

# Management of chronic wounds: the role of silver-containing dressings

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## Abstract

The last few years has seen an increasing interest in the area of topical antimicrobial dressings. In particular, dressings containing silver are being developed at a rapid rate. The use of silver-containing dressings is escalating and they are now widely utilised on many types of wounds. In particular, silver-containing dressings can be a valuable component of wound bed preparation and the management of chronic wounds.

This paper examines the current literature on silver-containing dressings. Implications for practice are discussed and two protocols for use of silver-containing dressings in practice are proposed. Many questions regarding the use of silver-containing dressings remain unanswered and this paper suggests directions for future research to assist clinicians to achieve optimal, economically sustainable client outcomes.

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## Chronic wounds

Chronic wounds can be defined as those wounds which fail to heal in an orderly and timely manner<sup>1</sup>. In the past, clinicians have applied acute wound healing models to manage chronic wounds. It is now recognised that the chronic wound environment is different to the acute wound environment<sup>2</sup>. The clinical signs of chronic wounds include<sup>1</sup>:

- Non viable wound tissue (slough and/or necrosis).
- Lack of healthy granulation tissue (wound tissue may be pale, greyish and avascular).
- No reduction in wound size over time.
- Recurrent wound breakdown.

Numerous molecular and biochemical imbalances are found within the chronic wound environment, including elevated inflammatory cytokines, elevated matrix metalloproteinases (MMPs) and decreased tissue inhibitors of metalloproteinases (TIMPs)<sup>1</sup>. The cells within the chronic wound exhibit low

mitotic activity, senescence and decreased growth factor activity<sup>1</sup>; chronic wounds are often referred to as being 'stuck' in the inflammatory or proliferative phases of wound healing<sup>3</sup>.

The emergence of wound bed preparation and the principles embodied in the TIME acronym are providing clinicians with a framework to better manage the local wound environment of chronic wounds<sup>3-6</sup>. The components of TIME are:

- T Tissue management.
- I Inflammation and infection control.
- M Moisture balance.
- E Epithelial (edge) advancement.

## The bacterial environment of the chronic wound

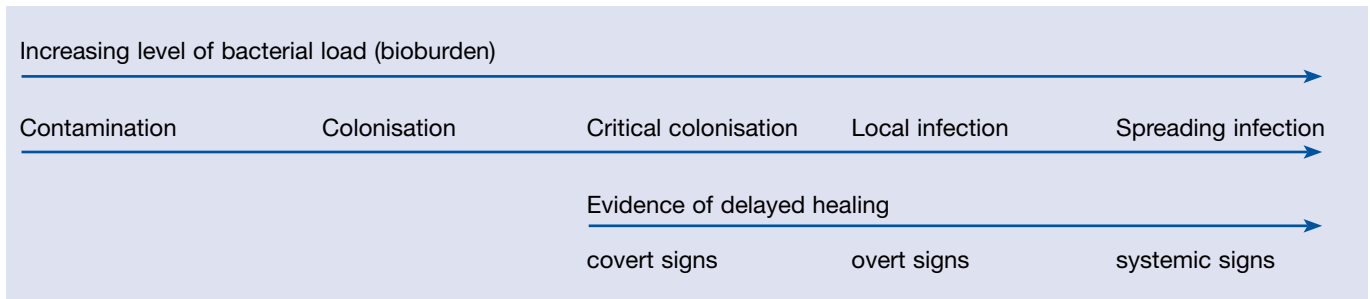
Within the TIME concept, management of inflammation and infection control plays a major role. The presence of high levels of bacteria, multiple bacterial strains, multi-drug resistant organisms and bacterial biofilms play a significant role in impairing the healing process within chronic wounds<sup>3</sup>. Bacteria can delay healing as they compete with cells within the wound for nutrients and oxygen. The metabolic by-products excreted by bacteria can also be toxic to human cells and promote the production of protein-degrading enzymes within the wound<sup>7</sup>. The wound infection continuum is conceptualised in Figure 1.

The term critical colonisation has been accepted to describe a level of bacteria between colonisation and infection. A critically colonised wound will fail to heal, but often does not display the overtly recognisable signs of infection<sup>5</sup>. Clinical signs of critically colonised wounds can be subtle and

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Figure 1. The wound infection continuum<sup>8</sup>.



therefore might go unrecognised by clinicians. The signs can include: failure of the wound to progress; increased wound pain or tenderness; increase in serous exudate; absent granulation tissue or increase in non-viable tissue; friable granulation tissue and an offensive odour<sup>9</sup>.

There are a number of methods to reduce bacterial load within a wound. Removal of non-viable tissue through debridement will reduce the number of micro-organisms, toxins and other substances within the wound bed which contribute to impaired healing<sup>4</sup>. However, a thorough assessment of the patient to determine their healing capacity must be undertaken prior to the removal of hard, dry eschar. The maintenance of eschar is clinically acceptable where the patient has inadequate blood supply to the wound to allow healing and support infection control<sup>10</sup>.

**Managing inflammation and infection control**

Wound bed preparation and the TIME concept is primarily concerned with managing the local wound environment to optimise healing<sup>5,6</sup>. However, a comprehensive assessment of the patient is a pre-requisite prior to applying wound bed preparation. As Sibbald *et al.*<sup>3</sup> states, “local wound management measures are unlikely to succeed if the patient is not receiving adequate treatment for conditions that are known to impair healing”. Factors such as poorly controlled diabetes, heart failure, poor vascularity, poor nutrition or continuing pressure will continue to impair healing and can thwart the best attempts to manage the local wound environment<sup>3</sup>. Other systemic conditions (e.g. rheumatoid arthritis), certain medications (e.g. corticosteroids) and some lifestyle choices (e.g. smoking) can also contribute to impaired wound healing.

Information gained from assessment is used to determine realistic long-term goals of wound management in conjunction with the patient. If factors impairing healing are severe and cannot be overcome, the wound may be unlikely to heal. In this situation, the management plan may be different to that for a patient with healing capacity.

**Implications for practice**

**Topical antimicrobials**

Table 1 outlines an overview of the antimicrobials that might be beneficial in managing various levels of wound bioburden. A number of terms are used to describe the reduction of bioburden. These include<sup>11</sup>:

- *Antibacterial*: a substance which is bactericidal (i.e. kills) or bacteriostatic (i.e. inhibits) bacteria.
- *Antimicrobial*: a substance that has cidal or static properties against microbes. This term is often used to include organisms other than bacteria such as fungi.

There has been renewed interest in topical preparations to assist in controlling wound bioburden. This brief review considers some of the topical antimicrobials utilised in wound management – povidone iodine, cadexomer iodine and honey.

Antiseptics have been used by clinicians for many years to control bacteria. Povidone iodine has been recommended as appropriate for the prevention and treatment of infected wounds<sup>12-14</sup>, and for reduction of bacterial load in wounds unlikely to heal<sup>9</sup>. However, Cooper<sup>15</sup> argues that the appropriateness of topical antiseptics for wound management remains controversial. In addition, whilst topical antibiotics can deliver high concentrations to the wound, the problems of

Table 1. A guide to antimicrobial management of wound bioburden<sup>3</sup>.

| Level of bioburden    | Primary treatment      | Adjunct treatment      |
|-----------------------|------------------------|------------------------|
| Non-healable wound    | Antiseptics            |                        |
| Critical colonisation | Topical antimicrobials |                        |
| Local infection       | Systemic antibiotics   | Topical antimicrobials |
| Spreading infection   | Systemic antibiotics   | Topical antimicrobials |

cutaneous sensitisation, impairment to healing and development of resistant strains means that topical antibiotics are not recommended for application to wounds<sup>16</sup>, although the author is aware that this practice still occurs.

Cadexomer iodine is an effective topical antimicrobial agent that offers controlled release of water-soluble iodine in response to exudate<sup>17</sup>. Cadexomer iodine can assist with autolysis of slough and management of exudate while maintaining a moist wound environment<sup>18</sup>. Clinical trials using cadexomer iodine on chronic wounds have demonstrated improved clinical outcomes compared to other treatments<sup>1</sup>. Anecdotal evidence suggests cadexomer iodine may be appropriate to use as an alternative to silver-containing dressings. However, as yet, there are no guidelines to assist clinicians in deciding whether to use cadexomer iodine or a silver-containing dressing.

Some honeys are also recognised for their antimicrobial properties<sup>19</sup>. The use of honey as a topical antimicrobial has seen a resurgence in recent years.

Unfortunately there is still a paucity of guidelines as to which topical antimicrobial preparation to choose in clinical practice. The number of topical antimicrobial preparations, conflicting views in the literature as to indications and efficacy<sup>20</sup>, and use based on tradition rather than evidence has led to confusion and variance amongst clinicians. In deciding whether or not to use topical antimicrobials for wound management, a risk/benefit analysis, including knowledge of the advantages and disadvantages of the particular antimicrobial, should be undertaken for each person and their wound<sup>20</sup>. These principles also apply to antimicrobial dressings containing silver, which will now be discussed in detail.

### Silver-containing dressings

Much has been written in the last few years regarding the antimicrobial properties of silver<sup>15, 21-25</sup>. Preparations including silver sulphadiazine cream and silver nitrate have been used for many years, particularly in burn units and for control of *Pseudomonas aeruginosa*<sup>22</sup>. An increasing number of dressings are now available which contain silver. The carrier mediums for these dressings vary and there are silver-containing dressings suitable for most wound exudate levels (Table 2).

#### Composition of silver-containing dressings

There is little doubt that silver-containing dressings offer valuable therapeutic effect<sup>26-30</sup>. However, it has become increasingly difficult for clinicians to determine which of these products offers the best efficacy and value. All the

products claim to contain or release ionic silver (Ag<sup>+</sup>), which is the form necessary for antimicrobial action<sup>15</sup>. However, many of the companies do not specify what type of silver complex is used in their dressing<sup>25</sup>. Two of the products claim to contain nanocrystalline silver. Nanocrystalline silver is produced using nanotechnology to reduce the silver particles to an extremely small size. This process greatly increases the surface area of the silver particles and nanocrystalline silver has been shown to allow more rapid delivery of silver with a faster kill rate of micro-organisms<sup>7</sup>.

No matter which silver complex is used, each company claims their silver-containing dressings are effective against a broad spectrum of bacteria and minimise wound infection<sup>25</sup>. However, further, independent confirmation of these claims is warranted.

Thomas & McCubbin<sup>31</sup> compared the antimicrobial effects of 10 silver-containing dressings on *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans* using three tests – zone of inhibition, challenge testing and microbial transmission test. A full description of their methods is available in Thomas & McCubbin's first report in which they tested four silver-containing dressings<sup>32</sup>. They demonstrated that some silver-containing dressings had limited or no antimicrobial effect when subjected to a number of *in vitro* (laboratory) tests. However, randomised, controlled clinical trials with sound methodology are required in order to provide clinicians with

Table 2. Some silver-containing dressings currently available in Australia.

| Carrier medium       | Product                  | Manufacturer      |
|----------------------|--------------------------|-------------------|
| Wound contact layer  | Acticoat (or Acticoat 7) | Smith & Nephew    |
|                      | Atrauman silver          | Hartmann          |
| Hydrocolloid         | Contreet H               | Coloplast         |
| Foam                 | Contreet Foam            | Coloplast         |
|                      | Avance                   | SSL               |
| Foam with additives  | Polymem silver           | Ferris            |
| Calcium alginate     | Acticoat Absorbent       | Smith & Nephew    |
| Hydrofibre           | Aquacel Ag               | ConvaTec          |
| Charcoal impregnated | Actisorb 220             | Johnson & Johnson |

unequivocal evidence of clinical efficacy of silver-containing dressings. Clinical trials might include studies with appropriate controls or studies that compare the new generation of ionic and nanocrystalline silver-containing dressings with like dressings.

#### Effective silver concentration

The amount of silver necessary to be bactericidal in the wound environment has also been debated. Lansdown<sup>25</sup> quotes one author as claiming that a concentration of ionic silver of 1.43ppm will kill or inhibit a wide variety of micro-organisms. Burrell<sup>33</sup> quotes Shierholz *et al.* as stating, "The Ag<sup>+</sup> kill rate is directly proportional to Ag<sup>+</sup> concentrations, typically acting at multiple targets. The higher the silver-ion concentration, the higher the antimicrobial activity".

Whatever the concentration, when silver is released into the wound bed only a small portion is taken up by bacteria. Much of the silver becomes bound to sulphhydryl groups, proteins in the wound bed and surrounding tissues<sup>25</sup>. Whilst in a pure water environment concentrations of silver as low as 1µg/mL or one part per 100 million are bactericidal<sup>34,35</sup>, in a complex organic environment, such as wound fluid, the minimum inhibitory concentration of silver required is much greater. In a wound environment, Burrell<sup>34</sup> claims a level of silver of 20-40µg/mL is required to be effective, whilst Thomas<sup>36</sup> claims concentrations of at least 50µg/mL and possibly up to 60.5µg/mL are necessary.

The concentration of silver in silver-containing dressings varies considerably between dressing types (Table 3). Differences within the dressing structure will also influence the efficacy of the silver as an antimicrobial. Dressings which contain silver as a surface coating are more effective than those where the silver is contained within the structure of the dressing<sup>31</sup>. The results of these tests and the relative efficacy of silver-containing dressings has sparked much debate between clinicians and companies<sup>33,37-39</sup>.

Numerous *in vitro* and animal studies are reported in the literature to support the antimicrobial properties of silver-containing dressings. Lansdown<sup>25</sup> states that caution must be exhibited when interpreting *in vitro* or animal studies. The test conditions in the laboratory are usually significantly different to the conditions found at the human wound site. Further, different studies use different *in vitro* methods, therefore comparison is difficult<sup>15</sup>. Sound, independent research to provide a definitive consensus as to the minimum effective concentration of silver required to be bactericidal in a human wound environment is urgently required.

Table 3. Silver concentration of some silver-containing dressings available in Australia.

| Name of dressing      | Silver concentration (mg/100cm <sup>2</sup> ) |                                 |
|-----------------------|---|---------------------------------|
|                       | Thomas <sup>25</sup>                          | Thomas & McCubbin <sup>21</sup> |
| Acticoat              | 105   | 101-109                         |
| Contreet Foam         | 85  | 47*                             |
| Contreet Hydrocolloid | 32  | 31.2-32.4                       |
| Aquacel Ag            | 8.3   | 8.3                             |
| Actisorb silver 220   | 2.7   | 2.4-2.9                         |
| Avance                | Not stated                                    | 1.6                             |

\* Results recognised as inaccurate: Thomas & McCubbin<sup>26</sup>.

#### The action of silver-containing dressings

Another consideration is the method with which the various silver-containing dressings act. Some claim to release silver from the dressing onto the wound bed, killing micro-organisms both in the wound and within the dressing<sup>40</sup>. Others only kill bacteria within the dressing, with no release of silver onto the wound.

Sibbald *et al.*<sup>41</sup> reported an evaluation of a nanocrystalline silver-containing dressing which released silver onto the wound. Comparison using semi-quantitative swabs determined that the flora on the surface of the wound was reduced. However, quantitative bacterial cultures demonstrated bacterial load and types were not reduced in the deeper wound tissues. This study suggests that even dressings which release silver onto the wound only penetrate the superficial wound tissue. Therefore, penetration of eschar and thick slough by silver is unlikely and it is recommended that non-viable tissue is removed prior to using these products.

A study undertaken by Bowler *et al.*<sup>42</sup> demonstrated that traditional hydrofibre and hydrophobic dressings (which did not contain silver) were very effective at sequestering and retaining micro-organisms. This function has also been recognised in alginate and hydrocolloid dressings<sup>42</sup>. Therefore, the clinical efficacy of silver contained only in the dressing needs further evaluation. At the present time, clinicians question the relative efficacy and clinical value of different product presentations and modes of silver delivery. The relative value of different modes of action of various silver dressings is an area which requires urgent research.

### Bacterial resistance

The issue of bacterial resistance to silver requires discussion. It is important that silver dressings are bactericidal, rather than merely bacteriostatic. It has been stated that silver shows a low tendency to develop resistance<sup>22</sup>. However, in a study undertaken by Richard *et al.*<sup>43</sup>, they found that some organisms were not affected by the two silver-containing dressings tested. It was proposed that this could have been due to resistance to silver. As the use of silver-containing dressings continues to expand, clinicians and researchers must be alert for the possibility of bacterial resistance to silver developing. As with any antimicrobial, the use of silver-containing dressings should be appropriate and judicious to help minimise the risk of resistance developing.

### Biofilms

Biofilms are created by bacterial colonies in order to optimise their survival. The initial colonies of bacteria modify their environment which encourages other bacteria to attach to them and multiply<sup>44</sup>. As part of their maturation, these bacterial communities secrete a slimy, protective, glycocalyx coating (biofilm) that helps the micro-organisms survive in harsh external conditions (e.g. extreme pH) and resist penetration by antimicrobial agents<sup>3,44</sup>. Biofilms have recently been identified as a potentially significant problem in some wounds, particularly those which are chronic<sup>44</sup>. The ability of silver-containing dressings to penetrate biofilm needs explicit investigation and articulation to ensure antimicrobial efficacy in all bacterial conditions.

### Evaluating wound progress

To optimise patient outcomes, a holistic approach to wound management is necessary. In order to maximise healing, a thorough assessment to determine wound aetiology and address systemic factors impairing healing is necessary<sup>10,45</sup>. The principles of wound bed preparation are used to overcome the local factors impairing barriers to healing<sup>1</sup>. If a healable wound is not progressing with standard care, reassessment or further investigations might be necessary to identify correct aetiology, deliver optimal local wound care and ensure patient-related issues are appropriately addressed<sup>9</sup>. Sibbald *et al.*<sup>9</sup> states that "a wound that is not 30% smaller between Weeks 0 and 4 is unlikely to heal by week 12".

Regular and systematic wound assessment of wound characteristics using standardised tools including forms, tracings, photographs and electronic or computer assisted measurement will assist the clinician to accurately determine wound progress<sup>46,47</sup>.

## Suggested protocols for use of silver-containing dressings

Like any treatment, silver-containing dressings should be used for appropriate indications and their use reviewed regularly. Protocols and standardised procedures provide guidelines for clinicians to deliver economically sustainable and optimal, reproducible outcomes<sup>48</sup>.

Two protocols are proposed. The first is most likely to be appropriate in tertiary care centres where advanced wound technologies are readily available or for inpatients where intensive therapies can be delivered. The second protocol is likely to be appropriate in outpatient and community-based settings where dressings form the mainstay of treatment and access to intensive, advanced therapies such as bioengineered skin is not appropriate or not available. Local care delivery factors and individual patient needs should be considered and treatments adjusted accordingly. However, "local practices, anecdotal remedies and treatments that provide no evidence of benefit are not acceptable for establishing appropriate levels of patient care"<sup>41</sup>. In this era of evidence-based practice, silver-containing dressings should only be instituted where there is justifiable, clinical evidence to support their use (Figure 2).

### Protocol 1: tertiary care centres

If, by the end of 1 month of standard treatment, the wound size is not reduced by 30% and systemic variables impairing healing have been controlled, topical antimicrobials should be considered. Sibbald *et al.*<sup>3</sup> recommend that if a wound fails to respond to a 2 week trial of topical antimicrobials, or develops signs of deep infection, systemic antibiotics should be considered. If the wound continues to be non-responsive, advanced biological therapies may be appropriate<sup>9</sup>.

For some persons, the factors impairing healing are such that they cannot be overcome or corrected. In this situation, the wound may be unlikely to heal. The objective of care for these persons is to optimise their quality of life whilst living with a wound. The principles of wound bed preparation might need to be modified for a person with a wound unlikely to heal. This may include topical antiseptics as the first choice to reduce bioburden<sup>1</sup>, and avoidance of extensive debridement<sup>3</sup>. Figure 3 outlines a management framework which applies these strategies.

### Protocol 2: outpatient and community-based settings

Silver-containing dressings are initiated in a variety of clinical settings. Not all these settings will have access to advanced

Figure 2. Criteria for use of a silver-containing dressing.

- Chronic wounds with a determined aetiology that have not responded to an appropriate management regime and conventional wound management products.
- Lack of wound progress, despite systemic and patient-related factors impairing healing being identified and addressed as able.
- Lack of wound progress, despite other local wound factors impairing healing being addressed as necessary.
- Heavily colonised wounds (as determined by sound clinical assessment).
- Wounds that are at high risk of or have exhibited repeated infections, the cause of which has been investigated and, where possible, treated.
- Clients who have agreed to follow a comprehensive wound management program which addresses lifestyle and psychosocial issues that may impact on healing.
- Silver-containing dressings should be used as part of a structured local wound management process to implement the principles of wound bed preparation (TIME). This includes wound debridement and management of exudate.

biological therapies. Figure 4 outlines an alternative management framework for settings where systemic antibiotics or biological therapies are not available or not appropriate. This framework is particularly applicable where nurses or clinic practitioners are initiating silver-containing dressings.

### Duration of treatment

Whilst topical antimicrobials, such as silver-containing dressings, can be a valuable adjunct to wound management, the length of time antimicrobial dressings should be continuously used is unclear. Some case studies using silver-containing dressings only report clinical effects after 2-4 weeks<sup>30</sup>. If a wound responds to the application of silver-containing dressings, it is difficult for clinicians to determine whether the product should be ceased after a certain period of time and, if so, what period is appropriate. In a study undertaken by Lansdown *et al.*<sup>49</sup>, it was noted that, after ceasing a silver-containing dressing following 4 weeks'

treatment, 50% of subjects' wounds increased in size and developed dull-looking granulation tissue within a week.

Further studies are needed to examine what is occurring in the wound bed when silver-containing dressings are used for extended periods. Certainly, if a wound fails to continue to respond to a silver-containing dressing, re-assessment should be undertaken. This might include re-evaluation of aetiology, local and systemic treatments and re-consideration of the factors impairing. Further investigations may be necessary. In some instances, the long-term goal of treatment may need to be re-defined.

### Cost implications and cost effectiveness

The number of patients using silver-containing dressings and the length of time they are being used has significant cost implications for those providing dressing supplies. The cost impact of these dressings is particularly relevant for community providers. It is widely acknowledged that cost effectiveness is more than the cost of products and the cost of labour<sup>50</sup>. The total cost of wound management involves direct and indirect costs, including factors not directly measurable such as reduced or lost productivity at work and home, reduced quality of life, pain, social isolation and reduced functional capacity<sup>51</sup>. Costs are offset against achievement of outcomes. However, there are no widely agreed outcome measurements in wound management and outcome measures will vary according to patient characteristics and care setting<sup>52</sup>.

The majority of persons with chronic and hard to heal wounds are treated in the community. There is the perception that community care is cheaper than hospitalisation; however, the long-term nature of community care makes it a particularly expensive care-delivery setting<sup>52</sup>. As community settings are bound by nursing or medical practitioner time, and do not have a defined number of beds, reducing the frequency of dressing changes often means another patient can be admitted and treated. If all these patients require a costly and prolonged regimen of dressings and treatments, the financial impact can be significant.

Norman<sup>53</sup> argues that "wound care remains poorly prioritized on the political agenda". Increased funding for expensive dressings and treatments is not currently available. Therefore, whilst new, expensive dressings, such as those containing silver can bring clinical success, they also bring high financial costs to those providing them. In Australia, there is considerable inequity in dressing product costs for the patient. In some States, community nursing organisations

Figure 3. Protocol 1.

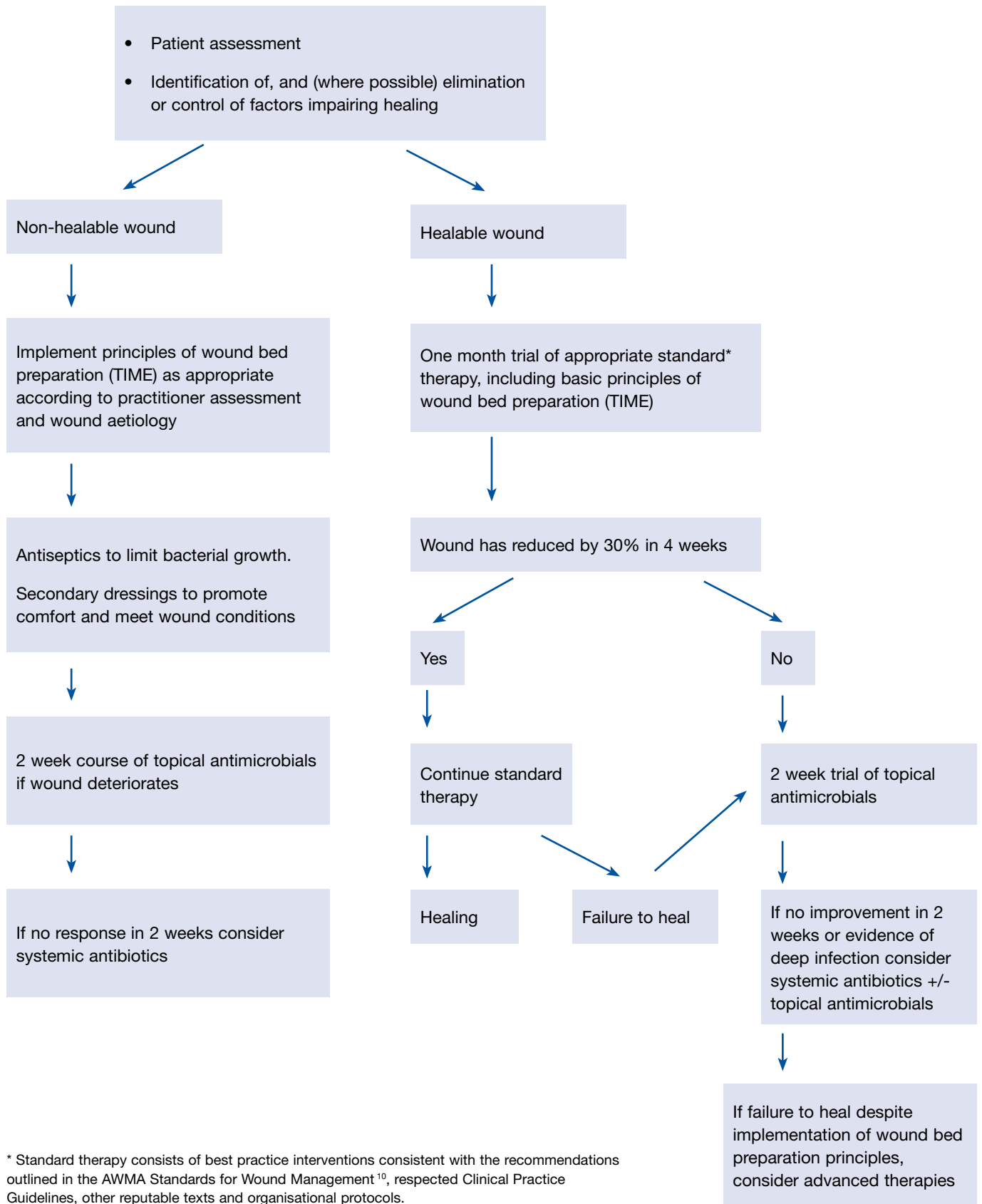
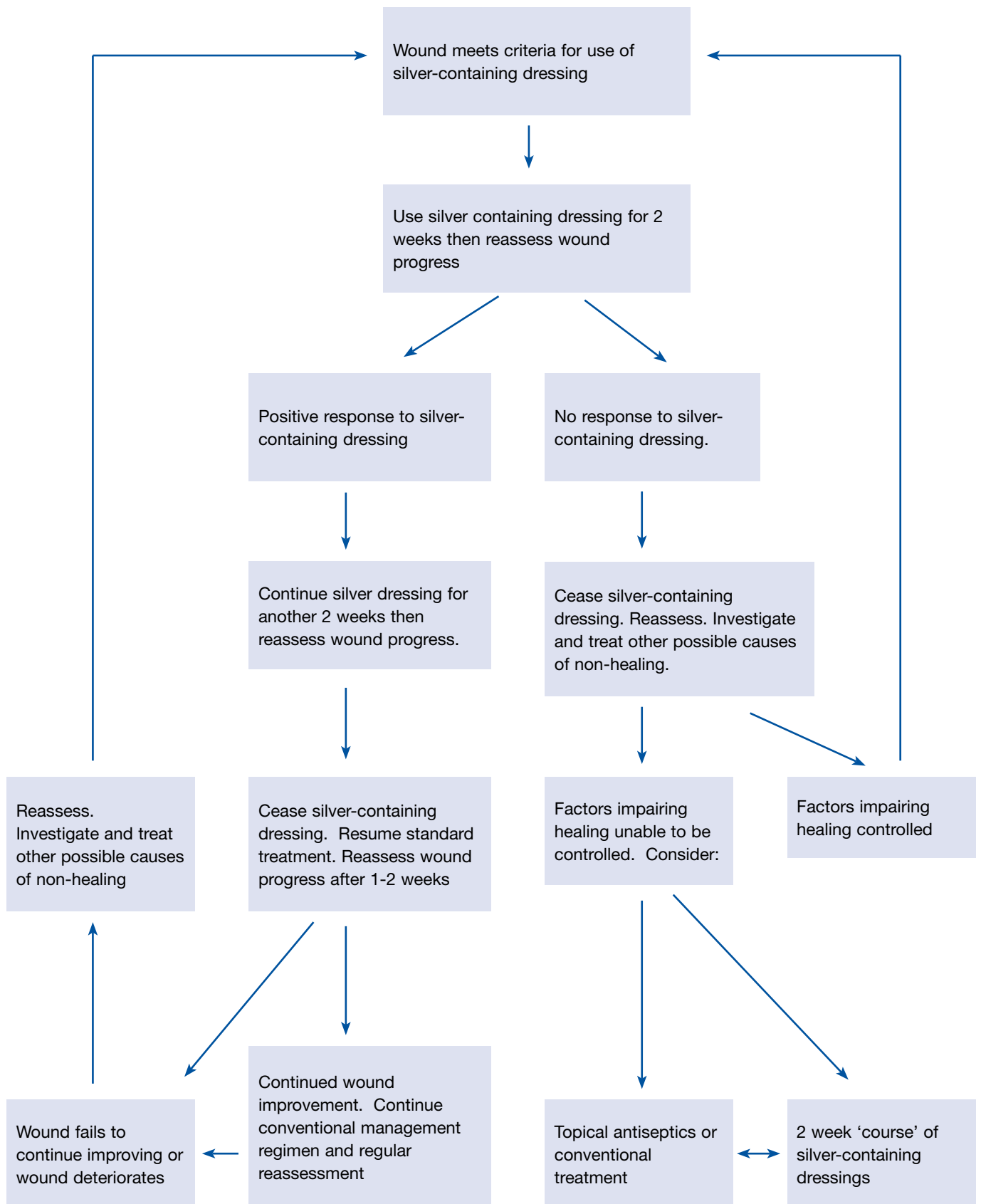


Figure 4. Protocol 2.





provide dressings free of charge to patients, whilst in other States patients must pay for their dressings. Residential aged care facilities and general practitioners do not receive additional funding to support wound dressings. These factors can have considerable influence on which products are available to and chosen by clinicians.

## Discussion

In order to promote cost-effective, evidence based practice, clinicians, researchers and wound management professional bodies need to debate, refine and endorse protocols and guidelines for the use of silver-containing dressings such as those suggested in this paper. At the present time, the explosion in the use of silver-containing dressings is based primarily on company data and marketing, expert opinion and case study reports. However, in a world of shrinking resources and increasing demand and accountability, clinicians cannot base decisions on opinion alone<sup>53</sup>. Standardised treatment protocols can provide clinicians with general guidelines to optimal treatment<sup>48</sup>. Whilst individual patient variance must be taken into account, standardised treatment protocols or guidelines can assist in achieving sustainable quality and cost-effectiveness<sup>53</sup>.

## Conclusion

Wound management in the 21st century will continue to bring technological advances which will undoubtedly radically change the way in which persons with wounds are treated. There are already numerous local and systemic therapies which are greatly improving outcomes and the quality of life for persons living with a wound. Greater understanding of the pathophysiology of the chronic wound and wound bed preparation are bringing about significant clinical changes in practice.

The advent of the new generation of antimicrobial dressings has provided clinicians with advanced, yet accessible tools to assist patients with wounds achieve optimal outcomes. However, whilst therapies such as the silver-containing dressings are improving wound healing rates, there are still some important questions which require further research and clarification. The enthusiasm with which silver-containing dressings have been taken up by wound management clinicians is astounding. However, clinicians should be mindful that silver-containing dressings vary considerably in their composition, method of silver delivery and amount of silver delivered. Like any local wound treatment, silver-containing dressings form only one part of a comprehensive wound management programme which considers the patient from a holistic perspective.

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