours of biofilms in clinical wounds. Therefore, we cannot assume that treatments that are effective in reducing or eradicating biofilms in laboratory settings will necessarily have similar impact in a wound.

Additionally, the ways in which antimicrobials are used in laboratory research often does not reflect the use of products in clinical settings.[161, 214] For example, contact time in laboratory research is often 24 hours or longer, while in the clinical setting an antiseptic might remain in contact with the wound bed for 10–15 minutes (e.g. during wound cleansing).[214] For leave-on antimicrobials, the influence on product efficacy of wound pH,[282] temperature, wound exudate and tissue repair activity is uncertain. Additionally, few laboratory studies explore the influence of the synergy between chemical and mechanical activity that is achieved when performing therapeutic cleansing.[161] For these reasons, we reviewed evidence regarding clinical efficacy (i.e. studies with real-life wounds), and the findings are summarised in Tables 12–16. The inclusion criteria for studies reported in these tables is outlined in the Methodology section. The identified clinical research was predominantly of low certainty. This finding reflected those of systematic reviews with moderate to high confidence ratings[165, 188, 283-287] that also concluded there is very limited evidence of high certainty on the use of antiseptics.

GUIDANCE ON THE USE OF TOPICAL ANTIMICROBIAL TREATMENTS

Despite the lack of clinical evidence with high certainty, it is evident that judicious use of topical antiseptics plays a role in preventing and managing wound infection.[70] When a wound is assessed as being at high risk of developing an infection (see *03 Wounds at Risk of Infection*), judicious use of some topical antimicrobial treatment[57, 188] may be appropriate (e.g. in immunocompromised patients or following high risk surgery). Topical antimicrobials play a role in treating the wound when it is likely to be clinically infected (i.e. when a wound displays signs and symptoms of local infection or is suspected or confirmed as containing biofilm). Selection of topical antimicrobial treatment should consider:[217]

- Broad-spectrum antimicrobial action and/or known efficacy for confirmed microorganisms
- Efficacy in achieving clinical goals of care of the individual
- No or low cytotoxicity, irritancy and allergenicity to wound tissue and the periwound skin
- Fast and long-acting activity
- No or low propensity to select bacterial resistance
- Local availability and guidance.

Use topical antimicrobial treatments to manage wounds exhibiting signs and symptoms of local wound infection and wounds suspected or confirmed as having biofilm.

Use topical antimicrobial treatments in combination with systemic antibiotics for wounds exhibiting signs and symptoms of spreading or systemic infections.

Evidence ranking in Tables 12 to 16 (see shading)
High certainty
Moderate certainty
Low and critically low certainty

Table 12: Clinical evidence for topical antiseptics in complete wound healing¥

Preparation	Evidence from reviews and randomised and/or controlled trials
Alginogel	No difference in complete healing rate for burns versus silver sulfadiazine dressing[288]
Cadexomer iodine	■ Higher complete healing rates for pressure injuries,[285] venous leg ulcers[289] and in chronic wounds[290] versus standard care ■ Higher complete healing at 12 weeks with 0.9% cadexomer iodine in both gel and powder forms versus standard care[291]
DACC	Higher complete health rates at 75 days for pilonidal sinus versus alginate dressing[292]
Honey	Higher rates of complete healing for surgical wounds versus EUSOL[284] ■ Higher complete healing rates for superficial burns versus silver sulfadiazine[293] ■ Higher complete healing rates for burns versus topical antibiotics[283] and versus silver sulfadiazine[294] ■ Higher complete healing rates for VLUs versus alternative dressings[289] ■ Higher complete healing ates for minor wounds versus standard care[294]
OCT	■ Similar complete healing rates for chronic leg ulcers with OCT versus Ringer's solution[295] ■ Complete healing was significant for partial thickness burns with OCT gel, similar rates to herbal gel[296]
PHMB	Higher rates of chronic wound healing with a PHMB dressing versus a silver dressing[186, 297]
Povidone iodine	Inferior complete healing rates for pressure injuries versus protease modulating dressing[285] ■ Conflicting findings for complete healing versus non-antimicrobial dressings with no difference shown for chronic ulcers[298] or donor-sites,[299] but faster healing shown for diabetic foot ulcers (DFUs)[299] ■ Reduction in time to complete healing in burns[283]
SOS	Improved healing for chronic wounds with no difference in healing outcomes for SOS versus tetrachlorodecaoxide[300] ■ Higher rates of chronic wound healing for SOS versus povidone iodine[301-303] ■ Faster complete healing of burns for sodium hypochlorite versus silver sulfadiazine[283]
Silver	■ Higher rates of healing for venous leg ulcers (VLUs)[286] and for burns[283] with silver dressings versus non-antimicrobial dressings ■ No difference in healing rates for burns between nanocrystalline silver dressing versus any other silver-impregnated dressings[304] ■ Higher rates of healing for chronic wounds[305] and for VLUs[286] with silver dressings versus antimicrobial dressings ■ Higher rates of healing for pressure injuries with silver sulfadiazine versus povidone iodine[285] ■ Higher rates of healing for DFUs with nanocrystalline silver dressing versus honey or nonactive dressing[306] ■ Lower or similar rates of healing for burns with silver sulfadiazine versus a range of other comparators[307, 308]

¥ reported as complete wound closure within 8–12 weeks

Table 13: Clinical evidence for topical antiseptics in preventing/reducing microbial burden+

Preparation	Evidence from reviews and randomised and/or controlled trials
Alginogel	No difference in colonisation rates for burns versus silver sulfadiazine dressing[288]
DACC	Significant greater reduction in bacterial load for VLUs versus non-binding silver dressing[233]
Honey	■ Faster bacterial clearance in DFUs versus iodine dressing[309] ■ Reduction in microbial burden for VLUs versus alternative dressings[289]
PHMB	■ Fewer surgical site infections (laparoscopic surgery) with PHMB dressing versus basic contact dressing[57] ■ Reduction in microbial burden in chronic wounds with PHMB gel versus standard care[265] ■ Reduction in polymicrobial counts and MRSA for chronic wounds with PHMB dressings[287] and PHMB irrigation[310] ■ Reduction in polymicrobial counts for burns with PHMB gel versus silver sulfadiazine[311] ■ Greater reduction in chronic wound critical bacterial load over 28 days with a PHMB dressing versus a silver dressing[186, 297] ■ Reduction in polymicrobial counts for acute wounds with PHMB versus Ringer's solution[312]
Povidone iodine	■ No difference in infection rates in traumatic wounds irrigated with povidone iodine versus normal saline[313]
SOS	■ Reduction in bacterial counts in chronic wounds with HOCl-based cleanser, with superior performance versus saline[314] ■ Reduction in microbial burden in chronic wounds for a range of hypochlorite and hypochlorous solutions, equivalent performance compared with other antimicrobial solutions[310]
Silver	■ Lower rates of infection in DFUs with 1.2% ionic silver versus calcium alginate dressing[188] ■ Superior reduction in bacterial load in burns for nanocrystalline silver versus silver sulfadiazine or silver nitrate[315] ■ Superior reduction in bacterial load in chronic wounds for silver dressings versus antimicrobial products[305]

+ reported as laboratory confirmed of absence of/reduction in critical levels of microorganisms

Table 14: Clinical evidence for topical antiseptics in reducing wound biofilm[$]	
Preparation	**Evidence from reviews and randomised and/or controlled trials**
PHMB	Limited impact on biofilm in VLUs for PHMB-surfactant versus saline cleanse[247]
Cadexomer iodine	Significant reduction in biofilm at 2–6 weeks observed in DFUs[316]

[$] reported as laboratory confirmed of absence of/reduction in wound biofilm

Table 15: Clinical evidence for topical antiseptics in reducing signs/symptoms of local wound infection	
Preparation	**Evidence from reviews and randomised and/or controlled trials**
Cadexomer iodine	Reduction in pus and debris and reduction in pain in chronic wounds at 6–8 weeks versus standard care[290]
DACC	Lower rate of signs/symptoms of local wound infection in surgical sites versus non-antimicrobial dressings[234, 235, 317-319]
Honey	Reduction in wound inflammation observed in burns treated with honey[283]
OCT	■ Superior management of pain in burns for OCT gel versus a silver sulfadiazine cream[320] ■ Superior management of pain in VLUs versus Ringer's solution[261, 262]
PHMB	■ Inconclusive findings on VLU pain reduction for PHMB versus saline cleansing[165, 321] ■ Reduction in pain in chronic wounds with PHMB gel versus standard care[265] ■ Reduction in wound pain for PHMB dressings[287]
SOS	Reduction in periwound cellulitis superior for SOS versus povidone iodine[188, 301, 302]
Silver	Improved exudate, odour and pain management in chronic wounds for silver-releasing dressing versus comparators[322]

Table 16: Clinical evidence for topical antiseptics in improving tissue type	
Preparation	**Evidence from reviews and randomised and/or controlled trials**
PHMB	■ Improvement in tissue type for chronic wounds with PHMB gel versus standard care[265] ■ Mixed findings on efficacy for PHMB dressings in achieving improvements in tissue type indicative of healing[287] ■ Improved BWAT score for VLUs with PHMB solution versus saline[215]
SOS	■ Improved BWAT score in chronic wounds treated with SOS, with no difference compared with ionic silver solution[278] ■ Similar rate of skin graft take at 14 days for SOS (HOCl) versus 5% Sulfamylon solution[323]
Silver	■ Improved BWAT score over time in chronic wounds treated with ionic silver solution, with no difference compared with SOS[278] ■ Faster improvement in wound tissue type in DFUs with silver ion dressing versus routine care[188]

Duration of topical antiseptic use should be individualised and based on regular wound assessment.[70] A 2-week challenge is often recommended, as this allows sufficient time for the agent to exert some observable activity to inform an evaluation of the management plan.[78] However, as noted in the step-down/step-up approach to biofilm-based wound care presented in the IWII-WIC, treatment may be required for up to 4 weeks to attain results.[70]

Alternating or rotating topical antiseptic treatments is popular.[324] The premise for this strategy is that suppression of a range of microorganisms is attained through the application of different antiseptics in 2- or 4-week rotation. In conjunction with therapeutic cleansing and debridement, alternating the type of antiseptic may assist in restoration of microbial balance; however, further research is required to support this clinical practice.[72, 169]

Use a topical antiseptic for at least 2 weeks before evaluating its efficacy in managing wound infection.

TOPICAL ANTIBIOTICS AND ANTIFUNGAL THERAPIES

Antibiotics target specific sites within bacterial cells while having minimal influence on human cells, thus they generally have a low toxicity.[188] They are administered either topically or systemically to manage wound infection. Topical preparations may include gels, creams or impregnated dressings.

The use of topical antibiotics, which contain a low-dose form of antibiotic, may induce resistance[325] (see *11 Antimicrobial Resistance and Stewardship*). Controversy surrounds the use of topical antibiotics, and the debate is compounded by extensive work on the wound microbiota and the limited evidence of clinical efficacy.[325] A review of clinical studies comparing topical antibiotics to antiseptics for preventing infection in uncomplicated wounds found a lower relative risk of infection associated with topical antibiotics but, importantly, there was no significant difference in absolute risk reduction.[326] Similarly, a review of local antibiotic delivery methods found a lack of good-quality evidence on their efficacy in reducing wound breakdown in DFUs.[327] Given the global concern regarding antibiotic resistance, use of topical antibiotics for wound management should only be considered in infected wounds under very specific circumstances by experienced clinicians[141, 326] (e.g. topical metronidazole gel for treating malodour in fungating wounds[328]).

Topical antifungal therapy can be used in conjunction with good wound care practice (e.g. management of wound exudate and other sources of moisture in which fungi proliferate). Accurate identification of fungi, although rare, is imperative when selecting appropriate treatment. Wound sampling and molecular analysis suggest that chronic wounds with fungal-associated biofilm have unique microbial profiles that require an individualised approach. Antifungal therapies (e.g. topical miconazole) may be appropriate; however, poor penetration throughout biofilm that contributes to selection of resistant phenotypes is a risk.[121, 329] The association of fungal infection with a high mortality rate in individuals with burns suggests more aggressive management with systemic treatment is appropriate.[330, 331]

10 Principles of Aseptic Technique in the Management of Wounds

Aseptic technique refers to a practice framework that is used to prevent the spread of infection both to and from a wound when completing a wound dressing procedure (WDP). This chapter focuses on the universal minimum standards for completing a WDP in a safe manner that reduces the risk of cross-infection and introduction of pathogens into the wound. In most clinical settings, local policies and procedures outline more specific requirements for aseptic technique during a WDP based on achievable infection control in the clinical and geographic setting.

When a wound occurs, the break in skin integrity is vulnerable to the introduction of transient or residential pathogens through direct or indirect contact.[332] The ultimate goal when performing any procedure when there is a break in the skin is to prevent introduction of pathogens. It is with this understanding that surgical procedures are undertaken using strict aseptic routines, including pre-operative skin cleansing, use of protective personal equipment (PPE), management of the surgical field and control of the environment in which the procedure is being conducted. However, such exacting procedures are not feasible in most settings in which WDPs are performed.[333]

ASEPTIC TECHNIQUES USED FOR WOUND DRESSING PROCEDURES

Two accepted standards of aseptic technique used for WDPs are described in the literature—sterile technique (also referred to as surgical technique) and clean technique (also referred to as standard technique).[162, 334, 335] The basic principles included in these techniques are described below. Wound service providers should have standards of aseptic technique that reflect local conditions (e.g. resources, standard of care, patient population and environmental risks). Wound clinicians should be guided by their local policies and procedures.

Sterile/surgical aseptic technique

When performing a sterile/surgical aseptic technique, universal precautions are implemented, hands are cleansed with alcohol-based sanitiser or skin cleanser and running water, and sterile gloves are worn. A sterile field, sterile equipment (including dressing tray, fluid well, scissors, forceps and cleansing solutions) and sterile wound dressings are used. Asepsis is maintained when preparing the wound dressing.[333, 335-337]

Clean/standard aseptic technique

When performing a clean/standard aseptic technique, universal precautions are implemented, hands are cleansed with alcohol-based sanitiser or skin cleanser and running water, and non-sterile gloves are worn. Clean equipment (e.g. towels, cleansing cloths and bowls) and a basic dressing tray (plastic tray with well, plastic forceps and gauze) are used. Potable water or sterile fluid is used. However, equipment used for performing debridement (e.g. scissors, curette and forceps) should be sterile.[164, 333, 335-338] Some local guidance[337, 338] suggests cutting wound dressings with clean scissors used exclusively for cutting wound dressings for the particular patient and storing the unused components appropriately between WDPs.

Universal infection control precautions

Regardless of which aseptic technique is selected, basic universal precautions are required, and the environment should be appropriate to the technique. This includes appropriate hand hygiene precautions, use of PPE appropriate to the aseptic technique (including an apron and eye protection if splashing is anticipated).[335] The environment should be appropriate for conducting a WDP, and basic principles of infection control should be implemented. For example, put animals/pets outside; stop fans or air conditioner flow in the direct area; select a space with cleanable, non-fabric décor; and establish a clean, flat, non-porous surface for setting up equipment.[339] Avoid performing WDPs in a toilet area where possible.

SELECTING AN ASEPTIC TECHNIQUE FOR WOUND DRESSING PROCEDURES

The most appropriate technique to use when performing a WDP has been an ongoing topic of debate. The clinical setting in which WDP is being performed has a direct impact on technique, because strict asepsis is impossible to achieve in uncontrolled and semi-controlled environments. For example, the ability to establish conditions conducive to asepsis is much lower in a community setting than in a wound clinic. The organisation's local policies and procedures related to infection control and antimicrobial stewardship should be observed.

A risk assessment should be undertaken to determine the most appropriate aseptic technique based on the patient and their wound, environmental considerations, the availability of equipment and the healthcare provider's clinical skills. Considerations include patient risk factors, characteristics of the wound and the context in which the WDP will be performed.[164, 336, 337, 339]

Several factors indicate that a sterile/surgical aseptic technique is appropriate. Presence of patient factors that increase the risk of infection development (e.g. comorbidities and low immunity) indicate a higher level of asepsis should be implemented.[336, 337] Wound-related factors that suggest use of sterile/surgical aseptic technique include a deeper and/or more severe wound, involvement of exposed structure such as tendon and bone, and whether it is anticipated that the wound can heal. More complex procedures – for example, those in wounds located in a difficult anatomical location, multiple wounds, or those with involvement of exposed structures – require sterile/surgical aseptic technique.[160, 335-337, 339]

Practical considerations also influence the selection of aseptic technique, such as the conditions of the environment in which the WDP will need to be performed, and the availability of sterile versus clean equipment, cleansing agents and wound dressings. Finally, the confidence and competence of the clinician[340] and their scope of practice in the context in which they practice is a consideration in aseptic technique selection.

Figure 5 summarises the process for selecting and implementing an appropriate WDP aseptic technique.

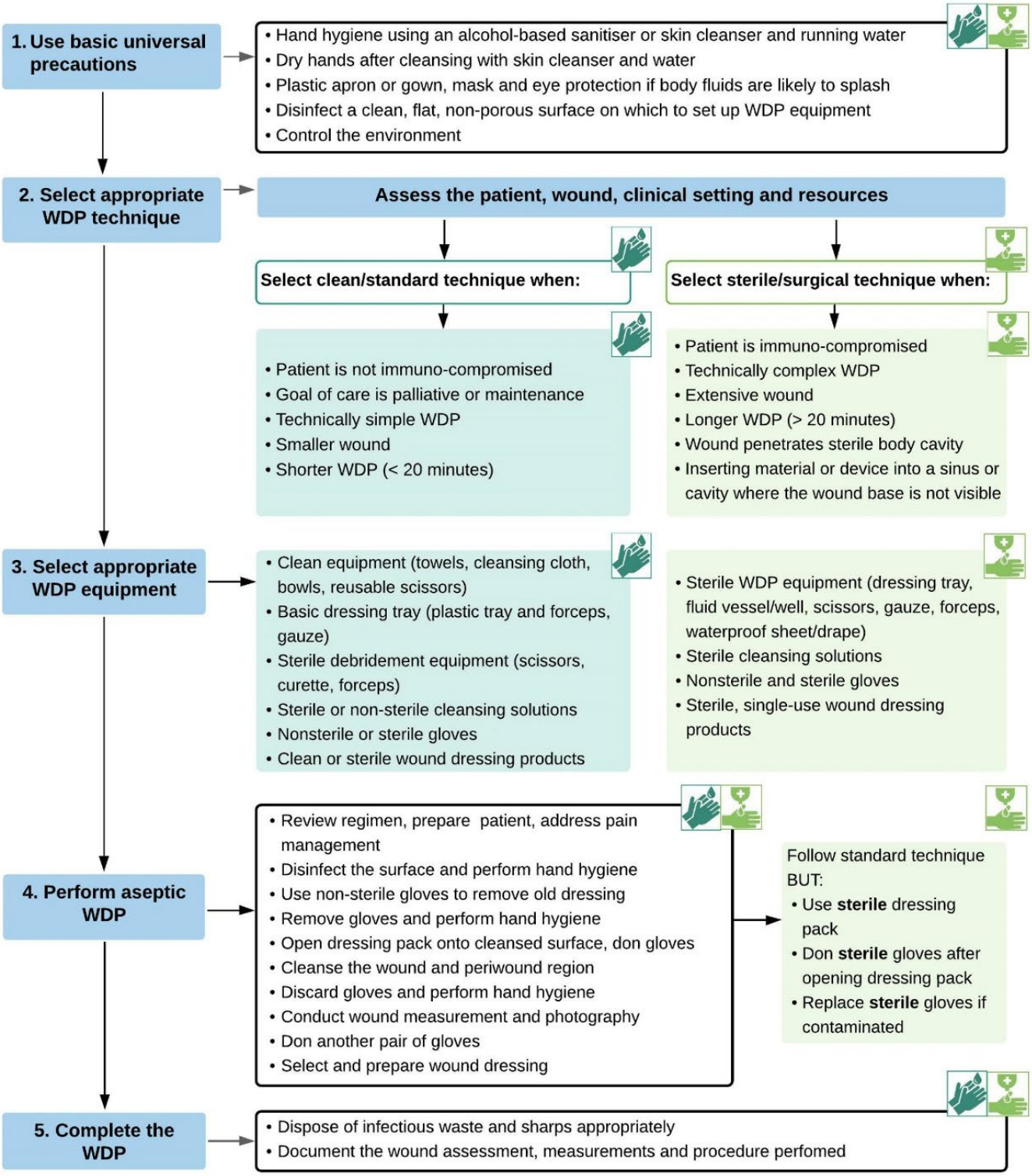
SEQUENCING A WDP CONDUCTED USING SURGICAL/STERILE ASEPTIC TECHNIQUE

Correct sequencing of a WDP is essential to maintain an appropriate level of asepsis and to prevent cross infection. Box 3 provides an example of sequencing for a surgical/sterile aseptic technique.

Box 3: Example of sequencing for a WDP using surgical/sterile aseptic technique

1. Review the individual's history, diagnosis, care goals, preferences, current wound condition and treatment regimen
2. Prepare the patient for the procedure by:
   - Outlining the WDP and its expected timeframe and gaining consent
   - Conducting a pain assessment and administering analgesia as required
3. Prepare the area in which the WDP will be performed:
   - Use a cleanser/wipe, disinfect work area, including non-porous surface on which equipment will be prepared
   - Address environmental factors that can increase pathogen spread (e.g. air conditioning or pets)
4. Collect and prepare the required equipment including:
   - Hand sanitiser
   - Sterile and/or non-sterile gloves and other PPE
   - Equipment to cleanse the periwound area
   - Sterile wound cleansing solutions
   - A simple or complex dressing kit/tray, anticipated equipment, wound dressings and devices
   - Equipment for assessing wound dimensions and depth, and a camera for wound photography
   - Rubbish bin/bag for infectious waste
5. Prepare and position the patient for the WDP, promoting comfort, privacy and safety
6. Perform hand hygiene and don non-sterile gloves
7. Remove the old wound dressing using moistened gauze or a cloth (with or without an adhesive remover); dispose of the wound dressing appropriately in infectious waste
8. Remove and dispose of the non-sterile gloves and perform hand hygiene
9. Open the sterile dressing pack/kit onto the cleansed surface
10. Perform hand hygiene and don sterile gloves
11. If there is a primary wound dressing, remove using sterile forceps. Hereafter, consider these forceps to be contaminated
12. Place a pack moistened with (preferably warmed) sterile solution on the wound for protection before proceeding to cleanse and pat dry the periwound area
13. Remove the moistened pack from the wound and dispose in contaminated waste
14. Proceed to cleansing and (when required) debriding the wound bed using sterile equipment; hereafter, consider this equipment to be contaminated
15. Conduct wound assessment (measurements and photography). Photography after wound cleansing is recommended, as this provides full viewing of the wound (before/after photographs may also be taken). This can be conducted by a second clinician, if available. If not, remove sterile gloves and perform hand hygiene after measuring the wound
16. Select a wound dressing based on wound condition, level of exudate, presence or otherwise of local infection, the frequency with which the wound dressing will be changed and the patient's preferences
17. Perform hand hygiene and don sterile gloves if they have been removed for wound assessment
18. Cut and apply the new wound dressing using sterile equipment that has not touched tissue or exudate
19. Discard contaminated waste appropriately
20. Document and communicate the wound assessment, the WDP and the ongoing wound treatment plan

Figure 5 | Flow chart for performing an aseptic wound dressing procedure (WDP)[164, 333, 335, 337, 339]



11 Antimicrobial Resistance and Stewardship

Antimicrobial resistance (AMR) occurs when microorganisms naturally evolve in ways that cause medications used to cure infections to be ineffective. When the microorganisms become resistant to most antimicrobials they are often referred to as 'superbugs'.[341, 342] Antimicrobial resistance is driven by a range of social and economic factors, including:[341, 343]

- Overuse of antimicrobials in humans and food-producing animals
- Using antimicrobials inappropriately
- Inadequate prevention and control of infection and disease, particularly in large facilities (e.g. healthcare and farms)
- Inadequate access to affordable, quality medicines, vaccines and diagnostics
- Lack of access to clean water, sanitation and hygiene
- Lack of awareness and knowledge regarding antimicrobials and their use
- Inadequate enforcement of legislation.

While aggressive measures in some countries[344] have led to the containment of some resistant Gram-positive organisms, AMR is emerging faster than the rate at which new and novel antimicrobial agents are being developed.[341, 345] The burden of pathogenic resistance to antimicrobials is predicted to be associated with up to 10 million deaths each year by 2050, equating to the death of one person every three seconds,[346] and exceeding deaths associated with cancer.[342]

ANTIMICROBIAL RESISTANCE IN THE CONTEXT OF WOUND INFECTION

Studies suggest there is excessive use of antibiotics in individuals with non-healing wounds. Mounting evidence identifies that the use of antibiotics to manage wound infection should and could be reduced significantly. This is supported by the observation that antibiotic therapy is frequently prescribed without clinical justification, without addressing the underlying aetiological causes of the wound,[342, 347, 348] and often without significant clinical benefit.[326] For example, a meta-analysis exploring the use of prophylactic topical antibiotics for the prevention of uncomplicated wound infection concluded that, although topical antibiotics were effective in reducing the risk of infections in uncomplicated wounds, the absolute risk reduction was minimal when compared to placebo, and not statistically significant when compared to use of antiseptics.[326]

More judicious antibiotic use in wound practice will contribute significantly to a reduction in antibiotic resistance and reduce both the poor health outcomes and economic burden associated with side effects of antibiotics. Reviewing wound care practice and aligning wound infection prevention and management with the goals and principles of antimicrobial stewardship (AMS) is an imperative to addressing the global problem of AMR. For example, a recent retrospective analysis found introduction of early detection of infection combined with improved wound hygiene practice was associated with a 33% reduction in use of antimicrobial dressings.[349]

WHAT IS ANTIMICROBIAL STEWARDSHIP?

AMS refers to the supervised and organised use of antimicrobial agents. In healthcare, this refers to a coordinated programme designed to decrease the spread of infections caused by multidrug-resistant organisms and improve clinical outcomes by encouraging appropriate and optimised use of all antimicrobials.[350]

There is an urgent need at the international, national, organisational, professional and general public levels to implement strategies to reduce the risk of AMR. Globally, AMS is promoted by numerous key groups, action plans and initiatives, including:

- The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR): a collaborative approach between Canada, the US and Europe to monitor use of antimicrobials in the care of humans and animals[351-353]
- The Global Antibiotic Resistance Partnership (GARP): a collaborative initiative between middle-and-low resource countries to develop policies addressing AMR[354, 355]
- The Global Health Security Agenda (GHSA): a strategic international initiative between governments and non-government organisations addressing health threats from infectious disease, including strategic objectives to address AMR in human and animal settings[356]
- Joint Programming Initiative on Antimicrobial Resistance (JPIAMR): an initiative addressing AMR through support of trans-national research, policy development and knowledge translation[357]
- The WHO, OIE and FAO Tripartite Partnership: a collaboration between the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO) and the World Organisation for Animal Health (OIE) that seeks to manage health risks at the human-animal interface[358]
- The World Antimicrobial Awareness Week: an annual international event coordinated by the WHO to increase AMR awareness.[359]

ANTIMICROBIAL STEWARDSHIP IN PREVENTING AND MANAGING WOUND INFECTION

Given the identified issues of AMR associated with wound care, the imperative to address AMS in preventing and managing wound infection is clear. Table 17 provides an overview of initiatives that should form a component of AMS in the context of wound infection at the government, organisational and clinical level.

First and foremost, leadership at Government and health organisation level is important in promoting and guiding responsible use of antimicrobials, research and development and resource allocation.[360] Governments have an ongoing universal role in promoting collaborative international approaches such as those listed above. At the national level, initiatives such as regulation of prescribing and supply of antimicrobials, monitoring use and prompting awareness underpin action at the organisation and clinical levels to address AMR.

Institutional level guidelines (based on national and international guidance), formularies and clinical decision pathways should provide direction to clinicians managing wound infection. An overarching committee responsible for AMS should be a focus for healthcare organisations to ensure a multidisciplinary and multifaceted approach to oversight of antimicrobial use.[345] Monitoring and clinical auditing of the use of antimicrobials underpins evaluation of the effectiveness of antimicrobial stewardship initiatives and informs quality improvement in managing wound infection. Verbal and written education focused on AMR, AMS and correcting the misbelief that an antimicrobial is a requirement for wound healing should be regularly provided to clinicians, patients and their families. The introduction of such initiatives will optimise antibiotic prescribing, reduce inappropriate antimicrobial use, reduce adverse consequences of antimicrobials (e.g. toxicity resistance) and reduce unnecessary economic burden.[232]

Clinicians play a significant role in ensuring their practice in prevention and management of wound infection is consistent with AMS. Clinicians should conduct an in-depth wound assessment to identify if the wound is clinically infected;[345] if there are no clinical signs and symptoms of wound infection there is no requirement for using topical antimicrobial agents or wound dressings. Antimicrobials should only be used in identified infected wounds, based on identification of the infecting organisms. Antimicrobial use for chronic prophylaxis should be avoided other than in exceptional circumstances.

Use of accurate diagnostic techniques to identify clinical wound infection, the profile of pathogens in the wound and their sensitivities to antimicrobials, as outlined in *05 Diagnosis of Wound Infection*, guides antimicrobial therapy. In light of AMR, judicious use of topical antibiotics is required and use of topical antiseptics should be considered as a reasonable alternative to topical antibiotics.[326]

Table 17: Antimicrobial stewardship initiatives[232, 345, 360, 361]
Government level antimicrobial stewardship initiatives
■ Promote global regulation of prescription and supply of antimicrobials ■ Support global initiatives focused on reducing AMR ■ Promote awareness of AMR in the health and animal sectors and the general public ■ Support and stimulate ongoing research on AMR and development of new antimicrobial agents
Organisational level antimicrobial stewardship initiatives
■ Provide adequate funding and resources to support AMS ■ Convene an AMS committee responsible for guiding and monitoring the use of antimicrobial agents in the facility ■ Develop institutional policies and procedures on the use of antimicrobial agents based on global guidance ■ Implement best clinical practice in wound infection prevention and treatment ■ Facilitate accurate diagnosis of wound infection with appropriate policies, resources and care pathways ■ Monitor trends in microbial sensitives in the facility ■ Audit antimicrobial prescribing and patterns of use ■ Monitor and publish incidence of wound infection, types of wounds being managed with antimicrobial agents and their effectiveness ■ Provide regular education to all stakeholders on AMR and AMS
Clinical level antimicrobial stewardship initiatives
■ Educate patients, their families and healthcare professionals regarding AMR and responsible use of antimicrobial agents ■ Avoid use of antimicrobials as a prophylactic therapy, except for wounds identified at high risk of infection ■ Use non-medicated options (e.g. non-medicated wound dressings) to manage infection when possible ■ Only use antimicrobials when a wound has been clinically identified as infected ■ Base antimicrobial selection on identification of the infecting organisms ■ Select antimicrobial agents with narrow-spectrum activity where possible ■ Reserve broad-spectrum agents for more resistant bacterial infections where possible ■ Continue the use of antimicrobial therapy for an appropriate duration to prevent development of resistance ■ Monitor therapeutic response to guide ongoing selection and use of antimicrobials

Implement an organisational-level antimicrobial stewardship committee to provide guidance, monitoring and education on antimicrobial use.

Prescribed topical agents should be narrow-spectrum, reserving broad-spectrum agents for more resistant bacterial infections, and therapy should continue for an 'appropriate' duration, guided by appropriate and timely monitoring of therapeutic response.[345, 362] For example, antiseptics and wound dressings containing silver, iodine and PHMB provide effective antibacterial action across a broad range of wound pathogens, and an increasing body of evidence supports their use.[361, 363-365]

Embed the principles of antimicrobial stewardship into the curriculum of undergraduate healthcare programmes.

NON-MEDICATED WOUND DRESSINGS

Non-medicated wound dressings (NMWDs) are dressings that have no active/pharmaceutical component. Some of these dressings have mechanisms of action that help to remove microorganisms from a wound, making them an effective option for reducing wound infection without the risk of AMR.[232] Examples of NMWDs include (but are not limited to) hydrogels, hydrocolloids, hydro-responsive wound dressings (HRWDs), DACC-coated dressings, super-absorbents and carboxymethylcellulose (CMC) dressings. The mechanisms of action of NMWDs include:[414]

- Promoting autolytic debridement that disrupts microorganisms
- Absorbing microorganisms and their by-products
- Sequestering microorganisms away from the wound bed
- Immobilising and retaining microorganisms in the dressing structure.

Some NMWDs (e.g. DACC-coated dressings, HRWDs) have multiple mechanisms of action, for example, ability to sequester microorganisms away from the wound bed and immobilise them in the dressing material for removal when the dressing is changed.[414]

12 Future Directions in Wound Infection Science and Practice

The ever-increasing resistance and tolerance of pathogens to antibiotics is increasing in its impact on healthcare delivery and concerns regarding our future ability to treat infection. As our understanding of the challenges in this field increases, including our understanding of the activity of microorganisms within a wound bed, new and novel wound infection assessment and management tools and technologies are emerging. Some of this recent and future work is discussed below.

BIOFILM RESEARCH

There has been recent, rapid development in scientific understanding of what biofilms are, and are not, in the clinical context of a wound. It is clear there are large gaps in knowledge and areas requiring further exploration. As summarised in *06 Wound Biofilms*, biochemical interactions between microorganism species (quorum sensing) are observed in *in vitro* models but their behaviours within a clinical wound are far less understood. Research has sought to expand understanding of the biochemical mechanisms through which different co-existing microorganisms interact in the wound microenvironment. More recent theories propose that the interplay between different microbial species may be beneficial in certain conditions and could be utilised as predictive markers of healing and/or exploited in future treatments to enhance wound healing.[15] Some biofilm experts[366] have also identified important other future directions in biofilm research, including:

- Developing relevant and reliable *in vitro* models
- Understanding the interaction between biofilms and antibiotics
- Adjuvants that could be used to render biofilms more susceptible to antimicrobial treatments (e.g. enzymes, metabolites or nutrients).

NEW AND EMERGING TECHNOLOGIES AND TOOLS TO ASSESS AND IDENTIFY WOUND INFECTION

There is currently no definitive method of establishing whether a non-healing wound is infected. As outlined in *05 Diagnosis of Wound Infection*, in many settings, laboratory testing is not easily accessible, is costly and/or lacks immediacy. Recent research has explored potential diagnostic options, including wound pH,[367] wound odour sensing[101] and laboratory biomarkers including neutrophil-derived enzyme activity[367] and presepin,[101] some of which could be applied at point-of-care.

However, more research is required to achieve diagnostic accuracy and accessibility of these indicators.[101] Although there is a range of wound assessment tools based on clinical signs and symptoms available for evaluating wound infection, few of these tools have undergone rigorous reliability and validity testing. This area is an important future direction to enhance the tools available at the bedside to aid wound infection diagnosis and assessment in all clinical and geographic settings.

However, there are some recent point-of-care wound infection diagnostic tools that are becoming more widely available and accessible. The use of autofluorescence light has recently been reported to directly identify the presence of bacteria density on a wound surface.[368-371] This technique provides information on bacterial burden in wounds in real time through the detection of bacterial fluorescence. The handheld imaging device emits violet light at 405nm, causing porphyrin-producing bacteria to fluoresce in a darkened room. Red fluorescence is observed in wounds that are moderately to heavily colonised with most Gram-positive and Gram-negative bacteria, aerobes, and anaerobes, while cyan fluorescence is seen when *P. aeruginosa* is present. Recent studies have reported that the device has a positive predictive value of >95% for detecting moderate to heavy bacterial presence on the wound.[372-374] Fluorescence imaging is currently being explored as an adjunct option to guide and

evaluate therapeutic wound care.[77, 375] However, the signal cannot differentiate between planktonic bacteria and bacteria contained within a biofilm.[371] In addition, only surface located bacteria can be observed.

Wound blotting, another newly emerging point-of-care technique, has successfully used wound staining to visually 'map' biofilms in a wound.[376-378] Wound blotting uses a cationically-charged nylon or nitrocellulose membrane sheet that is pressed into a chronic wound bed for a minute before staining with cationic dyes that selectively detect and localise the negatively-charged exopolymeric matrix of mature biofilms located on the chronic wound bed surface. Residual biofilm staining after wound debridement has been shown to predict increased slough formation and failure of the wound to heal in the following weeks.[376-378] A recent clinical study has further validated this "biofilm wound map" technique.[379]

NEW AND EMERGING WOUND INFECTION MANAGEMENT STRATEGIES

Research on, and experience with, antibiofilm agents including nanoparticles, antimicrobial peptides and bacteriophages continues to advance. Nanoparticles are particles on the nanometre scale that occur naturally or can be synthesised to perform specific purposes. Their small diameter allows penetration into cell membranes and biofilms, allowing opportunity for their use in destroying microorganisms. Nanoparticles are being explored for use in treating wound infection due to both their bactericide properties (e.g. silver, copper and other metallic nanoparticles) and their potential to as a drug delivery system to introduce other active substances into the cells of microorganisms.[380-383] Current research is exploring nanoparticle-based delivery systems, including wound dressings, encapsulated drugs and microneedle injection systems that allow transdermal delivery of drugs directly under the skin.[382]

Phage therapy is still being explored. Phages are small, naturally occurring viruses that can infect bacteria. In medical application, phages are isolated and evaluated for their efficacy in targeting specific microorganisms. Research is exploring whether phages used in conjunction with each other or with antiseptics that degrade the bacterial cell membrane can more readily penetrate bacteria and biofilm, treating infection more rapidly.[384, 385] This research is advancing in *in vitro* and animal modelling and in small clinical studies, demonstrating phage efficacy against a variety of host organisms, including *S. aureus, P. aeruginosa* and *E. coli*.[385] A range of delivery systems, including fibres, hydrogels and films are being explored. Work continues advancing regulation and commercialisation opportunities.

CONSENSUS PROCESS RELATED TO TERMINOLOGY

The IWII also undertook a consensus process with a goal of attaining agreement on standardised definitions for terms associated with wound infection.[20] This was undertaken as a formal, global consensus process with participant experts who were nominated to represent international wound organisations. The formal consensus process used to attain agreement on definitions has been previously reported.[12, 19, 412] Terms and definition explored in the consensus process were:

Antimicrobial resistance, antimicrobial tolerance, antiseptic, biofilm, colonisation, contamination, chronic wound infection, exudate, fibrinous wound base/surface, friable tissue, hypergranulation, local infection, maceration, microbial burden, pocketing, slough, surfactant, systemic infection, wound cleansing.

The consensus definitions for these terms are included throughout this document and incorporated into the glossary of terms in *13 Terminology*. The IWII website contains more information about the wound infection terminology definitions consensus process.

13 Terminology

ABBREVIATIONS

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
BBWC	Biofilm-based wound care
BEC	Benzethonium chloride
BWAT	Bates-Jensen Wound Assessment Tool
CFU	Colony forming units
CLSM	Confocal laser scanning microscopy
CRP	C-reactive protein
CSSC	Clinical Signs and Symptoms Checklist
DACC	Dialkyl carbamoyl chloride
DFU	Diabetic foot ulcer
DNA	Deoxyribonucleic acid
ESR	Erythrocyte sedimentation rate
FISH	Fluorescence microscopy
HOCl	Hypochlorous acid
IWII	International Wound Infection Institute
IWII-WIC	International Wound Infection Institute Wound Infection Continuum
MRSA	Methicillin-resistant *S. aureus*
NaOCl	Sodium hypochlorite
NMWD	Non-medicated wound dressing
OCT	Octenidine dihydrochloride
PCR	Polymerase chain reaction
PCT	Procalcitonin
PHMB	Polyhexamethylene biguanide
PICO	Population; intervention; comparator; outcome
PPE	Personal protective equipment
PSI	Pounds per square inch
RCT	Randomised controlled trial
SEM	Scanning electron microscopy
SOS	Super oxidised solution
TEM	Transmission electron microscopy
TILI	Therapeutic Index for Local Infections score
TIME	Tissue; infection/inflammation; moisture; edge
VLU	Venous leg ulcer
VRE	Vancomycin-resistant enterococci
WBC	White blood cell
WDP	Wound dressing procedure
WIC	Wound Infection Continuum
WIRE	Wound Infection Risk Assessment and Evaluation tool

Glossary of terms

Adjuvant/adjunctive interventions: Therapies that are used in addition to standard primary interventions for wound care. Adjuvant therapies enhance the impact of primary wound care interventions.

Antibiotic: A natural or synthetic medicine administered systemically or topically that has the capacity to destroy or inhibit bacterial growth[12] Antibiotics target specific sites within bacterial cells while having no influence on human cells, thus they have a low toxicity.

Antimicrobial resistance: Antimicrobial resistance occurs when microorganisms change over time in ways that render the medications used to treat the infections they cause ineffective.[12, 341]

Antimicrobial stewardship: The supervised and organised use of antimicrobials in order to decrease the spread of infections that are caused by multidrug-resistant organisms and to improve clinical outcomes by encouraging appropriate and optimised use of antimicrobials.[350]

Antimicrobial tolerance: Antimicrobial tolerance occurs when microorganisms have a lower susceptibility to an antimicrobial.[20]

Antiseptic: An antiseptic is a topical agent with broad spectrum activity that inhibits multiplication of, or sometimes kills, microorganisms. Depending upon its concentration, an antiseptic may have a toxic effect on human cells. Development of resistance to topical antiseptics is uncommon.[20]

Asepsis: A state of being free from infectious (pathogenic) agents.[335]

Aseptic technique: A practice framework to prevent microorganism cross-infection when performing a wound dressing procedure.[335] The two accepted standards of aseptic technique are: sterile/surgical aseptic technique and clean/standard aseptic technique.[160, 337]

Bioburden: See microbial burden.

Biofilm: Biofilms are aggregate microorganisms that have unique characteristics and enhanced tolerance to treatment and the host defences. Wound biofilms are associated with impaired wound healing and signs and symptoms of chronic inflammation.[20]

Cellulitis: An acute, diffuse and spreading infection of the skin and subcutaneous tissues that occurs when bacteria (usually *S. aureus* or Beta-haemolytic streptococci[386]) and/or their products have invaded surrounding tissues characterised by acute inflammation and erythema.[387] Requires culture and sensitivity, and management with systemic antibiotics.[386]

Chronic wound: A wound that makes slow progression through the healing phases or displays delayed, interrupted or stalled healing. Inhibited healing may be due to intrinsic and extrinsic factors that impact on the person, their wound and their healing environment.[12]

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 clinically observed.[20]

Contamination: Contamination refers to the presence within the wound of microorganisms that are not proliferating. No significant host reaction is evoked and no delay in wound healing clinically observed.[20]

Cytotoxic: Refers to a substance that has a toxic effect on an important cellular function. In the context of wounds, cytotoxicity generally refers to the potential adverse effect of destroying cells that are involved in tissue healing, including fibroblasts, macrophages and neutrophils that may be a risk associated with applying substances to the wound.

Cross infection: Transfer of microorganisms (e.g. bacteria, virus) from one person, object or location (e.g. anatomical location) to another person, object or location.

Debridement: The removal of devitalised (non-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.[97, 388]

Delayed wound healing: Wound healing that progresses at a slower rate than expected. Chronic wounds without infection can be expected to show signs of healing within two weeks.[97]

Devitalised tissue: Dead tissue presenting as necrotic tissue or slough.[97, 389]

Erythrocyte sedimentation rate (ESR): A blood test that provides a non-specific indicator of inflammation activity in the body.[390]

Erythema: Superficial reddening of the skin; however, it should be noted that erythema does not occur as 'red' across all skin tones.[97]

Eschar: Necrotic, devitalised tissue that appears black or brown, can be loose or firmly adherent and hard or soft, and may appear leathery.[97]

Exudate: Fluid that is released from tissue and/or capillaries in response to injury, inflammation and/or microbial burden. It is mainly comprised of serum, fibrin, proteins and white blood cells.[20]

Family caregiver: People with personal connection to the person with a wound and who are involved in their care. This might include significant others, family members, neighbours, colleagues and other people who are providing support (e.g. advocacy, care planning, direct care or other levels of support) to the individual.

Fibrinous wound base/surface: A metabolic by-product of healing occurring as a layer that is loosely or firmly adherent to the wound bed. It is composed of serum and matrix proteins that may be white, yellow, tan, brown or green, and has a fibrous or gelatinous texture and appearance.[20]

Foreign body: Presence in the wound of non-natural bodies that may be a result of the wounding process (e.g. gravel, dirt or glass) or might arise from wound treatment (e.g. sutures, staples, orthopaedic implants or drains).

Friable tissue: Fragile tissue that bleeds easily.[20]

Fungi: Single celled or complex multicellular organisms categorised in the biological kingdom Fungi. This includes a large number of ubiquitous organisms, a small number of which can be pathogenic in humans. Examples of fungi include yeasts, moulds and mildew.

Granulation tissue: The pink/red, moist, shiny tissue that glistens and is composed of new blood vessels, connective tissue, fibroblasts, and inflammatory cells that fills an open wound when it begins to heal. It typically appears deep pink or red with an irregular, granular surface.[97, 391]

Hypergranulation: Hypergranulation is an increase in the proliferation of granulation tissue such that the tissue progresses above or over the wound edge and inhibits epithelialisation. It presents as raised, soft/spongy, shiny, friable, red tissue.[20] Also referred to as over granulation.

Induration: Hardening of the skin soft tissue around a wound due to inflammation that may be due to secondary infection.[97]

Inert: An inert solution is one that is considered to be biologically inactive.

Infection: When the quantity of microorganisms in a wound become imbalanced such that the host response is overwhelmed and wound healing becomes impaired.[44] Transition from non-infected to infected is a gradual process determined by the quantity and virulence of microbial burden and the individual's immune response.[12]

Local infection: Local infection refers to the presence and proliferation of microorganisms within the wound that evoke a response from the host 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.[20]

Lymphangitis: Inflammation of lymph vessels, seen as streaking, linear erythema running proximally from a site of infection toward lymph nodes. Presentation reflects inflammation of the underlying superficial lymphatic system. Most often associated with acute bacterial infections including *S. aureus* and *S. pyogenes*, usually requiring management with systemic antibiotics.[392]

Maceration: Maceration refers to wrinkled, soggy and/or soft periwound skin occurring due to exposure to moisture. Macerated periwound skin usually presents as white/pale and is at increased risk of breakdown.[20]

Microbial burden: Microbial burden is the number of microorganisms in a wound, the pathogenicity of which is influenced by the microorganisms present (i.e. the species/strain), their growth and their potential virulence mechanisms.[20]

Microorganism: An organism that is microscopic in size (i.e. too small to see with the naked eye) including bacteria, fungi, yeasts, archaea and parasites. Although viruses are not considered to be living organisms, they are often included when using the general term 'microorganism'.

Necrotic tissue/necrosis: Dead (devitalised) tissue that is dark in colour and comprised of dehydrated, dead tissue cells. Necrotic tissue acts as a barrier to healing by preventing complete tissue repair and promoting microbial colonisation. It is usually managed with debridement, but only after a comprehensive assessment of the individual and their wound.[97, 148, 389, 393]

Osteomyelitis: Infection of the bone that occurs through infection of the bloodstream or from a wound that allows bacteria to directly reach bone.[97]

Periwound: The skin and tissue immediately adjacent to the wound edge extending out 4cm and including any skin and tissue under the wound dressing.[394] The periwound region can be affected by moisture (e.g. maceration and excoriation) or may be dry, or develop hyperkeratosis, callus or eczema.[394] The periwound region can be indicative of the wound infection (e.g. erythema, warmth and swelling indicates potential wound infection).[394]

pH: A measure on a scale from 0–14 of acidity or alkalinity, with 7 being neutral, greater than 7 being more alkaline and less than 7 being more acidic. The skin has a natural pH of around 5.5.

Phagocytosis: A cellular process by which certain living cells ingest and destroy other large cells or particles. Phagocytosis is a critical first line component of the host's defence, with phagocytes (e.g. neutrophils and macrophages) detecting and binding to the cell surface of invading microorganisms in order to eradicate them. The process of phagocytosis also initiates other host immune responses, including the release of proinflammatory cytokines.[395]

Planktonic bacteria: Unicellular bacteria growing in a free-living environment, meaning they are not part of a structured community or biofilm.[396]

Pocketing: Pocketing occurs when granulation tissue does not grow in a uniform manner across the entire wound base, leading to a dead space that can potentially harbour microorganisms.[20]

Potable water: Water that is of a quality suitable for drinking, cooking and bathing. Unless the water supply is known to be of safe for consumption, it should be considered non-potable. Tank water,

pool water and dam water may or may not be of potable quality.[397]

Prophylaxis: The use of one or more measures to prevent the development of specific disease.[398] In the context of wound infection, prophylactic interventions can include topical antiseptic use and debridement. Prophylactic antibiotics are sometimes used to prevent surgical site infection; however, antimicrobial stewardship should guide prescribing to prevent overuse. For most procedures, antibiotic prophylaxis is not recommended. Appropriate indications include pre-surgical infection, high risk of post-surgical infection (e.g. contaminated surgery) or when consequences of infection are high (e.g. cardiac valve surgery).[399]

Pyrexia: Abnormal elevation of the core body temperature (above 38.3°C), usually occurring due to the host's inflammatory response to infection.[400, 401]

Psychometric properties: A term that encompasses the reliability and validity of measurement scales, referring to the adequacy and accuracy of the measurement processes.[402]

Sepsis: Sepsis is suspected infection with acute organ dysfunction, characterised by a range of signs and symptoms, arising from an overwhelming host response to bacterial, fungal or viral infection.[403] Sepsis occurs on a wide spectrum, with the most severe being septic shock and imminent risk of death. Presentation of sepsis varies and can be influenced by age, comorbidities and time since onset.[404] Signs and symptoms can include excessive pain, confusion or disorientation, shortness of breath, shivering, high fever; high heart rate, and clamminess, often with local signs such as necrotising soft tissue.[404]

Slough: Slough is nonviable tissue of varying colour (e.g. cream, yellow, greyish or tan) that may be loose or firmly attached, slimy, stringy, or fibrinous.[20]

Spreading infection: Spreading infection arising from a wound refers to microorganisms spreading from the wound into adjacent or regional tissues, evoking a response in the host 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.[12]

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.[20]

Surfactant: A wound cleansing surfactant is a hydrophobic/lipophilic agent that reduces the surface tension between liquid and debris, slough and/or biofilm in a wound. The reduction in surface tension better disperses the liquid, improving the cleansing effect.[20]

Undermining: An area of tissue destruction extending under intact skin along the periphery of a wound. It can be distinguished from a sinus tract in that it involves a significant portion of wound edge.[97, 391, 405]

Wound culture: A sample of tissue or fluid taken from the wound bed for laboratory testing. In the laboratory the sample is placed in a substance that promotes growth of organisms and the type and quantity of organisms that grow is assessed by microscopy.[45, 406]

Wound cleansing: Wound cleansing is actively removing surface contaminants, loose debris, non-attached non-viable tissue, microorganisms and/or remnants of previous dressings from the wound surface and its surrounding skin.[20]

Wound dressing procedure: The process of undertaking therapeutic cleansing, preparation of the wound bed for healing and protection of the wound with a wound dressing (i.e. the process referred to as 'changing a wound dressing'). The procedure, which can be performed with differing considerations to asepsis, includes distinct steps and phases.[337, 407]

14 Methodology

This edition of Wound Infection in Clinical Practice is underpinned by a targeted literature search to identify relevant research published since the previous edition in 2016. The development team used a Search Builder to develop searches using MeSH terms and EBSCO terms that were then adapted for other databases. Key concepts searched were:

Wounds, infection, biofilms, debridement, cleansing, antimicrobials (including antiseptics and antibiotics), diagnosis, asepsis, holism

Controlled vocabulary searches were developed for each of the key concepts above. Literature for each section of this document was identified using the searches for each relevant concept for that section combined as appropriate. Searches were conducted in major medical databases: Medline, PubMed, Embase, CINAHL and the Cochrane Library. The search was limited to articles published in database-listed journals since 2016 in English language. After identification, publications were screened for their relevance to the project and grouped according to the concepts for which they provided evidence. References identified for the previous edition of this document (2016)[12] were re-screened for relevance and significance in the context of the expanding body of evidence. Publications considered to provide strong research and/or unique information were reviewed more thoroughly by the IWII experts. Additional publications known to the IWII experts were added to those identified in the literature search, including any previously unidentified seminal publications.

CLINICAL EVIDENCE ON TOPICAL ANTISEPTIC THERAPIES

To explore the evidence on the clinical efficacy of antimicrobial therapies, the development team identified clinical questions and conducted PICO searches to identify relevant evidence. The PICO elements are outlined in Table 18. The search identified literature published up to March 2021 in English language.

Table 18: PICO elements for clinical efficacy of topical antiseptics

Preparation	Evidence from reviews and randomised and/or controlled trials
Population	■ People with wounds with infection confirmed by quantitative measures ■ People with wounds with clinical signs and symptoms of infection
Interventions	■ Topical antimicrobial therapies: Alginate gels, Chlorhexidine, DACC, honey, iodine preparations, PHMB, silver preparations, super oxidised solutions and OCT
Comparators	■ Topical antiseptic application versus no or inactive topical application ■ Comparisons between different topical antiseptics
Outcomes	■ Reduction in microbial burden measured using laboratory evaluation ■ Reduction in clinical signs and symptoms ■ Improvement in tissue type in the wound bed ■ Complete wound healing – complete wound closure within 8–12 weeks

A scoping search was undertaken to determine the volume and types of literature providing evidence on efficacy of topical antiseptics. Due to the high volume of evidence available, including a range of systematic reviews that provided overviews of the primary evidence, inclusion was limited to existing systematic reviews in which critical appraisal of primary studies had been performed.[408] Systematic reviews were appraised using the AMSTAR-2 tool[409] and data was extracted to summary tables. Randomised controlled trials and non-randomised controlled comparative trials published after the most recently published systematic reviews were also considered. Studies without a comparator (e.g. non-comparative cohort studies, case series and case reports) were not considered. The quality of

studies was appraised using Cochrane Collaboration risk of bias (RoB) appraisal tools[408] relevant to the study design (RoB 2 tool[410] and ROBINS-I tool[411]).

For each topical antiseptic intervention and clinical outcome, evidence from systematic reviews, RCTs and controlled trials is reported in summary in *09 Topical Antimicrobial Therapy*, including certainty of the evidence[408] based on the critical appraisal. In this document, the ranking system based on guidance appropriate to each appraisal tool, summarised in Table 19 has been used. The full search strategy, critical appraisal results and data extraction tables are available as additional resources on the IWII website.

Table 19: Evidence ranking scale
High certainty
Moderate certainty
Low and critically low certainty

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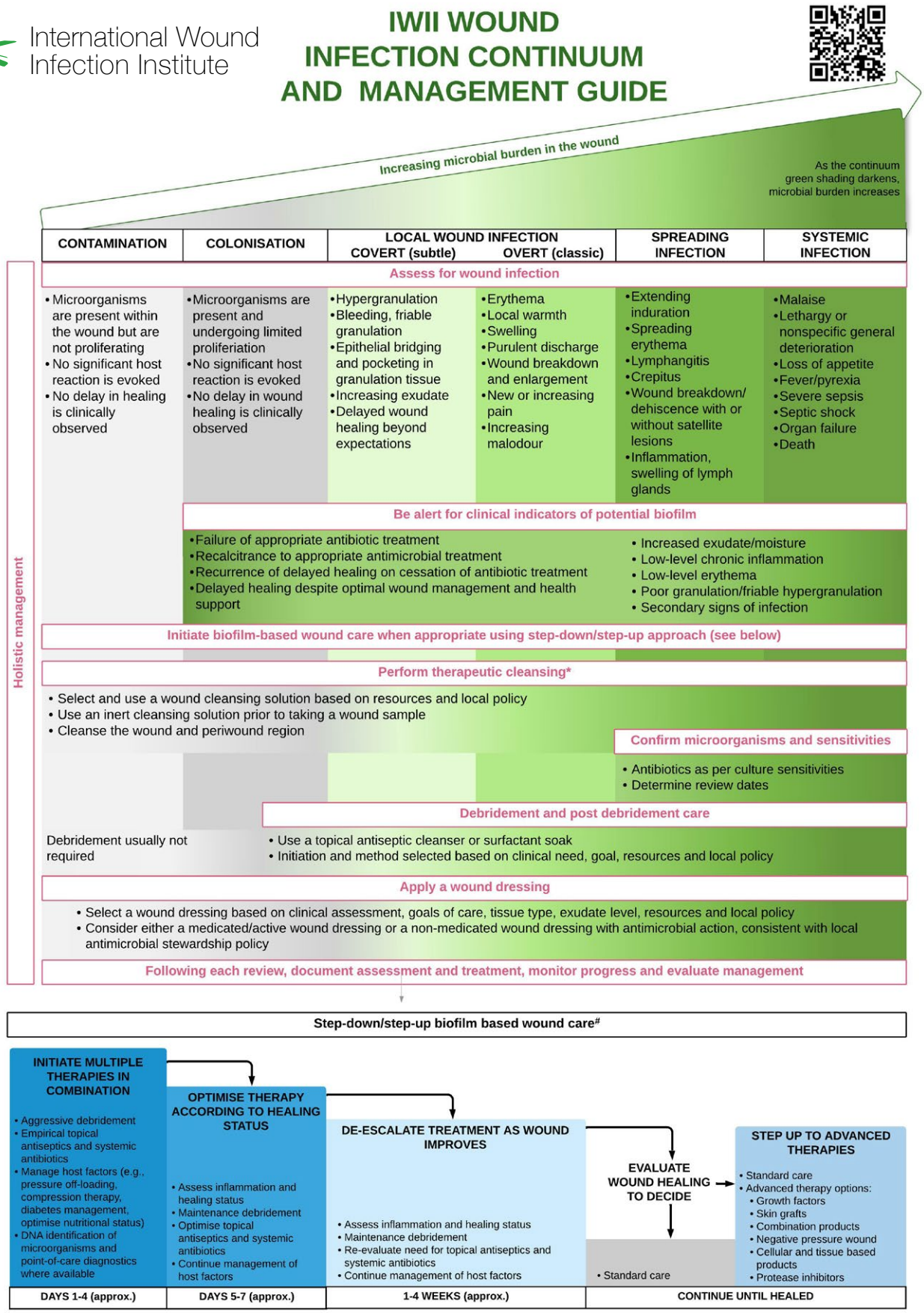

* refer to *Aseptic technique when performing a wound dressing procedure.*

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Notes

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