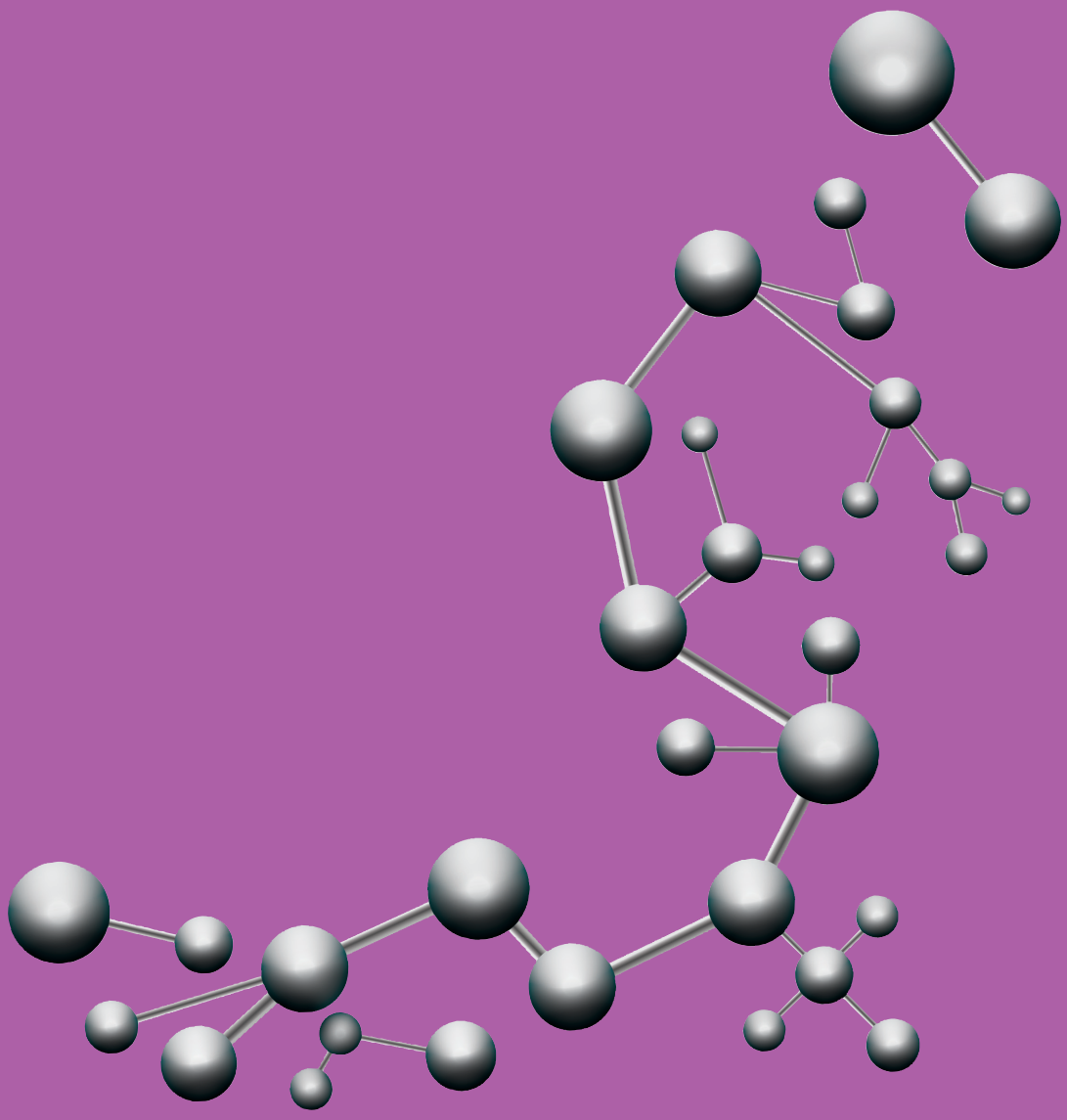
INTERNATIONAL
CONSENSUS

APPROPRIATE USE OF SILVER DRESSINGS IN WOUNDS



an expert working group consensus

Wounds INTERNATIONAL

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FOREWORD

Topical antimicrobial dressings, including those that contain silver, are used to prevent or manage infection in a wide range of wounds. Although silver dressings have been used extensively, a recent study[1] and two Cochrane reviews[2,3] have concluded that there is insufficient evidence to show that silver dressings improve healing rates. The overall effect has been to cast doubt into the minds of healthcare purchasers and to cause restrictions in the availability of silver dressings worldwide. There is growing concern amongst clinicians that arbitrary withdrawal of silver dressings could lead to increased morbidity and prolonged treatment time relating to uncontrolled wound bioburden.

A group of experts from Europe, North America, the Far East, South Africa and Australia met in December 2011 to provide internationally-recognised guidance for the proper use of silver dressings, based on experience in clinical practice and all the available evidence. This document presents the mechanisms by which silver dressings work, the relationship of *in vitro* and *in vivo* evidence to clinical practice and provides a rationale for cost-effective management.

Following the consensus meeting, a draft document was produced, which underwent extensive review by the expert working group. Additional international experts were also consulted to reflect practice across different parts of the world. This culminated in a consensus by all members of the extended expert working group on all statements presented in the document.

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Silver dressings — current issues

COMMON TERMS EXPLAINED

Bacteriostatic: prevents bacteria from growing or reproducing

Bactericidal: kills bacteria

Oligodynamic: active or effective in very small quantities

In vivo: experimentation on a whole living animal

In vitro: experimentation on components of an animal or organism

Antimicrobial tolerance: bacteria in a biofilm may take on a dormant state in which their slower metabolism makes them less susceptible to the effects of antimicrobials

Antibiotic resistance: the ability of bacteria to avoid harmful effects of antibiotic agents by undergoing genetic changes

THE HISTORY OF SILVER

The topical antimicrobial agent silver has been used for hundreds of years in wound care[4]. For example, silver has been used to prevent or manage infection in its solid elemental form (eg silver wire placed in wounds), as solutions of silver salts used to cleanse wounds (eg silver nitrate solution), and more recently as creams or ointments containing a silver–antibiotic compound (silver sulfadiazine (SSD) cream).

Silver nitrate solution is less widely used nowadays, but SSD cream has been an important part of burns management for many years[5]. SSD cream, however, is relatively short-acting, requires reapplication at least daily, and is time-consuming and messy to apply and remove.

In recent years, a wide range of wound dressings that contain elemental silver or a silver-releasing compound have been developed (see Appendix 1, page 20). These dressings have overcome some of the problems associated with the first silver preparations. They are easier to apply, may provide sustained availability of silver, may need less frequent dressing changes, and may provide additional benefits such as management of excessive exudate, maintenance of a moist wound environment, or facilitation of autolytic debridement[6].

The use of silver dressings in wound care has recently been faced with considerable challenges. These include a perceived lack of efficacy and cost effectiveness, and questions about safety[1–3,7,8]. In some healthcare settings, these challenges have led to restrictions in the availability or complete withdrawal of silver dressings[9,10]. This has left some clinicians in the frustrating position of not being able to use silver dressings for patients who may find them beneficial.

In the context of increasing resistance to antibiotics and the dramatic fall in the number of antibiotics in development, restriction of other potentially useful antimicrobial treatments such as silver dressings is particularly unfortunate[11,12]. Topical antiseptics, such as silver, differ from antibiotics: they have multiple sites of antimicrobial action on target cells and therefore a low risk of bacterial resistance[13]. As a result, antiseptics have the potential to play an important part in controlling bioburden in wounds while limiting exposure to antibiotics and reducing the risk of development of further antibiotic resistance. See Box 1 below for more information on antimicrobial agents.

BOX 1: Antimicrobial agents (modified from[14–16])

Antimicrobial – any agent that kills or prevents the multiplication of microorganisms, eg bacteria or fungi. Antimicrobials may be antibiotics, antiseptics or disinfectants

Antibiotics – agents that act selectively against bacteria and may be administered systemically or sometimes topically (although topical antibiotics are not recommended for wounds). They usually have one specific target of disruptive activity in bacterial cells and act against a narrower range of bacteria than antiseptics. Development of resistance to antibiotics is an increasing problem

Antiseptics – chemical agents that can be applied topically to skin or wounds. They are relatively non-selective agents that inhibit multiplication of, or kill, microorganisms. They may also have toxic effects on tissue cells, which has led to controversy and reduced their widespread use. Development of resistance to antiseptics is unknown in wound care. Antiseptics are often referred to as 'topical antimicrobials' even though the term also applies to topical antibiotics

Disinfectants – relatively non-selective agents often with multiple sites of action that kill a wide range of microorganisms including bacteria and fungi. Disinfectants are generally not suitable for use on body tissues because they are toxic to human cells

Challenging common misperceptions about silver

Misperception 1: 'Silver dressings don't improve healing rates'
The proportion of wounds that heal completely is a common endpoint in clinical studies of wound care and is insisted upon by regulatory bodies such as the Food and Drug Administration (FDA) of the USA. Given that chronic wounds are difficult to heal, the appropriateness of such an endpoint has been questioned[17–20]. The aim of treatment with silver dressings is to reduce wound bioburden, treat local infection and prevent systemic spread: their main purpose is not to promote wound healing directly. Clinical guidelines recommend that silver dressings are used for wounds where infection is already established or an excessive wound bioburden is delaying healing ('critical colonisation' or 'pre-infection'), and that they are used for short periods before re-evaluation[16].

Two influential Cochrane reviews and a high profile randomised controlled trial (RCT) of silver dressings have concluded that silver dressings do not improve healing rates[1–3]. However, the use of silver dressings in the reviews and in the RCT was not always as indicated by the manufacturers: in some cases they were used for extended periods and sometimes on wounds that were not infected or did not show evidence of heavy bioburden. The overall effect has been to cast doubt in the minds of healthcare purchasers on the efficacy of silver.

The experience of many clinicians, and more recent systematic reviews and meta-analyses, have confirmed positive effects of silver dressings when used appropriately[21–23]

Misperception 2: 'Silver dressings cause systemic toxic effects such as argyria'
Silver dressings occasionally cause local skin discolouration or staining which is harmless and usually reversible[24,25]. This discolouration is not true systemic argyria, which is rare and usually related to oral ingestion of silver solutions as an alternative health practice[26, 27]. True argyria is the result of deposition of silver compounds in the skin and internal organs and presents as generalised blue-grey skin discolouration, particularly in light exposed areas[24]. Argyrosis occurs when silver is deposited in the cornea or conjunctiva. True argyria and argyrosis are unsightly and irreversible, but not usually pathological or life threatening[24,28]. The total amount of silver required to cause argyria is unknown, but total body contents of 3.8–6.4g have been suggested[24].

Silver dressings are unlikely to cause true argyria because only low levels of silver are presented for systemic absorption[28]

Misperception 3: 'Silver dressings are toxic to wounds and delay healing'
Some *in vitro* studies have found that some silver-containing dressings are cytotoxic to keratinocytes and fibroblasts, and delay epithelialisation in animal wound models[24,29]. Conversely, other studies have found some silver preparations not to be toxic and have suggested that silver has actions that may promote healing[24,29-31]. Given the conflicting evidence, but wealth of positive clinical experience of silver, a pragmatic argument could be made that silver dressings should be used appropriately, in common with recommendations for antimicrobial dressing use.

Silver dressings should not be used on wounds where bioburden is not a problem, ie they should be reserved for use in wounds with or at risk of high bioburden or local infection

Misperception 4: 'Bacteria become resistant to silver'
The prevalence of resistance to silver is unknown, but resistance appears to be rare and much less common than might be expected given the considerable time that silver preparations have been in use and the widespread distribution of low levels of silver in the environment[25,32–35]. Silver has multiple actions against microbial cells. This reduces the chance that resistance to silver will develop. In contrast, antibiotics generally have a single target site and hence bacterial cells may more easily develop resistance[36]. Clinically, there may be alternative explanations for apparent silver resistance. For example, infected wounds that appear not to respond to an antimicrobial dressing may have a deeper unrecognised infection, may contain biofilm that facilitates antimicrobial tolerance, or may have an inadequately managed underlying comorbidity[37].

An apparent lack of response to silver does not relate to resistance, rather to inappropriate treatment of the underlying infection and/or wound aetiology

Misperception 5: 'Silver dressings could make bacteria resistant to antibiotics'
There has been concern that the use of silver dressings may lead to the emergence of bacteria that are resistant to antibiotics[8,13,38,39]. Although this is theoretically possible, there is no direct evidence that cross-resistance between silver and antibiotics has occurred[13,40].

The major cause of antibiotic resistance remains misuse or overuse of antibiotics themselves

Misperception 6: 'Silver dressings shouldn't be used in children'
Reports of increased blood silver levels in children with burns and epidermolysis bullosa have caused concern and withdrawal of silver dressings in some places[41–44]. However, it is possible that some paediatric wounds may benefit from use of silver.

Silver dressings should be used in the treatment of children with caution and the dressings should not be used for more than two weeks without good clinical reasons[45]

Misperception 7: 'Silver dressings are bad for the environment'
Concerns have been raised that silver released into the environment may be harmful[8]. Certainly, silver is used worldwide in a wide range of technologies and the environmental impact of silver is not clear[28]. A main silver dressing producer has estimated that it uses 0.0008% of global annual silver consumption[46].

The proportion of total silver production that is used in dressings is very small

Misperception 8: 'Silver dressings are too expensive'
The assessment of the cost effectiveness of wound treatments is not straightforward. The total cost of wound care involves many direct and indirect costs, and some costs are difficult to measure, eg reduced productivity at work or in the home, reduced quality of life, and social isolation[47]. Several silver dressing studies have demonstrated beneficial effects on overall cost of wound management and on quality of life parameters[48–51].

Silver dressings are generally no more expensive than other types of antimicrobial dressings

Understanding silver dressings

*Elemental silver in very small crystals that are about 10–100 nanometres (nm) in diameter (a nanometre is one billionth of a metre)[28]

Silver is found in dressings in a number of forms:

- **elemental silver** – eg silver metal, nanocrystalline silver*
- **an inorganic compound** – eg silver oxide, silver phosphate, silver chloride, silver sulfate, silver-calcium-sodium phosphate, silver zirconium compound, SSD (Box 2)
- **an organic complex** – eg silver-zinc allantoinate, silver alginate, silver carboxymethylcellulose[30,37,52].

BOX 2: SSD dressings and silver dressings – the difference

Dressings that contain SSD are often classified with other silver-containing dressings even though they are fundamentally different. The sulfadiazine element of SSD is an antibiotic and so SSD dressings contain two antimicrobial agents. Distinguishing the antimicrobial effects of the two agents is difficult and makes comparison with dressings that contain silver alone problematic. Difficulties and confusion may arise when study findings relating to the efficacy and safety of SSD are extended to silver dressings in general

The silver component of dressings may appear:

- as a **coating** – on one or both external surfaces of the dressing (elemental or nanocrystalline silver)
- **within the structure of the dressing** – either as a coating on dressing materials (elemental or compound silver), within the spaces of the dressing materials (elemental or compound silver), or as a compound that forms part of the dressing structure (eg silver alginate)
- as a **combination** of these.

Silver on the surface of the dressing may come into contact with the wound where it exerts the antimicrobial action. Silver within the dressing structure acts on bacteria absorbed into the dressing with wound exudate, but is likely also to diffuse to some extent into the wound[53].

The total amount of silver in dressings varies considerably[53], but in a wound environment the interaction of silver ions with wound components such as chloride ions and proteins, means that the amount of silver delivered to a wound does not correlate with the amount of silver contained in the dressing[37]. In addition, although in some laboratory experiments very low concentrations, eg one part per million (1ppm) of silver ions or less, have been shown to be effective against bacteria[54], it is unclear how silver content and availability measured in experimental settings relate to clinical performance[53].

Although attempts have been made to quantify the availability of silver from silver dressings, such measurements are currently of very limited value in predicting clinical efficacy

Mode of action of silver

HOW DOES SILVER WORK?

In metallic (elemental) form, silver is unreactive and cannot kill bacteria. To become bactericidal, silver atoms (denoted as Ag or Ag^0) must lose an electron and become positively charged silver ions (Ag^+). Elemental silver ionises in air, but ionises more readily when exposed to an aqueous environment such as wound exudate. In contrast, silver compounds contain positive silver ions bound to negatively charged ions or molecules. When exposed to aqueous environments, some of the silver ions become detached from the compound.

Silver ions are highly reactive and affect multiple sites within bacterial cells, ultimately causing bacterial cell death. They bind to bacterial cell membranes, causing disruption of the bacterial cell wall and cell leakage. Silver ions transported into the cell disrupt cell function by binding to proteins and interfering with energy production, enzyme function and cell replication[54,55]. Silver ions are active against a broad range of bacteria, fungi and viruses[13], including many antibiotic-resistant bacteria, such as meticillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococci* (VRE)[56].

Studies of the effects of silver dressings on experimental models of biofilms (Box 3) have suggested that silver may reduce bacterial adhesion and destabilise the biofilm matrix[57], as well as kill bacteria within the matrix and increase susceptibility of bacteria to antibiotics[58–60].

Other effects of silver

Some laboratory studies have suggested that silver may have beneficial effects on wound healing other than the control of bioburden alone. For example, silver nitrate, nanocrystalline silver, and some silver-containing dressings have been found to have anti-inflammatory effects and to encourage blood vessel formation (neovascularisation)[24,28,52,61]. The clinical relevance of these findings is not yet known.

WHAT HAPPENS TO SILVER?

Only a small proportion of silver presented to a wound site in a dressing is involved in antimicrobial action. Most of the rest remains within the dressing or binds to proteins in the wound or wound debris[4,52]. Very little is systemically absorbed[28].

Even if absorbed systemically, silver is excreted mainly via the biliary route in faeces. Some is also excreted in urine[24]. Silver is not absorbed into the central or peripheral nervous systems[24].

BOX 3: What are biofilms and how should they be managed?

Biofilms are complex microbial communities, containing bacteria and sometimes also fungi, which are embedded in a protective polysaccharide matrix. The matrix attaches the biofilm to a surface, such as a wound bed, and protects the microorganisms from the host's immune system and from antimicrobial agents such as antiseptics and antibiotics[62]. Biofilms are commonly present in chronic wounds, and are thought to contribute to, and perpetuate, a chronic inflammatory state that prevents healing[63].

Currently, the management of biofilms involves:

- reduction of biofilm burden through debridement and/or vigorous cleansing to remove the biofilm and the dormant (persister) bacteria
- prevention of biofilm reformation through the use of topical antimicrobials to kill planktonic (free-floating) bacteria[62].

Further research is required to further understand how biofilms form and to determine the best approach to treatment. In particular, the role of antimicrobial cleansing agents and the potential benefits of rotating the topical antimicrobial agent used need to be investigated

Recommendations for the appropriate use of silver dressings

NOTE: In this document, dressings containing antiseptic agents are referred to as 'antimicrobial dressings' (see Box 1, page 1)

This section summarises the recommendations for the appropriate use of silver dressings agreed by the consensus group

The major roles for antimicrobial dressings such as silver dressings in the management of wounds are to:

- **reduce bioburden** in acute or chronic wounds that are infected or are being prevented from healing by microorganisms
- **act as an antimicrobial barrier** for acute or chronic wounds at high risk of infection or re-infection[14].

REDUCING BIOBURDEN

The effects of bacteria in a wound are often described as a continuum which extends from **contamination** (the presence of bacteria without problems), to **colonisation** (the presence of multiplying bacteria), to **infection** with tissue invasion[14] (Figure 1). Infection may be localised to the wound, spread into nearby tissues, or cause systemic illness such as systemic inflammatory response syndrome (SIRS) or multiple organ dysfunction syndrome (MODS).

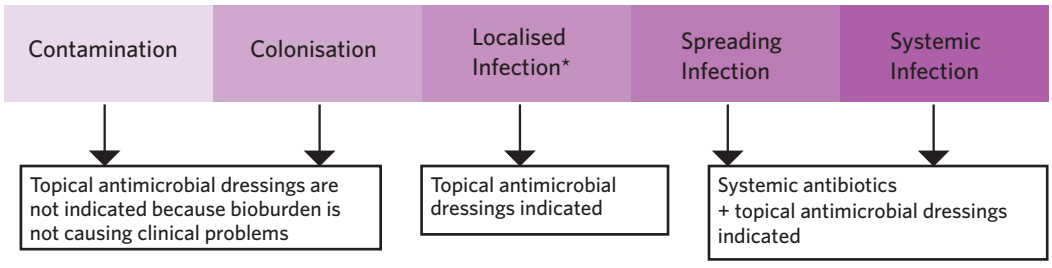
The classic signs of local infection are pain, heat, swelling, redness and loss of function, and may be accompanied by purulent discharge, pyrexia and malodour. However, in chronic wounds, the patient often has comorbidities that suppress the signs of inflammation[14,64]. As a result, identifying infection in chronic wounds may be difficult and clinicians need to rely on other signs and symptoms (see Box 4, page 7). This problem prompted the term 'critical colonisation' to be devised. The term is not universally accepted and some clinicians prefer 'covert infection' or 'subclinical infection' to convey a similar concept[64].

In practice, most healthcare practitioners rely on clinical signs and symptoms to diagnose wound infection[64,65]. Even where microbiological services are readily available, it is not recommended that microbiological tests are performed routinely[14].

Silver dressings may be used on acute wounds, such as traumatic wounds (including burns) or surgical wounds, and chronic wounds that present with localised (overt or covert), spreading or systemic infection (Figure 1). Manufacturer's instructions should be followed regarding wound cleansing and method of application of silver dressings (eg recommended cleansing materials and whether hydration of the dressing is required).

Inflamed wounds may be particularly suited to management with silver dressings because of the anti-inflammatory effects observed in experimental studies[24,66,67].

Figure 1 | When to implement antimicrobial dressings (adapted from[14,15,64])



*Including critical colonisation (also known as 'covert' or 'silent' infection or 'pre-infection'). Patients with chronic wounds often have comorbidities that suppress the signs of inflammation and make identification of infection difficult.
NB: Treatment for wound infection should take place in the context of standard care for the wound type, eg debridement, offloading and correction of underlying factors such as malnutrition, ischaemia and hyperglycaemia to enhance the patient's healing potential and ability to fight infection.

Box 4: Signs and symptoms of localised, spreading and systemic infection in wounds. Reproduced with permission from[14]

Localised infection	Spreading infection
ACUTE WOUNDS eg surgical or traumatic wounds, burns	
■ Classical signs and symptoms: – new or increasing pain – erythema – local warmth – swelling – purulent discharge ■ Pyrexia ■ Delayed or stalled healing ■ Abscess ■ Malodour	As for localised infection, plus: ■ Further extension of erythema ■ Lymphangitis ■ Crepitus in soft tissues ■ Wound breakdown/dehiscence
CHRONIC WOUNDS eg diabetic foot ulcers, venous leg ulcers, arterial leg/foot ulcers, pressure ulcers	
■ New, increased or altered pain ■ Delayed (or stalled) healing ■ Periwound oedema ■ Bleeding or friable granulation tissue ■ Distinctive malodour or change in odour ■ Wound bed discolouration ■ Increased, altered or purulent exudate ■ Induration ■ Pocketing or bridging	As for localised chronic infection, plus: ■ Wound breakdown ■ Erythema extending from the wound edge ■ Crepitus, warmth, induration or discolouration spreading into periwound area ■ Lymphangitis ■ Malaise or non-specific deterioration in the patient's general condition
SYSTEMIC INFECTION	
Sepsis: documented infection with pyrexia or hypothermia, tachycardia, tachypnoea, raised or depressed white blood cell count **Severe sepsis**: sepsis and multiple organ dysfunction	

A diagnosis of localised, spreading or systemic infection should be documented in the patient's health records along with treatment objectives, baseline data and rationale for use of the silver dressing, together with the timeframe for reviewing management[16].

Silver dressings should be used in the context of accepted standard wound care which involves a holistic assessment of the patient and the wound, management of underlying comorbidities, and wound bed preparation[68]

Silver dressings should not be used in the absence of localised (overt or covert), spreading or systemic infection, unless there are clear indicators that the wound is at high risk of infection or re-infection. Box 5 summarises the situations where silver dressings should not be used.

BOX 5: When not to use silver dressings

- In the absence of signs of localised (overt or covert), spreading or systemic infection
- Clean surgical wounds at low risk of infection, eg donor sites, closed surgical wounds
- Chronic wounds healing as expected according to comorbidities and age
- Small acute wounds at low risk of infection
- Patients who are sensitive to silver or any of the dressing components
- Wounds being treated with enzymatic debridement
- During pregnancy or lactation
- When contraindicated by the manufacturer, for example, some manufacturers recommend that their silver dressings are not used during magnetic resonance imaging (MRI), or on/near body sites undergoing radiotherapy

THE TWO WEEK 'CHALLENGE'

It has been recommended that antimicrobial dressings should be used for two weeks initially and then the wound, the patient and the management approach should be re-evaluated[16]. The consensus group has suggested that this initial two week period can be seen as a two week 'challenge' period during which the efficacy of the silver dressing can be assessed.

If after two weeks:

- **there is improvement in the wound, but continuing signs of infection** – it may be clinically justifiable to continue the silver dressing with further regular reviews
- **the wound has improved and the signs and symptoms of wound infection are no longer present** – the silver dressing should be discontinued
- **there is no improvement** – the silver dressing should be discontinued and consideration given to changing the dressing to one that contains a different antimicrobial agent and if the patient is unwell using a systemic antibiotic and re-evaluating possibly untreated comorbidities.

Once the bioburden is under control and the wound is improving, a non-antimicrobial dressing should be considered.

PROPHYLACTIC USE

Antimicrobial dressings such as silver dressings may be used as a barrier to microorganisms in wounds at high risk of infection or re-infection[69]. Examples of such wounds may include burns, surgical wounds, pressure ulcers near the anus, wounds with exposed bone, or wounds in patients who are immunocompromised, have poor circulation, unstable diabetes or neoplastic disease[69].

There may also be a role for antimicrobial dressings in preventing entry of bacteria to medical device entry/exit sites such as tracheostomy sites, externally placed orthopaedic pins, post-surgical drains, chest drains, nephrostomy sites, central venous lines, dialysis catheters, and epidural catheters[70-74]. The use of silver dressings in this way is yet to be fully defined and evaluated.

When a silver dressing is used for prophylaxis, the rationale should be fully documented in the patient's health records and use of the dressing reviewed regularly, eg every two weeks

APPLICATION TO PRACTICE – TIPS FOR USING SILVER DRESSINGS

- Conduct a comprehensive assessment of the patient, wound and environment before deciding whether a silver dressing is appropriate
- Document the rationale for using a silver dressing in the patient's healthcare records
- Choose the silver dressing on the basis of patient and wound needs, ie exudate level, wound depth, need for conformability, odour control, ease of removal and safety
- For infected wounds, initial use should be for a two week challenge
- Continued use of silver dressings should include regular review
- Use silver dressings in the context of a wound management protocol that includes wound bed preparation as appropriate for the wound type
- Follow manufacturer's instructions regarding indications, contraindications, method of application, wound cleansing procedures, need for dressing moistening before application, and use in patients undergoing MRI or radiotherapy
- Use silver dressings with caution in children and very large wounds
- Dressings containing SSD should not be used in patients with sensitivity to sulfonamide antibiotics or hepatic/renal impairment, or in pregnancy, during lactation or in newborns

Choosing a silver dressing

Differentiating between the many silver dressings that are available can be perplexing because of the variety of antimicrobial testing methods and clinical endpoints used in studies, and the complexity of comparing the data derived.

In practice, the factors most likely to influence choice of a silver dressing are:

- availability and familiarity
- the additional needs of the patient and the wound, eg level of exudate production and condition of the wound bed
- whether a secondary dressing is required
- patient preference.

For example, high absorbency would be preferable for a wound producing high levels of exudate, activated charcoal for odour, and low adherence for a patient who experiences pain at dressing change. In addition, if a patient has an irregular wound bed, enhanced dressing conformability may prevent the formation of pools of exudate where bacteria might flourish beneath the dressing.

The duration of silver availability may also be important. In general, silver dressings are intended to provide sustained delivery of silver over several days, so reducing the need for frequent dressing changes. If dressing changes are planned to take place once weekly, use of a dressing that is known to continue releasing silver for seven days would be advisable.

Table 1 | *In vitro* tests of the antimicrobial efficacy of dressings, adapted from[75]

Test	Outline of method	Advantages	Disadvantages	Generalised results for silver
Diffusion assay/Zone of inhibition assay	■ A piece of dressing is placed on the surface of a medium inoculated with test bacteria and incubated for up to 24 hours ■ Antimicrobial efficacy is demonstrated by production of an area of impaired bacterial growth around the dressing – the zone of inhibition (measured in millimetres)	Simple to perform Widely available	Production of a zone of inhibition does not differentiate bacteriostatic and bactericidal activity Sometimes mistaken as bactericidal activity Wide variations in technique makes comparisons difficult	Not ideal for testing silver activity because silver reacts with components of test media
Minimum inhibitory concentration (MIC)	■ Test tubes containing a series of concentrations of the antimicrobial agent are inoculated with the bacterium of interest and incubated for up to 24 hours ■ The test tubes are examined for signs of bacterial growth: the lowest concentration to show no growth is the MIC ■ MIC_{50} and MIC_{90} are the concentrations required to inhibit bacterial growth by 50% and 90% respectively	Can be helpful in determining levels of antimicrobial agents for clinical use	Provides no information about bactericidal activity Highly dependent on growth medium	Bacteria have MICs for silver generally >1mg/l in complex test media (eg those containing organic matter and chloride)
Minimum bactericidal concentration (MBC)	■ After MIC is determined, the tubes that show no growth are inoculated into growth media and incubated for up to 24 hours ■ The lowest concentration of antimicrobial agent to completely prevent bacterial growth is the MBC	Can be helpful in determining levels of antimicrobial agents for clinical use	Provides no information on rate of kill	MBCs for silver have been found to range widely from 1mg/l upwards depending on the test medium used
Logarithmic (log) reduction	■ The antimicrobial agent is incubated with the test bacterium of a known culture density for 0.5–24 hours ■ At various times, bacteria are recovered and the antimicrobial agent is neutralised ■ Viable cells are counted and the number expressed as a logarithm (log) ■ The difference in logs before and after exposure to the agent is the log reduction ■ A log reduction of >3 (ie >99.9% of bacteria are killed) may be used to define an agent as bactericidal rather than bacteriostatic. Log reductions of >1 but <3 indicate that some bacteria have been killed	Most appropriate *in vitro* test for dressing assessment Can provide information on rate of kill May be predictive of clinical outcomes	If the silver is not correctly neutralised a false impression of efficacy may result	Log reductions for silver are hard to compare because of different incubation times and media used
Direct counts	■ Involves using a microscope to count bacteria following exposure to silver for a set length of time	Useful in assessing growth inhibition (but not bactericidal activity)	Limited to detection of ≤2 log reduction, ie cannot distinguish bacteriostatic and bactericidal effects	See disadvantages

Choosing a silver dressing: clinical and cost effectiveness evidence

When choosing a silver dressing, it is important to balance the needs of the patient, the wound and the environment, and to consider how the overall characteristics of the silver dressing meet the other needs of the patient, eg in terms of exudate handling, adherence and frequency of dressing change

ANTIMICROBIAL EFFICACY – *IN VITRO* EVIDENCE

Silver has been shown *in vitro* to have antimicrobial activity against a wide range of microorganisms, including resistant forms such as MRSA and VRE, and fungi and anaerobes[6,75-77]. The techniques used to test antimicrobial efficacy (see Table 1, page 9) are often not standardised[64], so that comparisons between different studies may not be possible or may lead to incorrect conclusions.

Direct comparisons of several different dressings have revealed differences in silver content, silver availability, and scope and degree of antibacterial efficacy[53,56,76,78]. One study found no correlation between silver content or amount of silver released and antimicrobial activity in an *in vitro* dissolution assay, indicating that silver dissolution from a dressing is not a predictor of antimicrobial activity[56].

Other studies have concluded that although silver content is important, many other factors influence the ability of a dressing to kill microorganisms, eg the distribution of silver within the dressing, the availability of silver from the dressing, the ability of a dressing to closely contact the wound surface (dressing conformability), the dressing's ability to absorb fluid, the construction of the dressing, and its chemical and physical form[53,79,80].

In vitro tests of the antimicrobial efficacy of silver dressings are unlikely to be truly representative of performance in a wound because of the complexity of the wound environment

CLINICAL EVIDENCE

Silver dressings have been assessed in many different types of studies. RCTs have been performed in a range of acute and chronic wounds (see Table 2, page 13) using a number of different endpoints. Some studies have found silver dressings to have positive effects on wound healing parameters[49,81-91], whereas others have found no significant difference from comparators[1,92].

Difficulties in interpreting and comparing studies arise from the small number of patients in some studies (which may cause issues of insufficient study power and problems with randomisation), and the wide range of different inclusion criteria, study protocols and endpoints used. It is therefore not surprising that some systematic reviews and meta-analyses (see Table 3, page 16) have come to differing conclusions or have failed to find sufficient comparable data.

Validity of endpoints

Many of the studies of silver dressings have included endpoints related to healing. However, more appropriate endpoints for silver dressings may relate to measurement of microbial burden or assessment of clinical indicators of infection[16].

Some RCTs involving silver dressings have used such endpoints:

- **Bacteriological endpoints** – an activated charcoal and silver dressing was found to reduce laboratory assessed bacterial load significantly more than the control foam dressing ($p<0.05$)[90]. Another study comparing silver dressings with SSD found that both produced similar reductions in bacterial colonisation[93]. A further study of a silver alginate versus a plain alginate dressing found a trend for a higher rate of improvement of bacteriological status for the silver dressing[94]

- **Clinical indicators of infection** – a study which examined pre-specified indicators of infection found that significantly more wounds treated with a silver dressing had no signs of heavy bacterial colonisation after four or eight weeks of treatment in comparison with the control ($p<0.05$)[83]. Another smaller study, which used clinical infection scores, found no significant difference between a silver and a control dressing after two weeks of treatment and observation[94].

Levels of evidence

RCTs are conventionally seen as providing a high level of evidence because randomisation minimises the risk of bias and counteracts placebo effect. Unfortunately, multicentre RCTs are expensive and time consuming, and so are less likely to be undertaken[30]. Pragmatically, therefore, judgement of efficacy needs to examine other evidence, such as observational studies, and expert and patient opinion. This approach is also being considered in other fields of medicine[95].

VULCAN study

A particularly influential and controversial study of silver dressings has been the VULCAN study[1,7]. This study randomised 213 patients with venous leg ulcers to receive either one of a number of silver-containing dressings or a clinician-selected non-antimicrobial control dressing. The main outcome measured was the rate of complete healing at 12 weeks. The study concluded that there was no statistically significant difference between the use of silver-containing dressings and the control dressings for the proportion of ulcers healed, time to healing or rates of recurrence. The cost-effectiveness analysis found a higher cost associated with the silver dressings.

Many commentators have been concerned that, despite the care involved in the study design, the conclusions are potentially misleading[18–20].

The major concern is that the study did not use silver dressings in line with current recommendations, and so could not be expected to provide clinically relevant information on efficacy. For example:

- Silver dressings are indicated for the management of wound bioburden, or to prevent infection in wounds that are at high risk. The study did not report risk of infection, and did not evaluate wounds either clinically or microbiologically for presence of infection
- Silver dressings are not intended to be used for extended periods, particularly if infection is not present. In the study, they were applied for 12 weeks
- The goal of care when using silver dressings is not wound healing; it is control of wound bioburden. Wound healing is therefore an inappropriate measure of efficacy.

The conclusion that routine use of silver dressings in venous leg ulcers cannot be justified is therefore not surprising. However, it is unfortunate that the study findings have been generalised to suggest that silver dressings do not work and to justify withdrawal of their availability to clinicians.

COST EFFECTIVENESS

Thorough assessment of the cost effectiveness of a healthcare intervention is complicated and considers many factors, including resource use, quality of life issues and economic parameters such as ability to work[6] and ideally should be conducted separately from clinical trials[44].

A number of studies have found that silver dressings are associated with factors that may be beneficial in terms of cost effectiveness, eg:

- reduced time to wound healing[81,96]
- shorter hospital stays[50,51]
- reduced dressing change frequency[48,49]
- reduced need for pain medication during dressing change[48]
- fewer MRSA bacteraemias resulting from MRSA-infected wounds[97].

A formal cost-effectiveness analysis of silver dressings is needed and awaited. However, a retrospective study of hospital costs for burns in paediatric patients found that total charges and direct costs were significantly lower for patients treated with a silver Hydrofiber dressing than for those treated with SSD ($p<0.05$ for both)[50]. Similarly, another RCT found that treatment of burns patients with a silver Hydrofiber dressing cost significantly less than did treatment with SSD[81].

In practice, healthcare reimbursement is compartmentalised and costs of clinician time are kept separate from resource costs. This means that even if a dressing is shown to save money overall by reducing time to healing, hospital stay or nursing time, controllers of dressing budgets may choose to restrict reimbursement to simple low cost dressings.

Healthcare budget providers should be encouraged to think broadly about the potential for wider cost savings by dressings shown to reduce healing time, hospital stay or nursing time (see Misperception 8, page 3)

FUTURE RESEARCH

Research into the clinical effectiveness of silver dressings is ongoing. Box 6 lists some particular research needs identified by the consensus group.

BOX 6: Future research

- Clarification of the relationship between dressing formulation and silver availability
- Elucidation of how silver availability affects clinical performance
- Better understanding of the relationship between silver availability, systemic absorption and potential for systemic effects
- Further studies of silver dressings using endpoints related to bioburden and clinical indicators of infection
- Formal quality of life and cost-effectiveness analyses
- Clarification of how to choose appropriate antimicrobial agents/dressings
- Improved understanding of the best way to use antimicrobial dressings, including silver dressings, in the prevention of infection or re-infection in wounds at high risk
- Development of less invasive diagnostic tests for infection
- Improved understanding of biofilms and how they should be managed

Table 2 | RCTs of silver dressings in acute and chronic wounds

The studies summarised here are representative of the literature on silver dressings and do not comprise an exhaustive literature search. Studies that used dressings containing SSD or SSD cream as the active agent have been omitted.

ACUTE WOUNDS			
Wound type	**Product(s)**	**Reference**	**Outcomes**
BURNS			
Partial thickness burns	Askina Calgitrol Ag (silver alginate) versus SSD cream (n=65)	Opasanon S, et al. *Int Wound J* 2010; 7(6): 467-71	Healing time in the dressing group was significantly shorter than in the SSD group (p<0.02) Dressing group had significantly lower pain scores, fewer dressing changes and less nursing time than the SSD group (p<0.02 for all)
Partial thickness burns	AQUACEL Ag (silver Hydrofiber) versus SSD cream (n=70)	Muangman P, et al. *Int Wound J* 2010; 7(4): 271-76	Time to wound closure was significantly shorter for the silver Hydrofiber dressing group than for the SSD group (p<0.02) Number of hospital visits was lower for the silver dressing group (p<0.001) and total cost was significantly lower for the dressing group (p<0.01)
Freshly grafted burns	ACTICOAT versus 5% sulfamylon-soaked burn dressings (n=20)	Silver GM, et al. *J Burn Care Res* 2007; 28(5): 715-19	The median number of dressing changes was lower in the ACTICOAT group (p<0.05) and average cost per patient was lower with ACTICOAT There was no statistical difference between the two groups in wound healing and infectious complications
Partial thickness burns	AQUACEL Ag versus SSD (n=84)	Caruso D, et al. *J Burn Care Res* 2006; 27(3): 298-309	The silver Hydrofiber dressing was associated with less pain and anxiety during dressing changes, and less burning and stinging during wear than SSD (p<0.05 for these outcomes) The proportion of patients with full epithelialisation was not significantly different between the two groups Average cost-effectiveness for the silver Hydrofiber dressing was $1409.06 and for SSD was $1967.95 per burn healed
Second degree burns	Silver nanoparticle dressing versus SSD cream or vaseline gauze (n=191)	Chen J, et al. *Zhonghua Wai Ke Za Zhi* 2006; 44(1): 50-52	Silver nanoparticles and SSD cream produced a similar reduction in bacterial colonisation of the wounds; in the vaseline gauze group colonisation increased Healing time for superficial second degree wounds was significantly shorter for the silver nanoparticle group than for the SSD or vaseline gauze groups (p<0.01)
Partial-thickness burns	ACTICOAT versus SSD (n=47)	Varas RP, et al. *J Burn Care Rehabil* 2005; 26(4): 344-47	Pain during wound care was significantly lower for the ACTICOAT group than for the SSD group (p<0.0001)
Burns	ACTICOAT versus silver nitrate solution (n=30)	Tredget EE, et al. *J Burn Care Rehabil* 1998; 19(6): 531-37	There were fewer cases of burn wound sepsis and secondary bacteraemias in the ACTICOAT treated wounds than in the silver nitrate treated wounds (5 vs 16 and 1 vs 5 respectively)
SURGICAL/TRAUMATIC WOUNDS			
Colorectal surgical wounds	Silver nylon dressing (Silverlon) versus gauze (n=110)	Krieger BR, et al. *Dis Colon Rectum* 2011; 54: 1014-19	The incidence of surgical site infection was significantly lower in the silver nylon group than in the control group (p=0.011)
Colorectcal surgical wounds	AQUACEL Ag versus no dressing (n=160)	Siah CJ, et al. *J Wound Care* 2011; 20(12): 561-68	The silver Hydrofiber dressing applied post-operatively for 7 days reduced bacterial colonisation at the surgical site in comparison with no dressing (p<0.001) The rates of surgical site infection between the silver dressing and no dressing groups were not statistically significantly different (superficial SSI p=0.118; deep SSI p=0.115)
Pilonidal sinus	Silver Hydrofiber versus dry sponge dressing until wound closure (n=43)	Koyuncu A, et al. *EWMA Journal* 2010; 10(3): 25-27	Number of dressings used and time to complete closure were significantly lower in the silver group than in the control group (p<0.05 for both outcomes)
Open surgical and traumatic wounds	AQUACEL Ag (silver Hydrofiber) versus povidone-iodine gauze for 2 weeks (n=67)	Jurczak F, et al. *Int Wound J* 2007; 4(1): 66-76	The silver dressing was significantly better than the iodine dressing for overall ability to manage pain, overall comfort, wound trauma on dressing removal, exudate handling and ease of use (all p<0.01) Rates of complete healing between the two groups were not significantly different
DONOR SITE WOUNDS			
Donor sites	AQUACEL Ag versus Glucan II (n=20)	Bailey S, et al. *J Burn Care Res* 2011; 3296): 627-32	There was no significant difference between the two groups in healing time, infection rate and cosmetic outcomes
Split-thickness donor sites (n=70)	AQUACEL Ag with a gauze covering versus AQUACEL Ag with a transparent film dressing (n=70)	Blome-Eberwein S, et al. *Burns* 2010; 36: 665-72	77% of wounds had ≥90% epithelialisation by day 14; a greater proportion had healed in the transparent film group than in the gauze group (p=0.046) Pain scores decreased over time in both groups
Split-thickness donor graft sites	AQUACEL Ag versus paraffin gauze (n=20)	Lohsiriwat V, et al. *Ann Plastic Surg* 2009; 62(4): 421-22	Average time to complete epithelialisation was significantly shorter in the silver dressing group than in the paraffin gauze group (p=0.031) The average pain score on dressing removal was significantly lower in the silver dressing group than in the gauze group (p=0.027)

Table 2 | Continued

Wound type	Product(s)	Reference	Outcomes
ENTRY/EXIT SITES			
Vascular catheter sites	Arglaes (silver film dressing) versus Tegaderm (film dressing) (n=31)	Madeo M, et al. *Intensive Crit Care Nurs* 1998; 14(4): 187-91	No statistical difference was found in bacterial growth at the insertion site or on the catheter tips between the two dressings
Subclavian catheter entry sites	Silver-impregnated collagen cuff versus semiocclusive dressing versus collodion (n=50)	Babycos CR, et al. *J Parenter Enteral Nutr* 1993; 17(1): 61-63	There was no statistical difference in insertion site or catheter-related sepsis between the three groups

CHRONIC WOUNDS			
Wound type	**Product(s)**	**Reference**	**Outcomes**
PRESSURE ULCERS			
Pressure ulcers (grades III and IV)	Silver mesh dressing (Tegaderm) versus SSD (n=40)	Chuangsuwanich A, et al. *J Med Assoc Thai* 2011; 94(5): 559-65	After 8 weeks of treatment, the mean healing rate and percentage reduction in PUSH score were higher in the silver dressing group than in the SSD group, although the difference was not statistically significant The estimated average cost of treatment was significantly lower for the silver dressing than for SSD (p<0.01)
LEG ULCERS			
Venous leg ulcers at risk of infection	AQUACEL Ag for 4 weeks then AQUACEL for 4 weeks versus Urgotul Silver for 4 weeks followed by Urgotul for 4 weeks (n=281)	Harding K, et al. *Int Wound J* 2011; doi: 10.1111/j.1742-481X.2011.00881.x	After 8 weeks of treatment, the groups had similar relative wound size reductions The AQUACEL Ag group had significantly higher percentage of patients with better wound progression than in the Urgotul Silver group (p=0.0108)
Infected venous leg ulcers with signs of inflammation	Contreet Ag (silver foam) versus Biatain (foam) for 9 weeks (n=42)	Dimakakos E, et al. *Wounds* 2009; 21(1): 4-8	After 9 weeks, complete ulcer healing had occurred in 81% of the silver group and in 48% of the control group Wound healing rate was significantly higher in the silver group than in the control group (p=0.02)
Venous leg ulcers present for >6 weeks	Silver dressing chosen by clinician versus non-silver low adherence dressing for 12 weeks (n=213) VULCAN study	Michaels JA, et al. *Br J Surg* 2009; 96: 1147-56	There was no difference between the dressings in the proportion of ulcers healed at 12 weeks (59.6% in silver group; 56.7% in control group) There was no difference between groups in median time to healing or in health-related quality of life scores The significantly higher cost for patients treated with antimicrobial dressings was partly due to increased frequency of dressing change and partly due to cost of the dressings
Chronic venous leg ulcers with signs of critical colonisation	Restore Contact Layer Silver for 4 weeks followed by Restore Contact Layer (neutral contact layer) for 4 weeks versus Restore Contact Layer for 8 weeks (n=102)	Lazareth I, et al. *Wounds* 2008; 20(6): 158-66	At the end of 8 weeks, reduction of surface area and clinical score were significantly greater in the silver group (p=0.023) Median closure rate was significantly higher at week 4 (p=0.009) for the silver group, and remained so in the silver group up to week 8 after switching to the non-silver contact layer (p=0.001) At weeks 4 and 8 significantly more wounds in the silver group had no pre-specified signs of heavy bacterial colonisation (week 4 p=0.0097; week 8 p=0.044)
Critically colonised venous leg ulcers with delayed healing	Contreet Foam (silver-containing foam) versus ALLEVYN Hydrocellular (foam) for 4 weeks (n=129)	Jørgensen B, et al. *Int Wound J* 2005; 2(1): 64-73	After 4 weeks there was a significantly greater reduction in ulcer area in the silver group versus the control group After 1 and 4 weeks, significantly fewer patients had wound odour in the silver group than in the control group At final visit, there were significantly fewer leakages with the silver dressing than with the control dressing
Chronic venous or mixed venous/arterial leg ulcers with critical colonisation	Silver foam dressing versus foam dressing for 4 weeks (n=109)	Romanelli M and Price P. *J Am Acad Dermatol* 2005; 52: 21	After 1 week, odour perceived by the patient and by study personnel was reduced to a significantly greater extent in the silver group (p<0.02) The silver group had significantly less leakage after 4 weeks (p<0.01) Relative mean ulcer area reduction was significantly better for the silver dressing (p=0.03) No significant differences were found between the dressings for comfort during wear or pain
Venous leg ulcers	Activated charcoal silver impregnated dressing versus non-silver containing therapies for 6 weeks (n=38)	Wunderlich U and Orfanos OE. *Hautarzt* 1991; 42(7): 446-50	The silver group had significantly greater epithelialisation and reduction of ulcer size (p<0.05) 6/19 ulcers in the silver group healed vs 2/19 in the control group Exudate, granulation, colonisation of ulcers and odour, erythema and oedema were not significantly different between groups

Table 2 | Continued

Wound type	Product(s)	Reference	Outcomes
MIXED			
Chronic venous leg ulcers (n=12) and pressure ulcers (n=24) with critical colonisation	Silver alginate/ carboxymethylcellulose dressing vs calcium alginate dressing (Kaltostat) (n=36)	Beele H, et al. *Int Wound J* 2010; 7: 262-70	At 4 weeks, the average infection score was reduced for both groups The average infection score had reduced significantly more in the silver group than in the alginate group (p=0.013)
Infected chronic (86%) or acute wounds (14%)	Askina Calgitrol Ag (silver alginate) or Algosteril (alginate) for 2 weeks (n=42)	Trial C, et al. *J Wound Care* 2010; 19(1): 20-26	The silver dressing had superior antimicrobial effect to the alginate dressing The two dressings were similar in terms of reduction of local infection, local tolerance, acceptability and usefulness
Lower leg ulcers with clinical signs of infection or critical colonisation	Nanocrystalline silver dressing (ACTICOAT) versus cadexomer iodine dressing (Iodosorb) (n=281)	Miller CN, et al. *Wound Repair Regen* 2010; 18; 359-67	Over the 12 week observation period, there was no significant difference between the dressing groups in number of wounds healed (p>0.05) The silver dressing was associated with faster healing in the first 2 weeks of treatment and in larger, older wounds
Chronic wounds with delayed healing and moderate to high levels of exudate	Contreet Foam (silver foam) versus local best practice for 4 weeks (n=619) CONTOP study	Münter KC, et al. *J Wound Care* 2006; 15(5): 199-206	After 4 weeks, median reduction in ulcer area was significantly higher for the silver group than for the control group (47.1% vs 31.8%; p=0.0019) The silver group also had significantly improved (p<0.05) exudate handling, ease of use, odour and pain Significantly less time was spent on dressing changes and mean wear time was longer for the silver group (p<0.05)
Chronic wounds with at least 2 signs of local infection	Silvercel (silver alginate) versus Algosteril (alginate) for 4 weeks (n=99)	Meaume S, et al. *J Wound Care* 2005; 14(9): 411-19	None of the test group and 10.5% of the control group were treated with systemic antibiotics at final visit The 4 week closure rate was statistically greater in the silver group than in the control group (p=0.024)
Chronic wounds with delayed healing	Contreet Foam (silver foam) versus local best practice for 4 weeks (n=82) British arm of CONTOP study	Russell L. *Wounds UK* 2005; 1: 44-54	There was a 50% relative reduction in wound area in the silver group (25% in the control group) The silver dressing had greater ease of application and removal, and leakage control (all p<0.01)
Chronic wounds with no clinical signs of local infection	Actisorb Plus 25 (activated charcoal with silver) versus Tielle (foam) for 2 weeks (n=125)	Verdú Soriano J, et al. *J Wound Care* 2004; 13(10): 419-23	Bacteriological analysis was performed at baseline and at endpoint (2 weeks) After 2 weeks, 85.1% of wounds in the silver dressing group had a reduction in the number of bacteria in the wound compared with 62.1% in the control group (p=0.003)
DIABETIC FOOT ULCERS			
Non-ischaemic diabetic foot ulcers	AQUACEL Ag (silver Hydrofiber) versus Algosteril (alginate) for 8 weeks or until healing (n=134)	Jude EB, et al. *Diabetic Med* 2007; 24: 280-88	Ulcer depth in the silver group reduced significantly more than in the control group (p=0.04) Overall improvement and less deterioration was greater in the silver group (p=0.058), and particularly in the subset using antibiotics (p=0.02) The mean time to healing was not significantly different between the two groups

Table 3 | Systematic reviews and meta-analyses of silver dressings

The studies summarised here are representative of the literature on silver dressings and do not comprise an exhaustive literature search.

Wound type	Title	Reference	Studies included	Conclusions
BURNS				
Burns	A systematic review of silver-containing dressings and topical silver agents (used with dressings) for burn wounds	Aziz Z, et al. *Burns* 2011; http://dx.doi.org/10.1016/j.burns.2011.09.020	Of 14 RCTs identified, 4 RCTs compared silver-containing dressings with non-silver dressings The other RCTs compared SSD with non-silver preparations	Of the 4 silver-containing dressing RCTs: ■ The results of the 2 RCTs that reported healing time could not be combined because the study populations were different ■ One of these studies reported a significant difference in healing for the silver group; the other reported the converse
Burns	Nanocrystalline silver: a systematic review of randomized trials conducted on burned patients and an evidence-based assessment of potential advantages over older silver formulations	Gravante G, et al. *Ann Plastic Surg* 2009; 63(2): 201-5	5 RCTs were included in a meta-analysis of incidence of infection; 3 of these RCTs were included in a meta-analysis of pain	Meta-analysis showed that the nanocrystalline group: ■ had a significantly lower incidence of infection than the SSD/silver nitrate group ($p<0.001$) ■ had a more significant reduction in pain than the SSD group ($p<0.001$)
Superficial and partial thickness burns	Dressings for superficial and partial thickness burns	Wasiak J, et al. *Cochrane Database Systematic Reviews* 2008; 8(4): CD002106	26 RCTs were included	Burns dressed with hydrogels, silicon coated dressings, biosynthetic dressings and antimicrobial dressings healed more quickly than those dressed with SSD or chlorhexidine dressings Fewer dressing changes were required for hydrocolloid, silicon and silver dressings in comparison with SSD SSD delayed healing and required more dressing applications
LEG ULCERS				
Leg wounds/ ulcers	Silver treatments and silver impregnated dressings for the healing of leg wounds and ulcers: a systematic review and meta-analysis	Carter MJ, et al. *J Am Acad Dermatol* 2010; 63: 668-79	7 RCTs were included in a meta-analysis of complete wound healing 5 studies were included in wound size reduction meta-analysis 3 studies were included in the healing rate meta-analysis	The outcomes of the meta-analyses for complete wound healing and for healing rates were not statistically significant Meta-analysis of wound size reduction (%) was significantly in favour of silver dressings at 4 weeks and 8 weeks ($p=0.002$ at both times) The authors commented that 'complete wound healing is unlikely to differentiate between experimental and control groups because too short a time period has passed between initiation of treatment and evaluation'
Chronic wounds with delayed healing or a with clinical diagnosis of critical colonisation or infection	The effectiveness of silver-releasing dressings in the management of non-healing chronic wounds: a meta-analysis	Lo S-F, et al. *J Clin Nurs* 2009; 18: 716-28	8 RCTs of silver dressings versus non-silver dressings	Wound area reduction - meta-analysis of the results from the 8 studies showed a significant reduction in wound area for the silver dressing group ($p<0.001$) Odour was described in 3 RCTs - meta-analysis showed a significant reduction in the silver dressing group ($p<0.001$) Wound pain was reported in 2 RCTs - meta-analysis showed a significant reduction in the silver dressing group ($p<0.001$)
Infected chronic wounds	A systematic review of silver-releasing dressings in the management of infected chronic wounds	Lo S-F, et al. *J Clin Nurs* 2008; 17: 1973-85	14 RCT and non-randomised control trials of ionic silver dressings	4 studies (3 non-randomised trials and 1 RCT) assessed severity of infection and all found a statistically significant reduction in infection by silver-releasing dressings Odour control was measured in 5 studies (2 RCTs and 3 non-randomised trials), all of which reported reductions in odour
Leg ulcers	Silver treatments for leg ulcers: a systematic review	Chambers H, et al. *Wound Rep Regen* 2007; 15: 165-73	Of the 5 studies of silver dressings identified, only 2 were included in a meta-analysis of ulcer healing	Pooling the results of 2 eligible studies found no significant difference in proportion of ulcers completely healed There was a tendency for more ulcers to heal with silver The authors commented that poor reporting of methods and results limited inclusion of studies in the meta-analysis

Table 3 | Continued

Wound type	Title	Reference	Studies included	Conclusions
MIXED				
Uninfected wounds - burns and other wounds	Topical silver for preventing wound infection	Storm-Versloot MN, et al. *Cochrane Database Systematic Review* 2010; 17(3): CD006478	Burns - 13 trials of various silver preparations including silver nitrate and SSD Other wounds - 6 RCTs comparing SSD/silver containing dressings with non-silver dressings	Burns ■ 6 RCTs compared SSD with a silver dressing; only one found significantly fewer infections with a silver containing dressing and the rest found no difference ■ One RCT found a significantly lower rate of infection with silver coated gauze than with silver nitrate gauze Other wounds ■ Of 6 RCTs comparing SSD/silver-containing dressings with non-silver dressings, most found no significant differences in infection rates; one found significantly fewer infections with SSD/hydrocolloid ■ One RCT found a significant reduction in healing time with silver Hydrofiber in diabetic foot ulcers The authors concluded that there was insufficient evidence to establish whether silver dressings promote wound healing or prevent wound infection
Contaminated or infected acute or chronic wounds	Topical silver for treating infected wounds	Vermeulen H, et al. *Cochrane Database Systematic Reviews* 2007; 1: CD005486	3 RCTs were identified with a total of 847 patients	Silver-containing foam dressings did not significantly increase complete ulcer healing compared with standard foam dressings A greater reduction of ulcer size was observed with the silver-containing foam There were no differences between groups in pain, patient satisfaction, length of hospital stay, or costs The authors concluded that the 3 trials did not provide sufficient evidence to recommend silver-containing dressings for the treatment of infected or contaminated chronic wounds
DIABETIC FOOT ULCERS				
Diabetic foot ulcers	Silver based wound dressings and topical agents for treating diabetic foot ulcers	Bergin S and Wraight P. *Cochrane Database Systematic Reviews* 2006; 1: CD005082	No studies were identified that met inclusion criteria	No randomised or controlled trials existed at the time of the analysis to allow evaluation of the clinical effectiveness of silver dressings in diabetic foot ulcers

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APPENDIX 1 | Silver wound dressings

The dressings listed here are representative of the range and types of formulations currently produced. Availability of dressings varies worldwide.

Product name	Manufacturer	Formulation
KEY: CONTAINS SSD		
ALGINATE		
ACTICOAT Absorbent	Smith & Nephew	Nanocrystalline silver layer on alginate core
Algicell Ag	Derma Sciences	Alginate dressing with 1.4% silver (type not specified)
Algidex Ag	DeRoyal	Ionic silver with alginate and maltodextrin; available as a paste or thin sheets or with a foam backing
ALGISITE Ag	Smith & Nephew	Silver impregnated calcium alginate
Askina Calgitrol Ag Askina Calgitrol THIN Askina Calgitral Paste	B.Braun	Ionic silver alginate matrix with a foam backing Ionic silver alginate matrix in thin sheets Ionic silver alginate in paste form
Invacare Silver Alginate	Invacare	Alginate and carboxymethylcellulose dressing with silver sodium hydrogen zirconium phosphate
Maxorb Extra Ag	Medline	Alginate and carboxymethylcellulose with silver sodium hydrogen zirconium phosphate
Melgisorb Ag	Mölynlycke	Alginate and carboxymethylcellulose with silver (type not specified)
Restore Calcium Alginate	Hollister Woundcare	Alginate with 'ionic silver'
SeaSorb Ag	Coloplast	Alginate and carboxymethylcellulose with silver (form not specified)
Silvercel; Silvercel Non Adherent	Systagenix	Alginate and carboxymethylcellulose with elemental silver coated nylon fibres; Non Adherent has non-adherent contact layer
Silverlon Calcium Alginate	Argentum Medical	Calcium alginate with metallic silver plated nylon mesh core
Sorbsan Silver Flat; Sorbsan Silver Packing; Sorbasan Silver Plus NA; Sorbsan Silver Plus SA	Aspen Medical	Calcium alginate with 1.5% silver (form not specified); plus NA contains viscose pad; plus SA has viscose pad and film backing
Suprasorb A + Ag	Activa Healthcare	Calcium alginate with silver (form not specified)
Tegaderm Alginate Ag	3M	Carboxymethylcellulose and alginate with silver sodium hydrogen zirconium phosphate
UrgoSorb Silver	Urgo	Calcium alginate/hydrocolloid impregnated with silver
COLLAGEN		
BIOSTEP Ag	Smith & Nephew	Collagen and ethylenediaminetetracetic acid with silver chloride
COLACTIVE collagen with silver	Smith & Nephew	Collagen and alginate with silver lactate
Covaclear Ag Hydrogel	Covalon	Collagen-based hydrogel with silver (form not specified)
Promogran Prisma	Systagenix	Collagen and oxidised regenerated cellulose and 1% silver (silver-ORC compound)
Puracol Plus Ag+	Medline	Collagen with silver chloride
CREAM		
Flamazine	Smith & Nephew	SSD in a cream base
FIBROUS/FABRIC		
ACTICOAT; ACTICOAT 7	Smith & Nephew	Nanocrystalline silver/rayon-polyester core; ACTICOAT 7 is designed for 7 day wear
Actisorb Silver 220	Systagenix	Activated charcoal cloth impregnated with silver in nylon fabric sleeve
Atrauman Ag	Paul Hartmann	Polyester wound contact layer impregnated with silver
Physiotulle Ag	Coloplast	Knitted polyester net with hydrocolloid particles, petrolatum and SSD
Restore Contact Layer Dressing with Silver	Hollister Woundcare	Non-adherent dressing with silver sulfate
Silverlon Wound Contact Dressings	Argentum	Silver coated nylon fabric
Silverseal Contact Dressing	Derma Sciences	Knitted fabric with 99.1% elemental silver and 0.9% silver oxide
Tegaderm Ag Mesh	3M	Gauze with silver sulfate
Urgotul Duo Silver	Urgo	Polyester mesh with lipido-colloid coating and impregnated with silver salt; viscose backing
Urgotul SSD	Urgo	Polyester mesh with lipido-colloid coating impregnated with SSD
Vliwaktiv Ag	Lohmann and Rauscher	Activated charcoal dressing impregnated with silver (form not specified)
FILM		
Arglaes Film Island; Arglaes Island	Medline	Film dressing with ionic silver; Arglaes Island has an alginate pad
FOAM		
ACTICOAT Moisture Control	Smith & Nephew	Nanocrystalline silver coated polyurethane wound contact layer, foam core and film backing
ALLEVYN Ag Adhesive; ALLEVYN Ag Heel ALLEVYN Ag Non-Adhesive	Smith & Nephew Smith & Nephew	Adhesive foam, SSD, film backing Non-adhesive foam, SSD, film backing, shaped for heel
Avance	Mölnlycke	Non-adhesive foam dressing impregnated with silver
Avance A	Mölnlycke	Adhesive foam dressing with silver
Biatain Ag	Coloplast	Adhesive foam impregnated with silver, film backing
Mepilex Ag	Mölnlycke	Soft silicone contact layer, foam core containing silver, film backing
Optifoam	Medline	Foam pad with silver (form not specified)
Polymem Silver	Ferris Manufacturing Corp	Foam dressing impregnated with silver, starch and glycerin
Urgocell Silver	Urgo	Foam core with silver impregnated lipido-colloid contact layer and film backing
GAUZE		
Tegaderm Ag	3M	Non-woven mesh/gauze impregnated with silver sulfate
Urgotul SSD	Urgo Medical	Polyester mesh impregnated with hydrocolloid, petroleum jelly and SSD
HYDROCOLLOIDS		
Contreet Hydrocolloid	Coloplast	Silver impregnated hydrocolloid with vapour permeable backing
Silverseal Hydrocolloid	Alliqua	Hydrocolloid dressing with silver (form not specified)
Sureskin Silver	EuroMed	Hydrocolloid dressings with sodium hydrogen zirconium phosphate
HYDROFIBER		
AQUACEL Ag	ConvaTec	Hydrofiber with 1.2% silver
HYDROGEL		
AquaMed Hydrogel Sheet with Silver	AquaMed Technologies	Hydrogel with elemental silver
Gentell Hydrogel Ag	Concept Health	Hydrogel with SSD
Silvasorb Gel	Medline	Hydrogel with silver (form not specified)
Silverseal Hydrogel	Alliqua	Hydrogel with silver coated fibres
POWDER		
Arglaes Powder	Medline	Alginate powder with ionic silver (form not specified)

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