

# Experimental and clinical evidence for DACC-coated dressings: an update

**Objective:** To update the evidence in relation to the use of dialkylcarbamoyl chloride (DACC)-coated wound dressings in the prevention, treatment and management of wounds.

**Method:** PubMed and PubMed Central databases were searched to identify articles published since 2020 describing the experimental and clinical evidence for DACC-coated dressings, and their antimicrobial effect, as well as their impact on the prevention and treatment of infected wounds. The identified articles were then narratively reviewed.

**Results:** The search yielded 113 articles (plus references from ad hoc sources), of which nine met the inclusion criteria. Of the nine included studies, five related to clinical aspects and four were laboratory studies.

**Conclusion:** A number of new studies have provided further evidence for the mode of action of the antimicrobial effect of DACC-coated dressings and its wide spectrum effect (including World Health Organization-prioritised microorganisms). Additional clinical studies have provided evidence of new applications, such as in treating wounds in paediatric patients, and extended the evidence relating to their use in treating surgical site infections. Evidence also shows that DACC-coated wound dressings can aid in the binding of biofilms, and how this technology can align and support antimicrobial stewardship in the prevention of antimicrobial resistance.

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antimicrobial resistance • antimicrobial stewardship • antimicrobial resistant microorganisms • biofilms • DACC • dialkylcarbamoyl chloride • WHO-prioritised wound pathogens • wound • wound care • wound dressing • wound healing

Since both Chadwick and Ousey,<sup>1</sup> and Rippon et al.<sup>2</sup> reviewed this topic in the *Journal of Wound Care*, there have been advances in the available evidence—both scientific and clinical—for the use of dialkylcarbamoyl chloride (DACC)-coated dressings for the prevention and treatment of a variety of wounds. This article reviews the evidence now available since the publication of these earlier articles.

## Wounds and infection

The wound environment is ideal for the growth of bacteria and, as a consequence, wounds can support varying levels of microbes—ranging from colonisation to infection.<sup>3,4</sup> Colonisation is characterised by the presence of replicating bacteria in the wound without causing damage to tissues, whereas infected wounds have proliferating bacteria that are at a level that causes damage to tissues and prevents healing.<sup>3</sup> Acute wounds are generally characterised by low bacterial burden, whereas hard-to-heal (chronic) wounds have a high incidence of bacteria, including biofilms.<sup>5</sup> Biofilms consist of bacterial cells that naturally aggregate and attach within an extracellular polymer matrix. This matrix offers protection against systemic and topical antimicrobial agents,<sup>6</sup> and the impact of biofilms on hard-to-heal wound infections has been documented.<sup>7,8</sup> The presence of wound biofilms and the increasing incidence of antimicrobial-resistant microorganisms exacerbates these infections, and makes treating these wounds a major clinical challenge.<sup>9–11</sup> To heal infected wounds, it is imperative that antimicrobial agents (e.g.,

antibiotics, antiseptics and disinfectants) are used as part of their treatment regimen.<sup>12</sup>

## Antimicrobial wound dressings

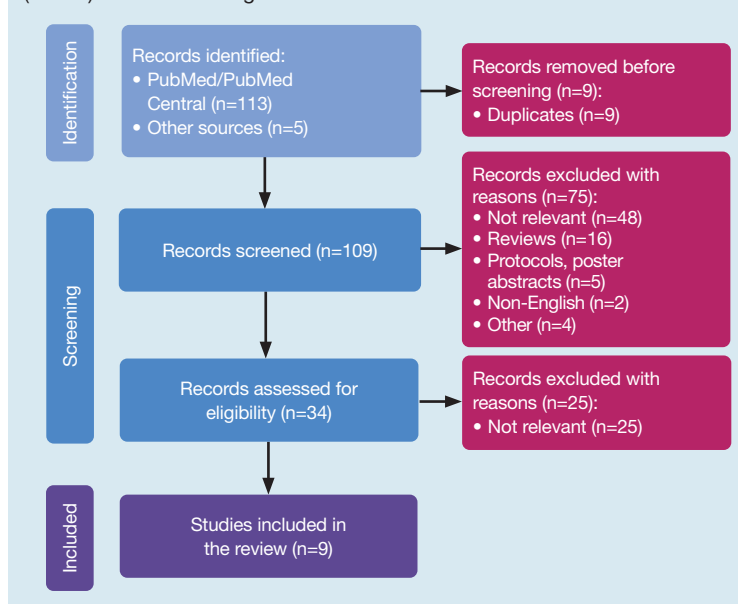
The choice of wound dressing depends on several factors, such as the specific wound being treated. It is essential to ensure that the selected dressing effectively addresses the challenges posed by the wound, such as the level of wound exudate, the presence or absence of infection, and the overall health status of the patient. There are many wound dressings currently available, and the large number of options makes choosing the appropriate dressing a complicated and difficult task for wound care practitioners.<sup>13</sup>

An 'advanced wound dressing' refers to a type of dressing or bandage that is designed to provide advanced therapeutic benefits beyond the basic function of protecting a wound. These dressings are specifically

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**Fig 1.** PRISMA flow diagram outlining the search strategy and identification of articles on the use of dialkylcarbamoyl chloride (DACC)-coated dressings



developed to promote optimal wound healing by creating an ideal environment for the healing process.<sup>14</sup> Antimicrobial wound dressings are defined as those which have, as part of their design, a component that has an antimicrobial effect. These dressings should also meet the criteria expected of any advanced wound dressing as put forward by the UK's National Institute for Health and Care Excellence (NICE).<sup>15</sup> These additional features include: having a broad spectrum effect against microorganisms (e.g., bacteria (including resistant strains), fungi, viruses); having a rapid but sustained effect; being non-irritant and non-toxic to wound tissue as well as healthy skin; and being cost-effective.<sup>16,17</sup> There are many antimicrobial wound dressings that meet these criteria and which contain several different active antimicrobial agents (e.g., silver, polyhexamethylene biguanide (PHMB), iodine).<sup>18,19</sup>

However, there are some antimicrobial wound dressings that do not act by using an active agent-dependent mechanism. An example of these is dressings coated in the fatty acid-derived dialkylcarbamoyl chloride (DACC), which have a physical mode of action (binding bacteria) resulting in an antimicrobial effect.<sup>1,2</sup> Generally, hydrophobicity plays a key role in the adherence of microorganisms to biotic (biological) and abiotic (physical) surfaces.<sup>20</sup> DACC is highly hydrophobic and readily irreversibly binds microorganisms commonly responsible for infections.<sup>21</sup> In vitro and preclinical animal studies have demonstrated DACC-coated dressings binding a number of different bacterial species (planktonic and biofilm).<sup>1,2</sup> It has been suggested that the irreversible binding of the microorganisms to the DACC-coated dressing facilitates the removal of these microorganisms at dressing change, leading to a

reduction in the wound bioburden.<sup>1,2</sup> Evidence has documented the use of DACC-coated dressings in both acute and hard-to-heal wounds in the treatment and prevention of infection.<sup>1,2</sup> NICE recommends the use of a DACC-coated dressing (Leukomed Sorbact, Essity AB, Sweden)<sup>22</sup> based upon evidence from three randomised controlled trials<sup>23–25</sup> and one non-randomised comparative study<sup>26</sup>—studies which provided evidence that the use of this DACC-coated dressing reduced the risk of surgical site infection (SSI).

The aim of this review is to provide an update on evidence relating to the use of DACC-coated wound dressing in terms of its antimicrobial effect (including mode of action), the prevention and treatment of a variety of wounds, and information on its cost-effectiveness.

## Methods

### Design

This review was conducted and reported following the guidelines defined in the Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The PRISMA statement and its included checklist provided guidance in order to assure transparent reporting of the review.

### Search strategy

A search of PubMed and PubMed Central databases from 1 January 2020 to 7 February 2023 was conducted to identify articles that reported the effect of the clinical use of DACC-coated dressing on acute or hard-to-heal wounds. The search also included laboratory studies of the in vitro effect of DACC-coated dressing on microbes and cells. The following keyword search strategy was used: '(dacc AND wound) OR Sorbact'.

### Eligibility criteria

Studies were included if they reported the outcomes of the clinical treatment of any wounds with, or laboratory studies using, DACC-coated dressings.

Articles that did not have access to full-text (i.e., not open access) or were not in the English language were excluded. Review articles, meta-analyses, poster abstracts and study protocols were also excluded.

### Data extraction and processing

The titles and abstracts of DACC-coated dressing articles identified by the literature search were assessed independently by two reviewers. Abstracts were reviewed for suitability (i.e., meeting the eligibility criteria) to include the use of DACC-coated dressings. Studies for which full texts were not found or did not meet the eligibility criteria were not included in the next stage of the review. Full texts of all included studies were then assessed. Articles thought to be relevant to the eligibility criteria but which were not identified during the PubMed searches were also evaluated for possible inclusion in the review. In addition, a manual search for papers in wound care journals not indexed in

PubMed/PubMed Central but related to the clinical use of PHMB in wounds was also carried out. Papers identified as relevant from references lists but which were not identified in the other searches were also included in this narrative review. A detailed search strategy is described in Fig 1.

## Results

The search yielded 113 articles (plus references from ad hoc sources): nine duplicate articles were initially excluded; 109 articles were reviewed for suitability with 48 being excluded for non-relevance and 27 additional articles being excluded for a number of different reasons (Fig 1). A full text review of the remaining 34 articles excluded a further 25 articles, leaving nine articles for review.

Of the nine included studies, five (55.6%) were clinical studies (Table 1): a DACC-coated dressing was applied in one (20%) study featuring patients with diabetic foot ulcers (DFUs);<sup>27</sup> two (40%) were related to surgical wounds (e.g., caesarean section, vascular);<sup>28,29</sup> one (20%) featured paediatric patients with mixed

(acute or hard-to-heal) wounds;<sup>30</sup> and one (20%) featured patients with traumatic wounds.<sup>31</sup> Overall, two (40%) clinical studies featured outcomes related to antimicrobial effectiveness (including treatment or prevention);<sup>27,30</sup> two (40%) studies featured outcomes related to wound progression or healing,<sup>28,30</sup> and two (40%) studies included outcomes related to cost-effectiveness.<sup>28,29</sup>

Of the four (44.4%) laboratory studies included in the review (Table 2): two (50%) demonstrated the effects of DACC-coated dressing on bacteria;<sup>32,33</sup> two (50%) detailed the effect of the dressing on cells important to the wound healing response (keratinocytes, fibroblasts, and macrophages);<sup>33,34</sup> and one (25%) study described the interaction between a DACC-coated dressing and bacterially produced and clinically important endotoxins.<sup>35</sup>

The clinical and in vitro evidence identified in this review update are summarised in Tables 1 and 2, respectively.

**Table 1. Summary of recent peer-reviewed clinical evidence for DACC-coated dressing**

Study	Study design	Aetiology	Sample, n	Outcome measures/ clinical challenge	Main findings
<b>Diabetic foot ulcers</b>					
Malone et al. (2022) <sup>27</sup>	Non-comparative, proof-of-concept study	DFUs	20	Reduced bacterial load with removal of DACC-coated dressing	Mean total microbial load of DFUs did not change after two weeks of therapy. Biofilms adhere to DACC-coated dressings
<b>Surgical wounds</b>					
Mahyudin et al. (2020) <sup>28</sup>	Comparative, observational study: DACC-containing dressing versus gauze/tulle dressing	Orthopaedic and traumatology surgery wounds	25	Wound healing (BWAT) score; patient comfort (frequency of wound care, pain VAS); cost-effectiveness (indirect and direct costs)	Slight improvement in wound healing (reduced BWAT score) and better patient comfort in favour of DACC-coated dressing. No difference in cost-effectiveness
Taylor et al. (2020) <sup>29</sup>	Audit study	Caesarean section wounds	N/A*	SSI rate	Use of evidence-base and guidelines, education and introduction of DACC-coated dressings reduced SSI rates
<b>Traumatic wounds</b>					
Avkan-Oğuz et al. (2020) <sup>31</sup>	Case series	Traumatic leg wound	1	Wound infected with <i>Aspergillus flavus</i> ; leg wound with exposed bone; tissue necrosis	Systemic antifungal initiated DACC-coated dressing applied daily. No fungal growth observed in third week of systemic antifungal therapy and dressing application. Wound improvement led to skin grafting
<b>Mixed wounds</b>					
Ciprandi et al. (2022) <sup>30</sup>	Non-comparative, retrospective assessment	Varied acute and chronic paediatric wounds	1232	Signs of infection; wound healing; SSI prevention	Use of DACC-coated dressing prevented SSIs, reduced signs of infection and promoted wound progression

DACC—dialkylcarbomyl chloride; DFUs—diabetic foot ulcers; BWAT—Bates-Jensen Wound Assessment Tool; VAS—visual analogue scale; SSI—surgical site infection; \*Sample size not available

**Table 2. Summary of in vitro evidence for DACC-coated dressing**

Study	Cell type	Comparators	Outcome measure	Main results
Husmark et al. (2022) <sup>32</sup>	WHO-prioritised wound pathogens	DACC-coated dressing, two silver dressings and a gauze dressing	Ability to bind potentially pathogenic microorganisms; antibacterial effect	DACC-coated dressing has a high and sustained antibacterial effect
Morgner et al. (2022) <sup>34</sup>	HaCaT keratinocytes; normal human dermal fibroblasts	DACC-coated dressing versus uncoated control	Ability of DACC-coated dressing to support cell viability; ability to induce growth factor and collagen production	DACC-coated dressing promoted cell viability and supported wound healing in vitro; DACC-coated dressing slightly induced growth factor production in cells
Ortega-Peña et al. (2022) <sup>33</sup>	<i>Staphylococcus aureus</i> ; murine macrophages (RAW 264.7 cells); murine fibroblasts (3T3 cells)	DACC-coated dressing versus gauze dressing	<i>Staphylococcus aureus</i> adhesion and growth; indirect effect of DACC-coated dressing on fibroblast and macrophage activity	DACC-coated dressing had an antibacterial effect and bound bacteria to dressing; filtered supernatants of bacteria treated with DACC-coated dressing did not stimulate growth factor or gelatinase activity in cells
Susilo et al. (2022) <sup>35</sup>	<i>Pseudomonas aeruginosa</i>	DACC-coated dressing and four antimicrobial dressings	Ability of DACC-coated dressing to bind Gram-negative bacteria-derived endotoxin	DACC-coated dressing binds purified and shed endotoxin

DACC—dialkylcarbonyl chloride; WHO—World Health Organization

## Discussion

### DACC and its antimicrobial activity

An ever-increasing number of resistant pathogens have been identified, some of which cause infection in wounds (Fig 2). A number of laboratory-based experimental studies have previously demonstrated DACC-coated dressings binding microorganisms, including antimicrobial-resistant microorganisms, when dressings are challenged with planktonic microorganisms.<sup>36–39</sup>

A recent study has extended the evidence for the antimicrobial effect of DACC-coated dressings, particularly regarding the antimicrobial effect against World Health Organization (WHO)-prioritised microorganisms (*Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Enterococcus faecium*, vancomycin-resistant *Enterococcus* (VRE), *Pseudomonas aeruginosa*; extended spectrum beta-lactamase (ESBL), *Enterobacter cloacae*, and *Acinetobacter baumannii*).

Using a standard laboratory test (the Japanese Industrial Standard (JIS) L 1902 challenge test), Husmark et al.<sup>32</sup> demonstrated a high antibacterial effect against the WHO-prioritised bacteria using a DACC-coated dressing. The authors identified that a necessity for effective antimicrobial action is close contact between the bacteria and the DACC-coated dressing. Strong binding of bacteria to the dressing was indicated by no release of bacteria from the dressing fibres despite extensive washing in the presence of surfactant. Furthermore, when evaluated under more challenging conditions, for example, at increased inoculation densities and augmented media protein content, the DACC-coated dressing still achieved an antibacterial effect. The authors also demonstrated that varying pH did not influence antibacterial performance.

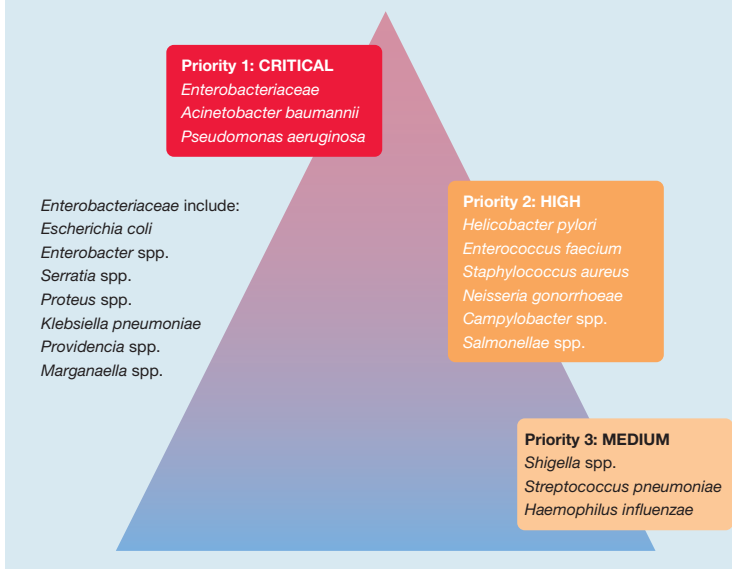
Ortega-Peña et al.<sup>33</sup> reported the direct effect of a

DACC-coated dressing on *Staphylococcus aureus* adhesion and growth in a laboratory-based study. A piece of DACC-coated dressing or cotton gauze (acting as control) was placed in each well of a 24-well culture plate and incubated for three hours in *Staphylococcus aureus* cultures. The results showed significantly less bacterial growth from DACC-coated dressing supernatants compared with gauze dressing ( $p < 0.01$ ) and control ( $p < 0.001$ ) samples. This study demonstrated that the DACC-coated dressing enabled the physical removal of bacteria, and that this removal was without bacterial killing or lysis. Examination of the dressing by light and electron microscopy demonstrated bacterial binding to the DACC-coated dressing.

DACC-coated dressings have been shown to exhibit antimicrobial activity in the clinical environment. In a small, proof-of-concept study conducted in 20 patients with DFUs with suspected localised infection, Malone et al.<sup>27</sup> investigated if the removal of DACC-coated dressings contributed an antimicrobial effect by reducing total bacterial numbers. A DACC-coated dressing was placed in contact with the ulcer bed and reapplied every three days, for a total of 14 days. All patients received standard of care for the study duration. The investigation showed, using scanning electron microscopy, that biofilm was adherent to DACC-coated dressings when they were removed, and that 8/20 patients experienced a reduction in total microbial load, although there was no change in the mean total microbial load in the 20 patients. The authors found no evidence that DACC-coated dressings alter the microbiome composition of DFUs, nor did they find evidence to suggest that specific types of microorganisms demonstrated a preference for adherence to the DACC-coated dressing.

The physical removal of intact bacteria reduces the potential for the release of molecules toxic to cells (e.g.,

**Fig 2.** World Health Organization priority pathogens list (adapted from Tacconelli et al.<sup>57</sup>)



bacterial endotoxins) involved in the wound healing response. Endotoxins cause inflammation and can impair wound healing.<sup>40–42</sup> Susilo et al.<sup>35</sup> studied in vitro the endotoxin-binding capacity of a DACC-coated dressing (Sorbact Compress, Essity AB, Sweden). The authors reported the overnight incubation of the DACC-coated dressing with various concentrations of purified *Pseudomonas aeruginosa* endotoxin reduced levels of free endotoxin by 93–99%. Endotoxin reduction was rapid, with a 39% reduction after five minutes. A one-hour incubation of a *Pseudomonas aeruginosa* cell suspension, after removal of the bacterial cells, was demonstrated to release 420 endotoxin units (EU)/ml. In contrast, the presence of a DACC-coated dressing resulted in >99.95% removal of endotoxin by binding to the dressing. The authors speculated that the DACC-coated dressing-mediated removal of both endotoxin and bacterial cells from wounds could promote the wound healing process.

#### Mode of action

DACC-coated dressings have a physical mode of action, are effective in wound bioburden management and support antimicrobial stewardship (AMS), as there is no risk of bacteria developing resistance.<sup>2,43</sup> The unique DACC-coated surface has special characteristics and highly hydrophobic properties—in the presence of water molecules, bacteria commonly responsible for causing infection will irreversibly bind to the dressing surface. These bound and intact microorganisms are then removed from the wound site at the dressing change.<sup>1,2</sup>

The study by Husmark et al.<sup>32</sup> identified anchoring points between the fibres of the DACC-coated dressing and WHO-prioritised bacteria, suggesting a strong

interaction between bacteria and dressing. The authors concluded that the antibacterial effect exerted on the tested bacteria was via bacterial binding, and speculated that the DACC-coated dressing exerted beneficial effects in controlling wound bioburden, reducing the overall demand placed on antibiotics, without using antimicrobial substances. They reported that no chemically or pharmacologically active substances were released from the DACC-coated dressing,<sup>32</sup> supporting previously published evidence for a physical mode of action rather than a release of active antimicrobial agent for DACC-coated dressings.<sup>1,2</sup> The findings of Ortega-Peña et al.<sup>33</sup> that *Staphylococcus aureus* binds directly to DACC-coated dressing further support the previously proposed physical removal mode of action,<sup>1,2</sup> and the authors suggested that the hydrophobic nature of the DACC-coated dressing enabled bacterial binding and physical removal of bacteria, and that this removal maintained bacterial structural integrity.

The findings of Malone et al.<sup>27</sup> of biofilm attachment to DACC-coated dressings used to treat patients with DFUs provides additional clinical evidence of the dressing's ability to bind microorganisms when removed as part of treatment. DACC-coated dressings, with their ability to effectively bind bacteria (including WHO-relevant pathogens) over a prolonged period of time,<sup>44</sup> can support AMS goals and counter the growing threat of antimicrobial resistance (AMR).<sup>45</sup>

#### DACC in prevention and treatment of infection

Any wounds can become colonised, which might then lead to infection, but some wounds are more prone to the risk of infection than others (e.g., hard-to-heal wounds, some surgical wounds, etc.). Risk factors for SSIs include those that are patient-based (e.g., age, nutrition status, comorbidities, etc.), procedure-related (e.g., the use of drains, poor skin preparation, long surgery duration, etc.), or related to the type of surgical procedure.<sup>46</sup> DACC-coated dressings have been demonstrated to be highly effective in both preventing and treating such infections. Meta-analyses comparing different types of surgical dressings indicated that DACC-coated dressings significantly reduced the rate of postoperative SSIs ( $p=0.008$ ) and SSI risk ( $p=0.01$ ).<sup>47,48</sup>

A number of clinical studies have demonstrated promising results in both the prevention and treatment of wound infections, and the clinical evidence for DACC-coated dressings has been recently reviewed.<sup>1,2,49</sup> Taylor et al.<sup>29</sup> reported on the adoption of a multifaceted approach to quality improvement in order to reduce SSIs in women giving birth by caesarean section. Following an increase in the SSI rate (from 3.07% to 5.86%) in this group across the region serviced by the Aneurin Bevan University Health Board, Wales, the approach taken involved a number of improvements including: the use of evidence-based practice and guidelines; education and engagement of clinicians, patients and staff; and the gradual



implementation of DACC-coated postoperative dressings. The introduction of DACC-coated dressings included a face-to-face training package for staff, and regular monthly training sessions on its use. A reported change to wound care practice was for the dressing to be left in place for 4–5 days as opposed to removal of wound dressings every 24 hours post-surgery to allow clinicians to visualise the wound and apply a fresh dressing. Keeping the dressing in place for the extended length of time allowed the wound to remain undisturbed, reducing the risk of external contamination. Between 2017 and 2018, adoption of the new approach (including use of a DACC-coated dressing) resulted in a decline in average SSI rate associated with caesarean section from 5.95% to 2.68%, and represented a 54% reduction in the SSI rate in one year; the authors concluded that this approach had been important in reducing the SSI rate.

A large, non-comparative, retrospective assessment of a clinical centre's experience of using DACC-coated dressings in the treatment of various acute and hard-to-heal wounds in paediatric patients reported that the use of a DACC-coated dressing prevented SSIs, reduced signs of infection and promoted wound progression.<sup>30</sup> A retrospective assessment of the 15-year experience of using DACC-coated dressings in paediatric care documented its use in a variety of acute and hard-to-heal wounds in neonates and children. The authors reported on the benefits of the DACC-coated dressing in the prevention and treatment of paediatric wounds related to wound infection. A total of 4223 patients (aged 0–16 years) with a variety of wounds were admitted and 1232 children affected by complex wounds underwent treatment with a DACC-coated dressing (Cutimed Sorbact or Cutimed Sorbact gel, both Essity AB, Sweden). Of the paediatric patients affected by complex wounds, 56% presented with an infected wound. During the 15-year use of DACC-coated dressings, 402 infants with infected stage I or stage II pressure ulcers were treated with a DACC-coated dressing. The authors reported a tenfold decrease in bacterial counts after the first two dressing changes. In 45 patients affected by mono- and polysutural craniosynostosis who underwent corrective surgery, a DACC-coated dressing was applied after the surgical procedure was complete. Superficial SSIs were managed with the DACC-coated dressing and no further antimicrobial therapies were required.

#### DACC and the support of wound progression

Wound dressings have intimate contact with the wound and periwound areas. It is logical to assume, therefore, that any wound dressing or its components may have an effect (positive or negative) upon the healing process. Mayhudin et al.<sup>28</sup> found a beneficial effect of a DACC-coated dressing on wound healing in a comparative study of patients with acute wounds treated with either DACC-coated dressing or gauze/tulle dressing. The study involved 25 orthopaedic and

traumatology patients with wounds treated in a surgical ward and who were assigned to receive either a DACC-coated dressing (Cutimed Sorbact) or gauze/tulle dressing (as control). An assessment of wound healing using the Bates-Jensen Wound Assessment Tool (BWAT), a wound condition assessment tool,<sup>50</sup> showed a significant reduction in the mean BWAT score in patients receiving the DACC-coated dressing compared with patients receiving the gauze/tulle dressing ( $31.26 \pm 1.69$  versus  $33.07 \pm 1.65$ , respectively;  $p=0.017$ ), indicating an improvement in wound condition and progression in wound healing.

A proof-of-concept study describing the binding of biofilm to a DACC-coated dressing in patients with DFUs noted a tendency for a reduction in wound area with its use.<sup>27</sup> Although the reduction in wound area was not statistically significant, there was a clinically relevant mean decrease in wound area from  $508.6 \pm 504.0 \text{ mm}^2$  at baseline, to  $329.3 \pm 314.0 \text{ mm}^2$ , respectively) after two weeks.

Ciprandi et al.<sup>30</sup> reported that almost 92% of the 1232 paediatric patients with a variety of complex wounds treated with DACC-coated dressings over a 15-year period exhibited complete healing of their wounds, and that there was no recurrence of wounds after a mean follow-up period of 90 days.

The *in vitro* testing of DACC-coated dressings in the presence of cells important to wound healing was undertaken to assess the potential effect of the dressing's close contact on wound healing.<sup>51</sup> In this early study, the authors demonstrated that the presence of the dressing in an *in vitro* wound model resulted in an increase in the proliferation rate of cultured fibroblasts. More recent studies have suggested that DACC-coated dressings are not cytotoxic to several cell types important for healing (e.g., keratinocytes, fibroblasts, macrophages). Morgner et al.<sup>34</sup> reported the potential effects of a DACC-coated dressing on fibroblasts and keratinocytes, and their production of growth factors. Contact with the dressing had no effect on the viability of keratinocytes (HaCaT cells) or normal human dermal fibroblasts cultures, and did not affect normal cell proliferation and migration of these cells (as measured by an *in vitro* scratch wound healing model). The authors observed that increased gene expression (growth factors and collagen) stimulated by wounding was minimally affected by the presence of the DACC-coated dressing. The authors speculated that the dressing supported normal wound healing progression by having little detrimental effect on the cells important to the healing response.

As stated previously, bacterially derived endotoxins that are released as a result of bacterial killing cause inflammation and can impair wound healing.<sup>40–42</sup> Ortega-Peña et al.<sup>33</sup> reported results of an *in vitro* study examining a DACC-coated dressing. The authors demonstrated that filtered supernatants of bacterial cultures treated with the dressing did not over-stimulate

the production of several growth factors (tumour necrosis factor (TNF)-alpha, transforming growth factor (TGF)-beta 1), nor did it increase gelatinolytic activity in fibroblast and macrophage cocultures. The authors speculated that the physical removal of bacteria by the dressing without killing the bacterial cells minimised the risk of the release of molecules proinflammatory or toxic for cells important to healing.

#### Patient comfort

DACC-coated dressings have also been demonstrated to be comfortable to wear. A prospective observational study involving patients with venous leg ulcers (VLUs) and DFUs assessed the dressing's clinical performance, safety and effect on patient quality of life. In the study, clinicians rated the following assessment parameters in relation to the dressing as 'very good' to 'good': wearing comfort (rated by the patient); application and removal; exudate absorption with or without compression; fluid retention capacity with or without compression; and infection management.<sup>52</sup>

When assessed in a series of 25 orthopaedic and traumatology patients with wounds treated on a surgical ward, the DACC-coated dressing was also found to have a good outcome with regard to patient comfort (as assessed by parameters including pain experienced).<sup>28</sup> Patient comfort was assessed using the frequency of wound care events (e.g., dressing change) over the course of the study and including the level of pain experienced at each event. The authors noted a lower mean frequency of wound care event for patients receiving DACC-coated dressing compared with controls ( $3.07 \pm 0.88$  versus  $4.60 \pm 1.84$ , respectively;  $p=0.021$ ) and a reduction in the mean Visual Analogue Scale pain score ( $4.59 \pm 0.72$  versus  $5.43 \pm 0.75$ , respectively;  $p=0.014$ ).

#### DACC and cost-effectiveness

Hard-to-heal wounds are associated with high treatment costs and previous data from Germany suggest that wound dressings can be a main cost-driver for the treatment of VLUs.<sup>53</sup> A number of studies have previously reported positive cost impacts for the use of DACC-coated dressings in wounds.<sup>53–55</sup> The introduction of a multifaceted treatment approach to reduce SSIs for women undergoing caesarean section, which included the introduction of DACC-coated dressings, resulted in a reduction in the average SSI rate associated with caesarean section, with an estimated cost saving for the maternity services between 2017 and 2018 of £163,816.<sup>29</sup>

Although a recent comparative study reporting the use of a DACC-coated dressing and gauze dressing in orthopaedic and traumatology surgery wounds found cost-effectiveness for both dressings were similar (for both direct (e.g., dressing costs, hospital costs, etc.) and indirect costs (e.g., productivity costs, etc.)),<sup>28</sup> cost modelling carried out as part of the NICE guidance for the DACC-coated dressing Leukomed Sorbact has

shown that the reduced rate of SSI with the DACC-coated dressing compared with standard surgical dressings led to cost savings of £107 per person after caesarean section and £18 per person after vascular surgery. They concluded that, by adopting use of the dressing, the National Health Service in England alone may save up to £5.3 million per year for caesarean sections and up to £1.2 million per year for vascular surgery as fewer patients will need to stay in hospital for SSI treatment.<sup>22</sup>

Furthermore, the introduction of the Leeds Wound Infection Framework in England (which included the use of DACC-coated dressings), as well as standardising care, led to improvements in cost-efficiency.<sup>45</sup> Spending on antimicrobial wound dressings (i.e., silver) reduced by almost 50%, antimicrobial spending overall was reduced by almost 15%, and there was a slight decrease in antibiotic prescribing.

Totty et al.<sup>56</sup> investigated the impact of SSIs on costs for healthcare providers, and their effect on hospitalisations, treatment costs and health-related quality of life after vascular surgery. Originally part of a study to assess the impact of DACC-coated dressings on the incidence of SSIs,<sup>25</sup> study participants were stratified into those who did not experience SSI within 30 days following surgery (No SSI:  $n=107$ ) and those who did (SSI:  $n=29$ ). A mean SSI-associated length of stay of 9.72 days resulted in an additional cost of £3776 per patient (including a mean antibiotic cost of £532). Adjusting for age, smoking status and procedure type, SSI was associated with a 92% increase in length of stay ( $p<0.001$ ). Readmission rates were higher with SSI ( $p=0.017$ ), and the rate of return to work within 90 days was lower. This study suggests that strategies to reduce the risk of SSIs—including the use of DACC-coated dressings—have the potential to reduce healthcare provider costs.

#### Limitations

Due to the general lack of larger studies addressing the efficacy of DACC-coated dressings in acute or hard-to-heal wounds, we were restricted to a limited range of reported data. There is a large degree of heterogeneity among reported outcomes in the studies. Bigger, randomised, multicentre studies are required to validate the results found from this updated review of the literature.

The inclusion of only papers in English is a limitation as there may have been significant clinical trials written in other languages. However, no non-English studies were identified in the early stages of the search process and we feel that this limitation was not applicable here.

The search for this review was limited to the PubMed/PubMed Central databases. There is the potential for this search to miss literature relevant to this review. However, we believe that a PubMed-only approach to the search captured all the main studies relevant to this review. However, for a more formal meta-analysis or systematic review, a search of multiple electronic literature databases would be appropriate.

## Conclusion

A number of new studies have provided further evidence for the mode of action of the antimicrobial effect of DACC-coated dressings and their wide spectrum effect, particularly regarding the antimicrobial effect against WHO-prioritised microorganisms. Additional clinical studies have provided evidence relating to new clinical applications, such as treating paediatric wounds, as well as extending the evidence

relating to SSIs, underpinned by the NICE guidance.<sup>22</sup> Specifically, DACC-coated wound dressings can help bind biofilms, which supports AMS and helps prevent AMR. Furthermore, recent laboratory-based work has added to the potential mode of action of DACC-coated dressings, the DACC-mediated removal of microbes and bacterial endotoxins from wounds which, together, could prevent and treat/manage infection and promote wound healing. **JWC**

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### Reflective questions

- What are the benefits of dialkylcarbamoyl chloride (DACC)-coated dressings in terms of treating wound infection?
- What is the basis of the mode of action of DACC-coated dressings?
- What are the top priority World Health Organization-listed pathogens?
- How cost-effective are DACC-coated dressings?

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