Supporting evidence-based practice: clinical review of TLC healing matrix
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>3</td>
</tr>
<tr>
<td>Evidence-based dressing selection</td>
<td>4</td>
</tr>
<tr>
<td>Pre-clinical evidence</td>
<td>11</td>
</tr>
<tr>
<td>The clinical evidence for dressings with TLC healing matrix (UrgoTul)</td>
<td>13</td>
</tr>
<tr>
<td>Dressings with hydro-desloughing fibres and TLC healing matrix (UrgoClean)</td>
<td>25</td>
</tr>
<tr>
<td>Dressings with TLC-NOSF healing matrix (UrgoStart)</td>
<td>29</td>
</tr>
<tr>
<td>Dressings with TLC-Ag and TLC-SSD healing matrix (UrgoTul Ag/SSD/UrgoCell Ag)</td>
<td>37</td>
</tr>
<tr>
<td>References</td>
<td>45</td>
</tr>
</tbody>
</table>

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**DECLARATION OF INTEREST:** Tracy Cowan is an employee of MA Healthcare, which Urgo Medical commissioned to summarise the clinical evidence presented in this supplement. Deborah Glover is an independent editorial consultant who received a fee for summarising this evidence. Richard White received a fee for reviewing the clinical data presented in this supplement, and also offers a consultancy service for various wound-care companies.
The requirements for evidence-based wound care have been evident for some years, despite continuing confusion over the definition and nature of this ‘evidence’, while the hierarchy of clinical evidence remains a topic of heated debate. Nonetheless, practitioners are faced with the inescapable task of compiling and evaluating all available evidence before making clinical judgements.

This review aims to provide clinicians, pharmacists and all others involved in the dressings supply chain with a thorough summary and assessment of the evidence relating to Urgo’s TLC range of wound dressings. While the compilation of this review has been financially supported by Urgo, it has been written with total academic freedom. Urgo’s philosophy of exhaustive clinical research manifests in the relative wealth of evidence now available. The emphasis here is on the word ‘relative’, for in order to understand this review, it is essential to consider the context in which it has been written.

In the ‘modern age’ of wound care, since George Winter’s key publications on moist wound healing in the early 1960s, dressings have been designed to support a moist wound interface. The growth of the industry that provides these products has been parallel to the development of a clinical specialty in many countries.

A variety of experts, both clinical and scientific, have striven to produce evidence in support of interventions and clinical observations. It has become apparent that wound healing is not as straightforward as first thought, requiring the reaching of various milestones along the path to healing — if, indeed, healing is the clinical objective. Thus, early goals include the debridement of slough and necrotic tissues and the control of infection. Later, the main objectives are promotion of granulation and epithelialisation. This is especially evident in ‘chronic’ wounds, such as leg ulcers, pressure ulcers and diabetic foot ulcers.

In the past three decades, millions of patients have benefitted from the use of modern wound dressings, and the evidence base reflects their clinical use. While early experiences warranted a case-by-case approach, thereafter, clinical trials were conducted — mainly against dry gauze, the standard of the day. It must be remembered that while many now decry the gauze comparator, such dressings are still widely used in many health-care systems. It is also vital to emphasise that the evidence for dry dressings remains very weak, considering current financial constraints and efforts to cut costs through restricting the use of ‘modern’ dressings.

The following compilation of clinical evidence covers Urgo’s entire range of lipidocolloid wound dressings, known as the TLC healing matrix range. There are randomised, controlled clinical trials, observational studies, and a number of cases and case cohorts; these involve many thousands of patients and a wide variety of wound types and clinical challenges. This evidence is collated and presented for your information, to assist you in making judgements on clinical use, purchasing and formulary processes. It is vital in such circumstances that you look at and appraise the totality of the evidence. Every effort has been made to present it here.
Evidence-based dressing selection

A wide range of considerations determine dressing selection. Taking into account the wound type, the patient’s holistic needs and his or her own clinical experience, the practitioner will then look to the literature for guidance. To support practitioners with their decision-making, this supplement provides an in-depth review of the evidence on the TLC healing matrix range of dressings. Its objective is to summarise the literature, as opposed to critiquing it.

Richard White, Professor of Tissue Viability, Institute of Health and Society, University of Worcester, and Director, Plymouth Wound Care Ltd, Tracy Cowan, Consultant Editor, Journal of Wound Care, and Deborah Glover, Independent Editorial Consultant

When faced with a plethora of dressings, how does the clinician decide which product to use? Clearly, clinical knowledge, based on experience complemented by evidence from the literature, will be the largest factor influencing the decision. The clinician will start by assessing both the wound (type, duration, size, exudate level, pain, presence of malodour, condition of the surrounding skin) and the patient (age, medical history, comorbidities, psychosocial factors) and will then consider the potential effectiveness of the selected product, evidenced by clinical outcomes and demonstrated cost-effectiveness. Naturally, the type/nature of the wound and stage of healing will also influence product selection and management options.

Identifying a chronic wound

The phases of the wound healing process are well known. For the purposes of this supplement, it is assumed that acute wounds, such as minor burns, surgical wounds, lacerations and other traumatic injuries, generally follow the three key stages of the healing trajectory — inflammation, proliferation and maturation — with little deviation.

Chronic wounds, in contrast, do not progress through these phases in an orderly and timely sequence and generally fail to heal in 4–6 weeks despite the provision of standard care. Chronic wounds (which are primarily leg ulcers, pressure ulcers and diabetic foot ulcers) may become ‘stuck’ in the inflammatory stage. In addition, matrix metalloproteinases (MMPs), which are protein-digesting enzymes, help remove dead and devitalised tissue. Their number is kept in check by tissue inhibitors of metalloproteinases (TIMPs), thereby preventing undue protease damage to healthy tissue. In chronic wounds, however, such anti-protease activity is diminished, resulting in significantly elevated levels of proteases. Studies have shown that chronic wounds can contain up to 65 times more proteases than acute wounds. The ensuing excessive MMP activity effectively stalls the healing process. Proliferation of keratinocytes, fibroblasts and endothelial cells is slowed or blocked. The MMPs degrade key components of the extracellular matrix (fibronectin, fibrin and collagen) as well as the viable marginal tissue, and impair the expression of growth factors. Similarly, the release of reactive oxygen species is much higher in chronic than acute wounds. This not only results in the degradation of viable tissue but also in local ischaemia. In this way, inflammation is prolonged and healing delayed, with 50% of chronic wounds becoming longstanding. This can have potentially devastating consequences for the patient, as well as huge resource implications for the individual, the health service and employers (Box 1).

Patient risk factors that may predispose a wound to become chronic include incontinence, under-
mining, peri-wound maceration, infection, oedema, chronic venous insufficiency or arterial disease of the lower leg, diabetes, chemotherapy, steroids and the presence of a wound biofilm. If any of these risk factors are present, the clinician must ensure that prevention measures are taken and the factors that may cause the wound to become chronic are addressed. This is of particular relevance to the management of MMPs, where effective ‘rebalancing’ of MMPs in the wound bed will accelerate healing in a chronic wound.

So how can the clinician determine whether the dressing is having this desired effect? A 20–40% wound area reduction at 3–4 weeks has been demonstrated to be highly predictive of complete closure at 20–24 weeks in leg ulcers. Therefore, if a wound (treated or not) has not shown signs of progression from the inflammatory stage to the proliferative stage within this time frame, it could have become chronic.

Management of chronic wounds
Evidence has shown that, for many patients, managing the symptoms of a wound is as important, if not more so, than promoting healing. The results of a multinational, multicentre trial undertaken in 2008 showed that wound pain, both ongoing and/or during dressing removal/procedures, was the most distressing and stressful aspect of having a wound. Impaired mobility, difficulties with bathing, leakage, malodour, bandage/dressing slippage and skin trauma were also considered important. These findings support those of other studies.

Therefore, the objective of treatment is not only to treat the underlying aetiology of the wound (with pressure-redistributing equipment for pressure ulcers, offloading for diabetic foot ulcers or compression therapy for venous and mixed aetiology ulcers), but also to select a dressing that will promote a wound environment that is conducive to healing and acceptable to the patient. To achieve this, a dressing will need to:

- Maintain a good moisture balance at the wound/dressing interface
- Allow gaseous exchange
- Provide thermal insulation
- Form a barrier to bacteria
- Be non-toxic and non-irritant
- Not cause pain or trauma at removal
- Require minimal disturbance or replacement
- Other desired properties include the ability to remove or inactivate proteolytic enzymes, remove excess exudate and devitalised tissue, have an antimicrobial effect and control malodour.

Inevitably, no one dressing has all of these properties and, as the patient progresses to the stated goals (healing or symptom management), the functions that will determine dressing selection, such as moisture balance, pain relief, management of infection or wound bed preparation, will change. When selecting a dressing, the clinician will therefore seek to identify one that can best meet the patient’s individual needs at that particular time. As stated above, the selection will be based on clinical knowledge, clinical experience and appraisal of the published evidence. Only in this way can it be claimed to be evidence-based.

Evidence-based dressing selection
Published evidence for the efficacy of an intervention can be found through a number of resources:

- National Institute for Health and Care Excellence (NICE)
- Professional bodies — for example, the World Union of Wound Healing Societies (WUWHS) and the European Wound Management Association (EWMA)
- Health databases (CINAHL, PubMed)
- Cochrane Database of Systematic Reviews
- York Centre for Review and Dissemination.

Received wisdom on clinical evidence is that it falls into a hierarchy depending on the type of study undertaken. The hierarchy of evidence and associated grading recommendations relate to the strength of the literature (Box 2). Meta-analyses of randomised controlled trials (RCTs), followed by the RCT, are considered to provide the best evidence for the efficacy of a treatment intervention. However, there is an ongoing debate about our apparent over-reliance on RCTs for constructing the evidence-base in wound care, with some arguing that the narrow inclusion/exclusion criteria used mean the findings are not necessarily

### Box 2. Hierarchy and source of clinical evidence

- Meta-analyses of well-designed randomised controlled trials
- Randomised controlled trials
- Evidence from well-designed, non-randomised controlled trials, such as cohort studies
- Case control studies
- Case series studies
- Expert opinion
applicable to the ‘real-life events that lie beyond the study confines’ and that other levels of evidence should also be used to inform practice.17

While no one denies that a well-conducted meta-analysis (or RCT) can produce robust results, or can reasonably argue that studies at all levels of the evidence hierarchy are equally valid, there is concern that the findings of some RCTs/meta-analyses relating to wound-care treatments do not support widely accepted empirical evidence. For example, a Cochrane systematic review concluded that there is insufficient evidence to support the use of silver dressings,18 even though it is a popular (and by association effective) antimicrobial in both primary and secondary care. Indeed, meta-analyses have even concluded that there is little or no compelling evidence of a significant difference in healing times between wounds treated with traditional and modern dressings,19 contrary to the received wisdom of clinical practice worldwide.

Such findings may be due to a wide variety of factors, including methodological inconsistencies between the various studies analysed, methodological flaws within individual studies, inadequate sample sizes, short follow-up periods, non-blinded assessment of outcomes, poorly defined control groups, and the subjectivity of those who decree the evidence to be ‘inconclusive’.

One of the most notorious examples of a poor methodological design is the VULCAN RCT, where the investigators inappropriately tested the efficacy (ulcer healing) of silver-donating dressings over 12 weeks in patients with leg ulcers showing no clinical signs of infection or bacterial colonisation.20 The finding that there were no significant differences in healing outcomes between the silver

<table>
<thead>
<tr>
<th>Dressing</th>
<th>Description</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>UrgoTul</td>
<td>Contact layer impregnated with TLC (hydrocolloid and petroleum jelly particles)</td>
<td>Wounds with no or low exudate levels at the granulation/epithelialisation stage: burns, skin grafts, skin tears, donor sites, traumatic wounds, postoperative wounds, amputation stumps, paediatric wounds, leg ulcers, pressure ulcers, diabetic foot ulcers, and epidermolysis bullosa. Can also be used in cavity wounds and under compression. Can be combined with an absorbent secondary dressing. Can be left in place for up to 7 days.</td>
</tr>
<tr>
<td>Urgotul Duo</td>
<td>As for UrgoTul, with light absorbent pad</td>
<td>Low exuding wounds at the epithelialisation stage of healing, such as burns, traumatic wounds and skin abrasions</td>
</tr>
<tr>
<td>UrgoTul Lite</td>
<td>As for UrgoTul, with light absorbent foam pad and backing (no border)</td>
<td>Low exuding wounds at the epithelialisation stage of healing, such as burns, traumatic wounds and skin abrasions</td>
</tr>
<tr>
<td>UrgoTul Lite Border</td>
<td>As for UrgoTul, with light absorbent pad and backing with border</td>
<td>Low exuding wounds at the epithelialisation stage of healing, such as burns, traumatic wounds and skin abrasions. Particularly recommended for wounds with a healthy peri-wound skin</td>
</tr>
<tr>
<td>UrgoTul Absorb</td>
<td>Soft adherent TLC healing matrix with absorbent foam pad and backing (no border)</td>
<td>Moderately exuding wounds at the epithelialisation stage of healing, such as burns, traumatic injuries and skin abrasions. Can be used under compression</td>
</tr>
<tr>
<td>UrgoTul Absorb Border</td>
<td>Soft adherent TLC healing matrix, with foam/highly absorbent layer and backing with a silicone border</td>
<td>Moderately exuding wounds at the epithelialisation stage of healing, such as burns, traumatic wounds, skin abrasions and postoperative wounds. Can be used under compression</td>
</tr>
<tr>
<td>Urgoclean</td>
<td>Soft-adherent TLC healing matrix, with hydro-desloughing pad</td>
<td>All exuding wounds in the desloughing stage, such as leg ulcers, pressure ulcers, diabetic foot ulcers and traumatic wounds. Also available as a rope (with no TLC healing matrix to facilitate application) for cavity wounds</td>
</tr>
</tbody>
</table>

Table 1. Dressings containing Technology Lipido-Colloid (TLC) healing matrix
dressing and the cheaper, non-silver comparator has been used as a rationale to remove silver dressings from wound formularies.

In response to such confusion about what actually constitutes evidence in wound care, the European Wound Management Association (EWMA) Patient Outcome Group produced useful guidance on how to conduct quality trials. The document acknowledges that very few wound care products have a sufficiently large market to justify the expense and time needed to implement a RCT. It proposes that generic or ‘me-too’ products, which abound in wound care, can be assessed by the process of equivalence, stating that only when a product is significantly different from anything that has already been approved is a new comparative clinical trial likely to be required. The implication is that observational (clinical) studies are sufficient in such circumstances.

The document also states that traditional endpoints (wound closure, wound area reduction and healing time) do not reflect the entire patient

<table>
<thead>
<tr>
<th>Dressings containing TLC healing matrix and silver (TLC-Ag and TLC-SSD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UrgoTul SSD</strong></td>
</tr>
<tr>
<td><strong>UrgoTul Ag/Silver</strong></td>
</tr>
<tr>
<td><strong>UrgoTul Ag Lite</strong></td>
</tr>
<tr>
<td><strong>UrgoTul Ag Lite Border</strong></td>
</tr>
<tr>
<td><strong>UrgoCell Ag/Silver</strong></td>
</tr>
<tr>
<td><strong>UrgoCell Ag Border</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dressings containing TLC healing matrix and protease inhibitor (TLC-NOSF)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UrgoStart Contact</strong></td>
</tr>
<tr>
<td><strong>UrgoStart</strong></td>
</tr>
<tr>
<td><strong>UrgoStart Border</strong></td>
</tr>
</tbody>
</table>
experience or even the primary indications of certain dressings, and proposes that other endpoints, such as the presence of wound infection, pain and change in wound condition (for example, exudate level, malodour etc.), can be equally valid, although they should be predefined and, wherever possible, measured in a way that can be validated independently. There is a very strong case for conducting ‘outcomes’ research and pragmatic trials in wound management.22

In summary, while case studies, observational studies and clinical studies may not be perceived to be of ‘high value’ in terms of evidence level and grading, in wound care, where demonstrable outcomes can influence practice, they are invaluable to the practitioner and, ultimately, the patient.

The evidence for the TLC healing matrix
Urgo provides a range of dressings that can meet the management requirements of most acute and chronic wounds (Table 1). Unique to the range is Technology Lipido-Colloid (TLC healing matrix), which is based on the impregnation of hydrocolloid (carboxymethylcellulose), petroleum jelly and/or paraffin and polymers into either a fine polyester mesh or a soft-adherent layer. According to the manufacturer, as exudate is absorbed, the hydrocolloid particles become hydrated and interact with the petroleum jelly/polymers to form a lipidocolloid gel that creates a moist environment within the wound, thereby promoting healing. As first identified by Winter,23 moisture is required for
granulation tissue formation as epithelial cells cannot easily migrate across a dry wound surface.

The newly formed granulation tissue is extremely fragile, so care must be taken to ensure that it does not adhere to the dressing and become damaged at dressing removal. To prevent this, the mesh present in some of the TLC dressings has a small pore size (500µm) through which granulation tissue cannot migrate. As a result, the dressing does not adhere to the newly formed tissue, with a significantly reduced likelihood of trauma — and, in turn, bleeding and pain — at dressing change (Figs 1 and 2). A key advantage of TLC dressings is that, depending on the one used, they can be left in place for up to 7 days as they are non-adherent.24

When in contact with the wound, the permanently open mesh pores prevent any risk of occlusion and allow exudate to drain into a secondary dressing, reducing the risk of maceration of the surrounding skin. Furthermore, continuous yarn

### Table 2. Summary of studies undertaken

<table>
<thead>
<tr>
<th>Product</th>
<th>Type of study</th>
<th>Number of patients</th>
<th>Wound types</th>
</tr>
</thead>
<tbody>
<tr>
<td>UrgoTul</td>
<td>3 randomised</td>
<td>144</td>
<td>Acute and chronic wounds: burns, donor sites, skin grafts, skin tears, traumatic wounds, postoperative wounds, leg ulcers, pressure ulcers, diabetic foot ulcers and epidermolysis bullosa. Used in combination with negative pressure wound therapy (NPWT) and compression bandaging</td>
</tr>
<tr>
<td></td>
<td>1 observational</td>
<td>5850</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11 clinical studies</td>
<td>554</td>
<td></td>
</tr>
<tr>
<td>UrgoTul Duo</td>
<td>1 clinical study</td>
<td>43</td>
<td>Acute and chronic wounds</td>
</tr>
<tr>
<td>UrgoTul Absorb</td>
<td>1 observational</td>
<td>2842</td>
<td>Venous leg ulcers</td>
</tr>
<tr>
<td></td>
<td>3 clinical studies</td>
<td>138</td>
<td></td>
</tr>
<tr>
<td>UrgoTul Absorb Border</td>
<td>1 observational</td>
<td>2125</td>
<td>Acute and chronic wounds</td>
</tr>
<tr>
<td>UrgoTul SSD</td>
<td>1 randomised</td>
<td>68</td>
<td>Burns</td>
</tr>
<tr>
<td></td>
<td>2 clinical studies</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>UrgoTul Ag/Silver</td>
<td>1 randomised</td>
<td>102</td>
<td>Venous leg ulcers</td>
</tr>
<tr>
<td>UrgoCell Ag/Silver</td>
<td>1 clinical study</td>
<td>45</td>
<td>Venous leg ulcers</td>
</tr>
<tr>
<td>UrgoStart Contact</td>
<td>1 randomised</td>
<td>117</td>
<td>Chronic wounds (venous leg ulcers, diabetic foot ulcers)</td>
</tr>
<tr>
<td></td>
<td>1 clinical study</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 observational</td>
<td>1248</td>
<td></td>
</tr>
<tr>
<td>UrgoStart</td>
<td>1 randomised</td>
<td>187</td>
<td>Chronic wounds (leg ulcers, pressure ulcers, diabetic foot ulcers)</td>
</tr>
<tr>
<td></td>
<td>2 clinical studies</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7 observational</td>
<td>9681</td>
<td></td>
</tr>
<tr>
<td>UrgoClean</td>
<td>1 randomised</td>
<td>159</td>
<td>Venous leg ulcers</td>
</tr>
<tr>
<td></td>
<td>1 clinical</td>
<td>50</td>
<td>Venous leg ulcers and pressure ulcers</td>
</tr>
<tr>
<td></td>
<td>2 observational</td>
<td>2968</td>
<td>Acute and chronic wounds: venous and mixed aetiology leg ulcers, pressure ulcers, diabetic foot ulcers, postoperative and post-traumatic wounds, and all types of acute and chronic sloughy wounds</td>
</tr>
<tr>
<td>TLC dressings</td>
<td>9 observational</td>
<td>22,936</td>
<td>Acute and chronic wounds</td>
</tr>
<tr>
<td>TLC-Ag dressings</td>
<td>2 observational</td>
<td>4960</td>
<td>Chronic wounds (leg ulcers, pressure ulcers, diabetic foot ulcers), traumatic wounds and postoperative wounds</td>
</tr>
<tr>
<td>Sequential treatment</td>
<td>1 observational</td>
<td>279</td>
<td>Chronic wounds</td>
</tr>
<tr>
<td>Total number of patients in clinical studies on TLC dressings</td>
<td>54,658</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
composition ensures that no fibres are shed into the wound (Fig 3 and Fig 4).

In this way, TLC dressings meet many of the requirements of the ideal dressing. A wide range of TLC dressings are available to suit the exudate level and clinical characteristics of the wound (Table 1).

**Urgo-specific wound-healing icons**

In order to prepare a wound for healing, it is necessary to remove any factors that have the potential to delay the healing process. This requires accurate assessment of the wound bed, identification of potential barriers to healing and implementation of therapeutic strategies to optimise the potential for healing. From a clinician’s perspective, a clear, simple and logically structured wound management system, such as the Urgo-specific icons system (Box 3), which incorporates a family of products designed to address the challenges and treatment objectives of each phase of wound healing, can help to achieve this.

In order to optimise and prepare the wound for healing, any wound infection present must be addressed, as this will delay healing or even result in a deterioration. Infected wounds may require systemic antibiotics alone, a combination of systemic antibiotics and topical antimicrobial dressings, or just topical dressings that have demonstrated robust clinical efficacy in the management of wound infection.

In the meantime, it is essential to debride any slough or devitalised tissue in order to clean the wound bed, reduce exudate levels and prepare the wound for the next phase of healing. Ongoing maintenance debridement may be required to encourage granulation tissue formation. Many different types of debridement methods are available; however, factors such as patient acceptability and ease of use need to be considered. Dressings, such as UrgoClean, that facilitate topical debridement have been found to promote safe, effective and atraumatic desloughing. Once these barriers have been removed, chronic wounds, in particular, may require dressings that accelerate granulation tissue formation. As stated above, chronic wounds contain high levels of MMPs. Products that contain inhibitors of MMPs (for example, TLC-NOSF, which is a component of UrgoStart) have been found to accelerate healing and avoid wounds from becoming longstanding.

In the final phase of healing, the aim should be to close the wound and achieve the best aesthetic and functional outcome for the patient. This is achieved by using products that promote a moist environment, which is conducive to healing, while also facilitating easy and atraumatic dressing removal, exudate management and patient and clinician acceptability. Products such as the UrgoTul range have been clinically proven to provide pain-free dressing changes and to optimise healing.

**Box 3. Urgo wound-healing icons**

- **Prepare the wound bed to initiate healing**
  - In cases at risk of infection, obtain a safe large-spectrum bactericidal effect
- **Achieve efficient and atraumatic desloughing**
- **Tailor the treatment to each patient**
- **Accelerate wound healing and avoid wounds becoming longstanding**
- **Optimise wound healing**

**A substantial body of clinical evidence**

This supplement summarises the evidence from RCTs, comparative and non-comparative clinical studies, observational studies and *in vitro* studies on the efficacy, tolerability and acceptability of the TLC dressing range. Poster evidence is also included when the findings are likely to be of particular value to clinicians or there are no published peer-reviewed data on the use of TLC healing matrix on a particular wound type. In all, the efficacy, tolerability and safety of TLC dressings have been evaluated in more than 50,000 patients drawn from 170 clinical areas across Europe. Over 600 clinicians were involved in these evaluations (Table 2).

This body of clinical evidence amounts to eight RCTs involving 777 subjects, 25 observational studies involving 52,889 patients (some evaluated several TLC products) and 22 other clinical studies involving a further 992 patients. When pooled together, the results provide ‘good’ evidence, as defined by Evans, that TLC dressings promote healing and avoid pain and trauma at dressing change.
Pre-clinical evidence

Long before any wound dressing prototype is put onto a patient, many in vitro tests are conducted in the laboratory. Each test is designed to evaluate a particular performance characteristic — for example, exudate handling,\(^4^6\) bacterial barrier properties,\(^4^7\) toxicity of dressing constituents and the full formulation,\(^4^8\) plus the dressing’s antimicrobial activity.\(^4^9\) As a result, anyone with experience in wound care will have encountered and, in many cases, be guided by the evidence available from in vitro tests.

Fibrogenesis is an important mechanism in wound repair. Fibroblasts (a dermal cell type) play a key role in producing extracellular matrix components that are vital for granulation tissue formation and, later, wound closure and remodelling.\(^5^0\) In chronic wounds, where prolonged inflammation has disrupted normal healing, altered fibroblast functions can lead to fibrosis, oxidative stress and impaired closure.\(^5^1\) It follows that any intervention that is likely to ‘normalise’ fibroblast function will elicit noticeable clinical responses, which suggests that a dressing that can stimulate fibroblast proliferation will promote wound healing.

Effects on fibroblasts

The first in vitro study to assess the effect of TLC dressings on fibroblasts looked specifically at whether or not dressings modified their behaviour. The effects of UrgoTul and five other non-adhesive wound-contact dressings — Adaptic (then produced by Johnson & Johnson), tulle gras Lumiere (Solvay Pharma), Mepitel (Mölnlycke Healthcare), Ialuset (Genevrier Laboratories) and Physiotulle (Coloplast) — on cultured human fibroblasts were evaluated. Fibroblasts were taken from healthy volunteers aged 12, 32 and 51 years. The MTT assay was used to assess fibroblast viability (MTT is a colourimetric assay that assesses the overall activity of cells). Cultures in monolayer were used to study fibroblast morphology and growth. To characterise the effects of the dressings on cell phenotype, fibroblasts were seeded within collagen gels and labelled for alpha-SM and F-actin, which are markers of myofibroblast differentiation (during the wound healing process, fibroblasts transform into myofibroblasts, which have contractile properties that facilitate wound closure). Fibroblast cells were exposed to the dressing samples for 1 and 3 days.

The results demonstrated that, for all skin ages, UrgoTul, Mepitel, Physiotulle and tulle gras had no significant effects on cell growth on day 3, whereas cell proliferation was significantly reduced with Adaptic and Ialuset (p<0.05). Changes in cell morphology were noted with these two dressings, with the fibroblasts appearing round in shape on day 3, which is indicative of cell death. Cells in contact with UrgoTul, Mepitel, Physiotulle and tulle gras demonstrated the same bipolar and elongated morphology as did the controls, again indicating that the dressing did not have any cytotoxic effects. However, only fibroblasts exposed to UrgoTul exhibited long stress fibres, which is a precursor to transformation into myofibroblasts.\(^5^2\)

The next step was to assess the effect of UrgoTul on fibroblast proliferation. An in vitro study therefore compared the level of fibroblast proliferation achieved with UrgoTul with that of two similar comparators: a soft-silicone wound-contact dressing (Mepitel) and tulle gras.\(^5^3\) Proliferation was determined by whether or not there was an increase in tritiated thymidine incorporation in the DNA of replicating normal human dermal fibroblasts (a validated assay for evaluating the rate of fibroblast proliferation). In addition, cell viability/cytotoxicity was assessed using the MTT assay. Finally, following contact with the dressings, fibroblasts were also visualised using confocal laser microscopy.

In terms of cell proliferation, of all the dressings UrgoTul was associated with the highest levels of thymidine incorporation at all time points tested (24, 48, 76 and 96 hours). The difference was most marked at 48 hours (p<0.01), when it was 45% greater than in the controls (cultures with no dressings). Mepitel was associated with an overall non-significant tendency to reduce cell proliferation, although this became significant when the medium was not changed every 24 hours (Fig 5).

The MTT results confirmed those of Viennet et al.,\(^5^2\) showing that none of the test dressings significantly modified the overall metabolic activity of the fibroblast culture. However, visual observation of the cell layers showed clear differences: very little of the print pattern of the net comprising the UrgoTul and
Mepitel dressings was apparent on the cell layer, whereas with tulle gras the cell layer appeared to be significantly damaged, indicating that it was cytotoxic to fibroblasts.

Finally, cells treated with UrgoTul and Mepitel had a normal morphology, whereas those from tulle gras samples were abnormal and often rounded. However, following exposure to UrgoTul, the density of the dividing fibroblast cells increased when compared with the other dressings, again confirming that it stimulates proliferation in these experimental conditions.53

The third in vitro study (presented as a poster) focused on cytotoxicity, but this time with Atrauman (Paul Hartmann) as the comparator. Here, the MTT assay was repeated three times using three different batches of Atrauman. Results confirmed the above findings that UrgoTul does not have a cytotoxic effect on normal human dermal fibroblasts at any time point (24, 48 or 72 hours). In contrast, Atrauman clearly decreased fibroblast viability after 24 hours, and presented a cytotoxic effect after 24, 48 and 72 hours with two different batches, and after 72 hours with the third batch.54

This lack of cytotoxicity was also demonstrated for UrgoTul Absorb.55 MTT assay and assessment of tritiated thymidine incorporation, followed by confocal laser microscopy, demonstrated that UrgoTul Absorb is not toxic to cells, and that it significantly stimulates cultured fibroblast proliferation after 24 hours (p<0.001), 48 hours (p<0.001) and 72 hours (p<0.05) when compared with the control.

Effects on collagen

The effect of UrgoTul on extracellular matrix protein production was also explored, again using normal human dermal fibroblasts.56 Production of (Pro)collagen 1 and fibronectin were quantified by specific immunoenzymatic assays (ELISA) and the extracellular matrix organisation was visualised by immunofluorescence microscopy, after immunolabelling of type 1 collagen, type III collagen or fibronectin. Results showed that the fibroblasts in contact with UrgoTul produced significantly more soluble (pro)collagen 1 than did the control (180% of the control; p<0.01). This result was validated by a confirmation test using the same methodology. The results also show that UrgoTul stimulated the production of hyaluronic acid,57 which helps promote cell proliferation. This is a key early stage of dermal repair, and these findings therefore give an insight into how TLC dressings can facilitate healing.

Table 3 summarises the in vitro evidence on TLC dressings.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Urgo product</th>
<th>Comparative product(s)</th>
<th>Main results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viennet et al.52</td>
<td>Urgo T ul</td>
<td>Tulle gras, Adaptic, Mepitel, Ialuset, Physiotulle</td>
<td>Cell proliferation reduced with Adaptic and Ialuset</td>
</tr>
<tr>
<td>Bernard et al.53</td>
<td>Urgo T ul</td>
<td>Mepitel, tulle gras</td>
<td>UrgoTul stimulates fibroblast proliferation by 45%. Mepitel showed a tendency to reduce cell proliferation</td>
</tr>
<tr>
<td>Juchaux et al.54</td>
<td>Urgo T ul</td>
<td>Atrauman</td>
<td>Atrauman is cytotoxic to fibroblasts</td>
</tr>
<tr>
<td>Bernard et al.55</td>
<td>Urgo T ul Absorb</td>
<td>None</td>
<td>UrgoTul Absorb stimulates fibroblast proliferation</td>
</tr>
<tr>
<td>Bernard et al.56</td>
<td>Urgo T ul</td>
<td>None</td>
<td>UrgoTul stimulates soluble (pro)collagen 1 production by 43% and stimulates production of hyaluronic acid</td>
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</table>
Clinical evidence for dressings with TLC healing matrix

As seen from the in vitro evidence, neutral TLC dressings create a moist environment that stimulates fibroblast proliferation. Furthermore, their non-adherent properties are designed to avoid pain and trauma to newly formed tissue at dressing removal, which can delay healing. For patients, the prospect of uninterrupted healing and pain-free dressing removal can greatly improve quality of life. While this may sound aspirational, numerous clinical studies at all levels of the evidence hierarchy show that TLC dressings regularly achieve these desired clinical outcomes in different wound types as discussed below.

Acute and chronic wounds
Evidence relating to outcomes achieved in acute and chronic wounds is discussed first. A recent unpublished observational evaluation involving 2125 patients with various wound types treated with UrgoTul Absorb Border found that just over half (54.7%) healed within 8 weeks. Of the wounds, half (50%) were chronic and the rest were mainly acute (43%) or classed as ‘other’ (7%). Chronic wounds included venous leg ulcers, diabetic foot ulcers and pressure ulcers; and acute wounds included ‘dermabrasion’ and postoperative wounds. In total, 54.7% of the wounds healed, with a higher mean healing rate for patients with acute wounds (69.7%) compared with chronic wounds (42.3%).

Most patients considered UrgoTul Absorb Border easier to use/better than other neutral foam dressings with a border in terms of application, conformability, absorption, adhesiveness of the border and the effectiveness of the waterproof backing. Furthermore, at the final visit, 49% of patients stated that UrgoTul Absorb Border caused less pain than similar dressings. Sixty-nine per cent of the sample regarded the dressing as extremely useful.

Scores for tolerability and acceptability were high. Almost all participants (99%) rated its tolerability as ‘very good’ (84%) or ‘good’ (15%); the same percentage rated its acceptability as ‘very good’ (76%) or ‘good’ (23%). High scores were also given for its handling properties: ‘very good’ (69%) or ‘good’ (28%).

A large-scale multicentre observational study conducted approximately 10 years prior to this, which involved almost 6000 patients with acute or chronic wounds, clearly demonstrated that UrgoTul reduces pain at dressing change. The prevalence of pain at dressing change was measured, and the subsequent effect of UrgoTul on this was evaluated. At the screening visit, patients experiencing moderate or severe pain at dressing change were identified using a simple four-point pain scale. Those who met this criterion then self-evaluated, in a questionnaire, the intensity and frequency of pain experienced during subsequent wound-care procedures. Dressings in use at baseline comprised mostly simple wet or dry gauze dressings, paraffin gauze, hydrocolloids or foams. A second questionnaire enquired about the practitioner’s approach to the management of painful wounds.

Acute wounds (n=2914) comprised traumatic injuries, burns and post-surgical wounds. Chronic wounds (n=2936) were mainly leg ulcers, but also included pressure ulcers, diabetic foot ulcers and chronic post-traumatic/post-surgical wounds.

At the screening visit, 80% (n=2308) of patients with acute wounds and 80% (n=2341) of those with chronic wounds reported moderate or severe pain at dressing change.

Fig 6. UrgoTul was associated with no or less pain at dressing change12
dressing removal. Of these, 1879 switched to UrgoTul during the treatment period (1023 with acute wounds and 856 with chronic wounds). Median follow-up periods were 10 and 23 days for acute and chronic wounds, respectively. Compared with the period before the switch, 95% of patients with acute wounds and 88% of those with chronic wounds reported no pain or less pain at dressing change (Fig 6). Furthermore, 83% of patients stated that, after switching to UrgoTul, they felt substantially less anxious before treatments, while 80% of patients with acute wounds and 71% with chronic wounds wanted to continue with this dressing.

A smaller study, undertaken in Spain, involving 28 patients with acute wounds (n=7), chronic wounds (n=10) or burns (n=11) found that UrgoTul was highly efficacious and caused either no or minimal pain at dressing change. The wounds, which were mostly located on the lower limb, were assessed until full healing occurred. Previous treatments used included sterile gauze, ‘greasy’ gauze, hydrocolloids and foams. Surface area was measured using planimetry. Mean baseline measurements were 20.91cm² ± 24.63 (range 0.50–62.16cm²) for acute wounds and 5.18cm² ± 3.22 (1.78–10.83cm²) for chronic wounds. The mean baseline duration of chronic wounds was 24.6 months. For burns, the mean duration was 13 days ± 8.9 (1–30 days) and the mean surface area was 37.5cm² ± 90.0 (2.1–308cm²).

All of the wounds healed. Chronic wounds healed in a mean of 67 days ± 30.7 (28–130 days), acute wounds in a mean of 11.0 days ± 6.6 (3–24 days) and burns in a mean of 20.3 days ± 3.0. None of the burns developed clinical signs of infection. The dressing, which was almost always non-adherent, was considered to be very easy/easy to both apply and remove at every dressing change. No local adverse events were reported.

The first study on UrgoTul undertaken in the UK confirmed its efficacy and acceptability. This single-centre, 4-week clinical study involved 22 patients with acute (n=12) or chronic (n=10) wounds. Chronic wounds comprised sacral pressure ulcers, venous/arterial ulcers, a diabetic foot ulcer and a traumatic haematoma on the skin. Acute wounds comprised burns, postoperative abdominal wounds, traumatic wounds and cellulitis. Wound area was measured by tracing and photography. Average baseline surface areas were 84.36cm² (1.35–290cm²) for the acute wounds and 26.68cm² (3.54–59cm²) for chronic wounds.

Seven of the acute wounds healed in a mean time of 15 days (range 7–20 days), while one chronic wound healed in 10 days and the rest showed a ‘marked reduction’ in size. Good results were also reported for acceptability. All nurses agreed that UrgoTul was ‘very easy’ to apply because of its flexibility and conformability, and ‘very easy’ to remove, even after 14 days in one instance. Furthermore, they all gave the highest score (‘very good’) for conformability, which is noteworthy as the wounds varied in type, depth, shape and part of the anatomy (in one patient the base and sides of a full-thickness abdominal wound were carefully but easily laid with UrgoTul under V.A.C. (KCI) to prevent ingrowth of granulation tissue into the V.A.C. foam, a commonly encountered problem in practice). Similarly, all dressing removals were atraumatic (no bleeding occurred), and no patients experienced pain at dressing change. There were no treatment-related adverse events. While dressing-change frequency was not measured, UrgoTul was left in place for 6–7 days on average, saving nursing time and avoiding excessive disturbance of the wound. Full results for acceptability of the UrgoTul dressing are given in Fig 7.

A 4-week multicentre clinical trial reported good efficacy, acceptability and tolerability for UrgoTul in a similar patient population that also included patients with partial-thickness burns. The sample comprised 92 patients with acute wounds (n=34), leg ulcers (n=24), other chronic wounds (n=14), or burns (n=20). Wounds were measured by planimetry and photography. Mean baseline surface areas were 19.1cm² (±21.0cm²) for the acute wounds, 19.1cm² (±35.5cm²) for the leg ulcers and 10.3cm² (±7.2cm²) for the other chronic wounds (primarily five pressure...
ulcers and four amputation stump wounds).

Eleven acute wounds, three leg ulcers and two other chronic wounds healed within 4 weeks. In the remaining wounds, the surface area decreased, on average, by 76%, 64% and 44%, respectively. Conformability was considered appropriate in almost all acute wounds, but less so in the chronic wounds, where it was classed as poor in 11% and 14% of changes, respectively. However, of the 771 dressing changes undertaken, application was considered easy/very easy in ≥90% of acute wounds and other chronic wounds, and in ≥80% of leg ulcers. Almost all (>96%) dressing removals were easy/very easy, with no pain recorded in just over three quarters of dressing removals for each wound type (range 76–79%). The prevalence of adhesion, maceration, malodour and bleeding was very low.

Nineteen of the burn injuries healed in 5–19 days (mean 11.0 ± 4.5 days). Conformability was considered good/very good in 61% of dressing changes, reflecting the challenge of dressing burns located on the hand and fingers. Of the 97 dressing changes undertaken, application and removal were considered easy/very easy in 81% and 80% of them, respectively. Again, the prevalence of maceration, malodour and bleeding was low.

For all wound types, safety was good, with only seven adverse events: two cases of peri-wound erythema, which were dressing related and resulted in both patients dropping out of the study, and one case each of peri-wound ulceration, overgranulation, bleeding, pain and inflammation, and pain/dressing adhesion.

The success of UrgoTul led to the development of UrgoTul Duo. This has all of the properties of UrgoTul plus a light absorbent pad, which avoids the need for a secondary dressing in wounds with low exudate. This reduces the risk of peri-wound maceration and excoriation, which delay healing.

A multicentre clinical study\(^58\) reported similar efficacy, tolerability and acceptability results as those for UrgoTul. The sample comprised 43 hospitalised patients with acute (trauma) (n=27) or chronic wounds (leg ulcers/pressure ulcers) (n=16). The acute wounds had been previously treated with a wound contact layer dressing, paraffin gauze or a hydrocolloid, the leg ulcers with a hydrocolloid or alginate, and the pressure ulcers with hydrocolloids or alginate.

Forty patients were evaluated for 4 weeks; the three withdrawals were non-dressing related. Wound area was measured by planimetry and photography. Mean baseline wound areas were 13.4cm\(^2\) (± 16.6cm\(^2\)) for the acute wounds, 7.6cm\(^2\) (± 4.6cm\(^2\)) for the leg ulcers and 8.5cm\(^2\) (± 4.0cm\(^2\)) for the pressure (mostly heel) ulcers.

Twenty-three wounds (53%) healed by the end of the 4-week study period (20 acute wounds and three chronic wounds). The acute wounds healed in a mean of 17.4 days (±8.1 days) and the chronic wounds in a mean of 25 days and 21 days (pressure ulcer).

By the end of the treatment period, the wound surface area had reduced by 94%, 76% and 75% for acute wounds, leg ulcers and pressure ulcers, respectively. The dressing also improved any inflammation of the peri-wound skin, which either disappeared or improved to ‘healthy’ in 83% of the acute wounds, 57% of the leg ulcers and 100% of the pressure ulcers.

Conformability was considered ‘very good’ in 76% of acute wound and 83% of leg ulcer dressing applications, but in only 59% of pressure ulcer applications, although it was never ‘poor’. The nurses considered the dressing either very easy/easy to apply/remove at almost every dressing change. Similarly, pain was not experienced at most dressing removals (89% or better in all wound types) and was ‘marked’ in 1.7% of acute wounds. Adhesion was ‘marked’ in only 2.8% of acute wounds. There was no bleeding in ≥91% of wounds at dressing change, or any confirmed dressing-related adverse events. During this study dressings were changed, on average, every 2.5–2.8 days, although in some cases nurses were able to leave them in place for up to 8 days. Secondary dressings were rarely needed at acute wound dressing changes (2%), but were required more often for leg ulcers (14%) and pressure ulcers (21%). As a result, nurses considered the dressing application and changing times to be shorter in 75% of cases, and operations to be facilitated in 84% of cases.\(^58\)

The acceptability of a range of TLC dressings (mostly UrgoTul Duo) was further demonstrated in a large-scale (but as yet unpublished) study involving 1448 patients, which reported that TLC dressings are highly conformable and thus easy to apply to acute and chronic wounds initially judged to be ‘difficult to dress’\(^39\). Wound types included traumatic injuries, postoperative wounds, pressure ulcers, leg ulcers, burns and ‘other’. At baseline, two-thirds of the wounds were painful and 31% bled easily. The TLC dressings applied mainly comprised UrgoTul Duo (49%), UrgoTul Absorb (12%) and UrgoTul Lite (27%). The dressings achieved the highest score for conformability in 82% and
87% of applications to ulcers/traumatic and post-operative wounds, respectively, and in over 75% of applications to burns and other wound types.

The evidence that UrgoTul Duo reduces the need for secondary dressings suggests it may have economic benefits. An observational multicentre study was conducted to compare the resource utilisation with UrgoTul to that of UrgoTul Duo in four emergency departments in France. The study involved 305 outpatients with predominantly traumatic wounds treated with either UrgoTul Duo (n=166 patients) or UrgoTul (n=139) for 2 weeks. Demographic data and wound characteristics for the two groups were similar. The study population was mainly male, with an average age of 34.9 years. Wounds treated with UrgoTul were significantly more likely to require secondary dressings compared with UrgoTul Duo: 98% versus 12% (p<0.001). Further investigation found that the use of secondary dressings with UrgoTul Duo was largely attributed to one emergency department, which recorded a higher incidence of bleeding at dressing removal.

Nevertheless, acceptability results also favoured UrgoTul Duo over UrgoTul:
- 88% of nurses considered that UrgoTul Duo saved them time
- 98% reported that care was easier
- 100% said they preferred UrgoTul Duo.

These results demonstrate that use of UrgoTul Duo can produce cost savings by avoiding the need for secondary dressings.

In 2010, Urgo launched a new version of UrgoTul, which is more flexible and comfortable. Anecdotal reports suggested that the older version of UrgoTul tended to slip when applied to vertical surfaces such as the digits or thigh, to epidermolysis bullosa wounds and paediatric wounds. To overcome this, the manufacturer increased the conformability of the dressing, so that the new version stretches and moves with the body, thereby avoiding the risk of slippage.

A multicentre clinical study involving 44 patients with acute (n=32) and chronic wounds (n=12) reported that the conformability of new UrgoTul is generally better than that of the original UrgoTul, particularly in relation to paediatric and surgical wounds. Acute wounds comprised post-operative wounds, traumatic injuries, partial-thickness burns and amputation sites. Chronic wounds comprised leg ulcers, pressure ulcers and ‘other’. Mean baseline wound surface areas were 21.64 cm² ± 25.30 (range 1.63–89.64 cm², median 9.38 cm²) and 6.61 cm² ± 3.12 cm² (range 2.19–13.40 cm², median 6.05 cm²) for acute and chronic wounds, respectively. Previous treatments included hydrocolloids, foams, contact layers, alginates, greasy gauze or ‘other’ dressings. Wounds were measured by planimetry and photography.

Efficacy of new UrgoTul was good, although it should be noted that 10 patients with acute wounds were excluded from the efficacy analysis, primarily due to lack of planimetric data. Seventeen acute wounds and three chronic wounds healed. The mean healing times were 14.2 days (±7.7 days) and 26.3 days (±2.9 days), respectively. Acute wounds reduced by an average of 78% and chronic wounds by an average of 42% during the 4-week study period. Two adverse events (infection and infected necrotic tissue) were reported in patients with acute wounds only, one of which resulted in discontinuation of treatment.

Conformability was reported to be good/very good in 93% of acute wound dressing changes and in 85% of chronic wound dressing changes, while the dressing was considered to have stayed in place at 89% of the evaluations. In addition, the clinicians considered new UrgoTul to be more conformable than original UrgoTul at 73% of dressing changes (assessed on all patients who had used the older version before entry into the study). There was no pain during 87% of dressing changes, with moderate bleeding reported in only 8%.

Traumatic wounds
Assuming there are no complicating comorbidities and depending on the patient’s age, traumatic...
wounds often progress through the stages of the healing process in an orderly and timely fashion, although the speed of healing will depend on the cause of injury, the degree of tissue loss and the anatomical site. Wounds should be cleansed to remove any debris and potential contaminants, and then dressed with a non-adherent dressing in order to keep the area moist and avoid pain at dressing change. A dressing that can optimise healing and achieve a good cosmetic effect is desired.

A small, independent, clinical study that compared the effectiveness and acceptability of five dressings on traumatic and surgical wounds showed that UrgoTul achieved faster than expected healing rates. This study, which took place in an orthopaedic outpatient department in the UK, assessed Mepitel (Mölnlycke), N-A Ultra (then produced by Johnson & Johnson), UrgoTul, Atrauman (Paul Hartmann) and Tegapore (3M). All patients who attended the department with superficial wounds healing by secondary intention received one of the five dressings for a 2-week period. The different dressings were allocated on a rotational basis, based on five 2-week allotments. Fifty-two patients participated, with wounds including digital amputation, digital crush injury, toenail avulsion, skin tear, laceration, post-surgical cellulitis, post-surgical incision and pretibial laceration. Seven patients received Atrauman, 13 patients received Mepitel, eight received N-A Ultra, nine received Tegapore and 15 received UrgoTul. Forty-six wounds had either healed or were healing at the study end, although details are not given.

Results showed that UrgoTul required the lowest mean number of dressing changes, Tegapore and Atrauman required the most dressing changes per patient (mean of 4.6 and 4.4, respectively) and N-A Ultra, Mepitel and UrgoTul the least (mean of 2.4, 1.8 and 1.7, respectively). Ease of application was comparable for all five dressings. However, there were variations in ease of removal, with UrgoTul achieving the highest score (being 'easy' to remove in 96% of cases), closely followed by Mepitel and N-A Ultra, while Atrauman and Tegapore had the lowest scores as they dried and adhered to the wound bed in 16% and 22% of cases, respectively. Only with UrgoTul did patients always consider themselves 'comfortable' during dressing removal.

UrgoTul achieved faster than expected healing rates, particularly following toenail avulsions, and it appeared to facilitate autolytic debridement of superficial slough and necrosis. The investigator concluded that, of the five dressings, UrgoTul achieved the best results on wounds in areas that are more sensitive, difficult to dress, with changing exudate levels and superficial slough and necrosis. Results are summarised in Fig 8.

Another independent study — this time a randomised controlled trial (RCT) undertaken in Hong Kong — provides more detailed data showing that UrgoTul optimises healing of traumatic wounds. Patients attending an emergency department with full-thickness traumatic digital wounds were randomised to receive either UrgoTul or gauze (the control). Outcome measures were the time taken to heal the wounds and the wound size at each dressing change. Over a 7-month period, 28 patients participated (16 experimental and 12 control), allowing a 5% level of significance at a power of 60%. Wound size was determined by regular tracing. Full healing was defined as complete epithelialisation.

No patients withdrew from the study or were lost to follow-up. Most patients were male (75%) and healthy, with a mean age of 32.5 years (± 17.1). Both groups were comparable at baseline in terms

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Fig 9. Traumatic wound at presentation (a); healing was achieved after 23 days (b)
of patient demographics and wound characteristics. Results show that wounds treated with UrgoTul achieved a greater reduction in size. The average healing time was 12.1 days (± 3.3, range 7–20 days) in the UrgoTul group and 16.8 days (± 5.1, range 9–21 days) in the control group, representing a statistically significant difference in favour of UrgoTul (p=0.024). The authors suggest that the fewer dressing changes required for UrgoTul not only avoid traumatising the wound, but also produce savings in both time and resources. Unfortunately, due to an outbreak of severe acute respiratory syndrome (SARS) in Hong Kong at the time of the study, the number of admissions dropped, resulting in the low statistical power, limiting the generalisability of the findings.

Fig 9 shows the healing outcome following use of UrgoTul on a traumatic wound.

Skin lesions
A comparative study comparing the postoperative use of a paraffin tulle dressing impregnated with chlorhexidine acetate (Bactigras, Smith & Nephew) versus UrgoTul found significant benefits during removal for the latter in terms of pain, adherence and bleeding. Hessam et al. randomised 42 patients undergoing surgical excision of a single skin lesion (basal cell carcinoma, squamous cell carcinoma, keratoacanthoma, lentigo maligna, melanoma in situ and Bowen’s disease) to receive either Bactigras or UrgoTul, administered both on the day of surgery (modified microscopically controlled surgery, MCS) and on the day of second-stage MCS or defect reconstruction. There were no significant differences between the two groups in the evaluation with respect to defect size and dressing change frequency, although patients in the Bactigras group were significantly older than those in the comparator group.

Results showed that there was significantly less adherence to the wound bed with UrgoTul than with Bactigras (16 vs. 2 patients, p=0.001). This, in turn, resulted in significantly less bleeding at dressing removal (16 vs. 2 patients, p=0.001) and lower mean visual analogue scale (VAS) pain scores (1.9 ± 2.2 vs. 0.7 ± 1, p=0.022). Only one patient developed clinical signs of infection, for which antibiotics were required.

Fig 10 shows the healing outcome following use of UrgoTul on a basal cell carcinoma on the nose.

Negative pressure wound therapy
Negative pressure wound therapy (NPWT), also known as topical negative pressure, is widely regarded as an extremely effective (albeit expensive) method of promoting healing in a wide range of acute and chronic wounds. In most NPWT systems, a polyurethane or polyvinyl alcohol foam dressing is placed between the wound and the device, but there is a risk that granulation tissue can grow through the foam, causing trauma and pain at removal. To avoid this, a wound contact layer can be used under the NPWT foam. It is proposed that UrgoTul’s small mesh size prevents such growth, increasing the likelihood of painless removal.

This was confirmed in a trial in which patients being managed with NPWT experienced substantially less pain at dressing change after using UrgoTul under NPWT. Sixty-six patients with 42 acute and 24 chronic wounds given UrgoTul plus NPWT (V.A.C., KCI) were followed-up for an average of 17 days. At baseline, pain was noted between two consecutive dressing changes in 66% of patients, even though 60% were receiving oral analgesics, and was either ‘moderate’ or ‘marked’ in 69% of dressing-care procedures. During the treatment period with UrgoTul plus NPWT these percentages fell to 34% and 13%, respectively. Patients considered the combination easy/very easy to remove in 95% of dressing changes, and there was no adherence in 88% of removals. No or minor bleeding was reported in 91% of dressing changes. Finally, the appearance of the surrounding skin improved from inflamed, oedematous, eczematous or macerated to ‘healthy’ in 18 patients. No UrgoTul-related adverse events were reported. It appears, therefore, that dressing changes were less painful when NPWT was used with UrgoTul because granulation tissue did not adhere to the wound bed.

Fig 11 shows the healing outcome following use of UrgoTul on an amputation stump.
**Grafts**

If there has been a loss of a large percentage of skin — for example, as a result of a burn or soft-tissue trauma — then split-thickness skin grafting may be required. The ensuing donor site wound will be treated as an acute wound, and so will require a dressing that maintains a moist environment, is non-adherent, absorbent, easy to apply and remove, and helps relieve postoperative pain. Traditionally, paraffin gauze (or tulle gras) was used for this purpose, with an absorbent secondary dressing, but this often dries out and adheres to the wound, causing pain and trauma at dressing removal.

An independent, open-label, randomised, intra-individual comparison trial found that, compared with tulle gras, UrgoTul was not only associated with more painless dressing removals, but also significantly improved healing times for both burn injury and the graft donor sites. Twenty-five patients were recruited into the study over 6 months. Partial-thickness burns selected for comparison were of similar depth, as assessed by two blinded observers; all grafts were harvested at a fixed depth. Each patient had two burns (or one large burn divided by an imaginary line), one of which was dressed with tulle gras and the other with UrgoTul plus a standard secondary dressing. The same treatment protocol applied to the donor sites. In this way, each patient acted as his or her own control. Two blinded observers used photography and planimetry to assess wound healing every week for a mean of 3 months.

Two patients were lost to follow-up, so 23 (92%) were followed up. The mean age was 44 years (range 23–65 years) and the mean areas dressed with UrgoTul and tulle gras were 118cm² and 112cm², respectively.

The mean time to complete epithelialisation significantly improved with UrgoTul compared with tulle gras: 9.6 days (range 7–14) versus 11.9 days (range 7–21 days), respectively (p< 0.05). Furthermore, 100% of the nurses considered UrgoTul ‘very easy’ to use/change at each dressing change, compared with 0% for tulle gras, while the latter was ‘difficult’ to use in 13% of dressing changes. Bleeding at the first dressing change was observed in twice as many tulle-gras sites as UrgoTul: 100% versus 52% (p<0.05). During the treatment period, significant bleeding occurred in 17% of tulle gras dressing changes but in none of the UrgoTul ones. Finally, none of the UrgoTul dressing changes were ‘very painful’ (defined as intolerable pain requiring extra analgesia), compared with 35% of the controls. Pain was more likely to be ‘minimal’ with UrgoTul than tulle gras: 65% versus 26%, respectively (p<0.05). No adverse events were reported.

Fig 12 shows the healing outcome achieved following use of UrgoTul on a skin graft on a mixed aetiology leg ulcer.

**Paediatric wounds**

Most wounds presenting in children are acute, generally burns, traumatic injuries and surgical wounds. Given the anxiety that wounds are likely to cause children (and their parents), plus the potential sociopsychological consequences, it is vital that dressings are easy to apply and that removal is pain-free. The stature of young children also makes it essential that dressings are conformable, so that they can fit into small, awkward places when necessary.

![Fig 12. A 72-year-old patient presenting with a mixed aetiology leg ulcer of 18 months’ duration: wound appearance after grafting (a) and progression towards healing after 8 weeks of treatment with UrgoTul (Fig b)](image-url)
A 4-week clinical study conducted in both France (11 centres) and Germany (five centres) involving children with burns or other acute and chronic wounds found that removal of UrgoTul was atraumatic, with limited pain and adhesion. A total of 100 children (aged 1–12 years) with 77 burns (29% superficial partial-thickness, 71% deep partial-thickness) and 23 ‘other’ wounds (principally traumatic, postoperative and burns sequelae, but also postoperative necrotic and recent pressure under plaster) participated. Analgesia was administered at 21% of the documented 529 dressing changes undertaken on all wounds in the two countries. Children assessed their pain at dressing change using either the faces scale (children aged over 3 years) or a VAS where 0mm = no pain and 100mm = very painful (children aged over 6 years). In addition, nurses assessed pain in those aged 1–6 using both the objective pain scale (four items: crying, motion, restlessness and verbal/non-verbal expression) and the VAS.

At a majority of dressing changes (59%) the children selected the ‘smiling faces’ on the faces scale, while the mean VAS values ranged between 0.9mm and 10.1mm, depending on the country and the wound type. These VAS values were very similar to those noted by the nurses (1.1–6.7mm) and supported the investigators’ qualitative evaluation.

Results for the objective pain scale show that most dressing changes (50–65%) did not cause the children to cry, move, or become restless, regardless of wound type.

The nurses’ evaluations (both objective and subjective) showed that UrgoTul was associated with either no pain or moderate pain at almost every dressing change. The vast majority of dressing applications/removals were either easy or very easy, with minimal bleeding or adherence. Conformability was largely good/very good for nearly 90% of all dressings changes.

Fig 13 shows full healing achieved following use of UrgoTul on a partial-thickness burn on a one-year-old child, while Fig 14 shows the progression towards healing after application of the dressing to a paediatric traumatic wound.

Epidermolysis bullosa

Epidermolysis bullosa is a group of inherited skin conditions that result in potentially extensive skin lesions and blistering following minimal trauma. The open lesions are susceptible to infection. Skin management is mainly supportive, and predominantly comprises good wound care. Given the fragility of the skin and mucous membranes in these patients, a non-adherent, atraumatic dressing must be used to avoid pain at dressing change wherever possible and so improve quality of life.

The largest published wound care study involving this patient group found that use of UrgoTul improved healing rates and reduced pain at dressing change when compared with the previous treatment regimen. This clinical study involved 20 patients (11 adults and nine children aged over 12 months), of whom half had previously used other non-adherent dressings or petrolatum gauze. The target lesion had been present for 1–45 days (mean 8.8 ± 12.1 days).

Nineteen of the 20 epidermolysis bullosa lesions healed in a mean 8.7 days (± 8.5); 50% of the sample stated this was shorter than with the previous dressing. Excellent results were also reported for acceptability, with 91% of dressing changes being pain free and no reports of very severe pain. Indeed, 75% of patients stated that dressing changes were less painful than with the previous dressing. Analgesia (paracetamol) was only needed...
before 13% of dressing changes. Correspondingly, dressing removal was easy/very easy in 98% of cases, with strong adhesion being reported in only three dressing changes. Mild bleeding was reported in only five patients in 18 dressing changes. Based on these findings, 11 patients (55%) concluded that their quality of life had improved following use of UrgoTul. Most of the adults and all of the children said they felt less apprehensive about the procedure than they had with their previous dressing. Nineteen of the 20 patients said they would use the dressing again.41

While these results demonstrate that UrgoTul is a valuable treatment modality for patients with epidermolysis bullosa, its lack of tack and flexibility may rarely result in slippage, and thus wound extension, when used on large areas. Furthermore, the UrgoTul range did not include a size big enough for the large lesions often seen in epidermolysis bullosa. A study involving 14 patients (nine adults and five children), presented as a poster, found that new UrgoTul (which is available in a wider range of sizes, including a 20 x 30cm) was considered more comfortable and associated with a better quality of life than previous dressings used, including UrgoTul.77 Prior to the study, all patients had used a non-adherent soft silicone primary dressing or UrgoTul. When asked to compare new UrgoTul with their previous dressing, 50% of patients said their quality of life had improved, 33% said the new dressing was less painful, 33% considered it more comfortable, and 17% felt less apprehensive at dressing change. Thirty-three per cent found that dressing changes were quicker. All patients considered new UrgoTul to be very easy/easy to apply and its conformability to be very good/good. In all, 75% were willing to continue using new UrgoTul on all of their wounds.77

Fig 15 gives an example of the efficacy of Urgotul on epidermolysis bullosa in a 9-month-old child.

### Venous leg ulceration

Venous leg ulcers are the most prevalent of all chronic wounds, with a reported incidence of between 1 and 2 per 1000 of the general population.78 Compression bandaging is the gold standard therapy for venous and mixed aetiology ulcers. However, clinical studies show that TLC dressings, when used in conjunction with compression, can promote healing still further, when compared with other dressings.

The first 8-week RCT to investigate the use of UrgoTul with compression showed that, although efficacy was similar, it was significantly more acceptable to patients than the hydrocolloid comparator.79 Ninety-one patients with venous or mixed aetiology ulcers were randomised to receive either UrgoTul (n=47) or DuoDERM E (known in the UK as Granuflex, ConvaTec) (n=44) in combination with high-compression bandages. Results showed that efficacy of the two dressings was similar in terms of healing rates and healing times. In terms of acceptability, there was a significant difference in favour of UrgoTul (ease of removal, maceration, odour and pain on removal) over the comparator (p<0.002). In addition, fewer dressing changes were made per week in the UrgoTul group (2.31 ± 0.45 versus 2.54 ± 0.57 [mean ± SD; p=0.047]).79

The efficacy of UrgoTul plus four-layer compression bandaging was also demonstrated in a clinical study, which again confirmed its acceptability to patients and clinicians.40 Thirty-six patients with venous leg ulcers, 84% of which were indolent or deteriorating, were treated with UrgoTul plus a four-layer multilayer compression bandaging system (K-Four, Urgo). Wound area was measured by planimetry and photography.

At the final visit (week 12), 18 patients had healed in 46.8 days (± 27.4) of treatment. Of the 16 patients whose ulcer had not healed, the area decreased by a mean of 49.3%, from a mean of 15.2cm² to 7.3cm². The average wear time was 6.7 days (± 2.3), which the authors say is close to the ideal of 7 days required for cost-effective community leg ulcer care. There was only one dressing-related adverse event (skin irritation around the wound), which resolved spontaneously without

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**Fig 15. Non-Herlitz junctional epidermolysis bullosa on a 9-month-old child (a); same wound after 7 weeks of treatment with UrgoTul (b)**
Fig 16. A 78-year-old female patient presenting with bilateral circumferential leg ulcers (a); the same wounds after 6 weeks of treatment with UrgoTul (b)

the need to exclude the patient from the study. Once again, the dressing was ‘very easy’ to apply/ remove in almost all cases, with very little pain, adherence or bleeding at removal. Conformability was rated as ‘very good’ in 96% of dressing changes.

There was also an improvement in the condition of the surrounding skin: at baseline, only 17% had healthy surrounding skin, whereas at the study end it was considered healthy/normal at 50% of dressing changes and compromised in some way (dry/scaly, macerated, erythematous, oedematous) in 50%.

However, healing can be delayed in exuding venous leg ulcers, despite compression. Other studies have investigated the effect on chronic leg ulcers of combining compression therapy with UrgoTul Absorb, a foam dressing with TLC healing matrix. The results show this combination was generally efficacious, acceptable and well tolerated. These results are summarised briefly below.

An observational study conducted in general practice settings in France showed that the combination of UrgoTul Absorb and compression was not only efficacious, but also helped to improve adherence rates. The sample comprised 2532 consecutive patients with venous leg ulcers who were about to receive a non-adherent primary wound dressing (almost always UrgoTul Absorb). At baseline, 64% of the patients who had access to compression said they regularly wore it, indicating the difficulties in achieving adherence. However, this increased to 80% at the follow-up visit at least 3 weeks later.

The mean ulcer length at baseline was 5.3cm ± 4.1 (range 0.1–35.0cm) and the mean duration was 9 months ± 15 (0–240 months). After an average of 32.4 days, the mean reduction in ulcer length was 38% (median 33%), while 14% of the ulcers healed and 71% improved. Either no or minimal pain was experienced at removal in 94% of dressing changes. High scores were also reported for tolerability, conformability and acceptability.

The next study, also multicentre and clinical, involved 43 patients with non-healing venous or mixed aetiology ulcers given this treatment combination for a maximum of 6 weeks. Results show that the mean baseline area of 10.71cm² ± 7.31) had reduced by 38%, to 7.67cm² ± 9.27, by the study end. UrgoTul Absorb was well accepted; four treatment-related adverse events, mainly ‘erosion’ and eczema lesions, were reported, but none required discontinuation of treatment.

Similar results were obtained in a slightly larger clinical study on UrgoTul Absorb Border (previous acrylic adhesive version), involving 50 patients who had chronic wounds with a mean duration of 7 months. Ulcers were measured by planimetry and photography. Previous dressings used were another hydrocolloid, foam, alginate or greasy gauze. Following treatment with the new dressing combination, six patients healed in a mean of 28 ± 8 days. For the group as a whole, the surface area reduced by a mean of 47%, from a mean baseline surface area of 8.34cm² ± 6.95, range 0.8–30.7cm², during the 6-week study period. The investigators considered that 72% of the wounds had improved. The dressing was also associated with an improvement in the condition of the peri-wound skin, which was considered healthy in 28% at inclusion versus 36% at study end. There were only four (unspecified) dressing-related local adverse events. Again, good results were reported for all acceptability parameters, with nearly 90% of dressing removals being pain-free.

The next study was conducted after UrgoTul Absorb was improved by the inclusion of a soft-adherent TLC healing matrix, with a view to making it more conformable and easy to use. This multicentre clinical study, presented as a poster, involved 45 patients with venous or mixed aetiology leg ulcers. It found that the mean baseline area, 13.15cm² ± 10.54, range 1.96–45.02cm², reduced by 37.4% (± 52.2) after 6
weeks of treatment (wounds were measured by planimetry and photography). Two ulcers healed. In addition, scores for ease of use and conformability were excellent, while pain during dressing removal was minimal or non-existent in nearly 98% of cases.

An example of a healing outcome achieved following use of UrgoTul on a venous leg ulcer is given in Fig 16.

**Diabetic foot ulcers**
The prevalence of foot ulcers in people diagnosed with diabetes mellitus is estimated as 4–10%. The major aetiologies of diabetic foot ulcers are neuropathy, peripheral vascular disease and neuroischaemia. Approximately half of all diabetic foot ulcers become infected over the course of therapy. Diabetic foot ulcers are a severe complication of diabetes, and are associated with a reduced quality of life, morbidity and premature mortality. They are also associated with 85% of major amputations. Standard treatment comprises debridement, offloading, treatment/prevention of infection and use of modern wound dressings to promote a moist environment.

A multicentre 6-week clinical study involving 35 patients with diabetic foot ulcers has provided preliminary evidence on the efficacy and acceptability of UrgoTul. Mean baseline ulcer surface area was 13cm², measured by planimetry. The mean ulcer duration was 5.2 months. The surrounding skin was healthy in only 21% of patients. Thirteen patients healed completely, while there was a 55% reduction in mean wound surface for the group as a whole. An improvement in the condition of the surrounding skin was noted in all but three patients. Conformability was almost always (99%) regarded as very good/good. Only one adverse event (erysipelas of the right lower limb) was reported, but this was not considered to be dressing related.

Fig 17 shows the healing outcome achieved following use of UrgoTul on a diabetic foot ulcer.

**Other wounds**
TLC dressings have been evaluated on a number of other wounds such as bullous pemphigoid, deep caustic burns, pyoderma gangrenosum, cancerous wounds, post-tattoo wounds and pressure ulcers. Figs 18–20 illustrate healing outcomes achieved following use of UrgoTul on a category III pressure ulcer, caustic burn, and a wound that was secondary to breast cancer, respectively.

Table 4 summarises the main outcomes of the clinical studies on the use of TLC dressings.

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**Fig 18. An 84-year-old patient with a category III pressure ulcer of 4 weeks’ duration on a knee stump (a); the wound healed after 6 weeks (b)**

**Fig 19. Caustic burn following contact with wet cement (a); complete wound healing after 72 days (b)**

**Fig 20. A 65-year-old woman presenting with breast cancer (a); the same wound after 12 months of radiotherapy, chemotherapy and TLC dressings (b)**
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Wound types</th>
<th>Product used</th>
<th>Outcome measures</th>
<th>Key results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meaume et al.12</td>
<td>5850 patients</td>
<td>Acute and chronic wounds</td>
<td>UrgoTul</td>
<td>Incidence of pain at dressing change</td>
<td>At baseline, incidence was 80% for both acute and chronic wound types. After switching to UrgoTul, 95% of patients with acute wounds and 88% with chronic wounds reported no or less pain</td>
</tr>
<tr>
<td>Meaume et al.39</td>
<td>92 patients</td>
<td>Acute and chronic</td>
<td>UrgoTul</td>
<td>Efficacy, tolerability and acceptability</td>
<td>11/34 acute wounds, 3/24 leg ulcers and 2/14 other chronic wounds healed in 4 weeks. Wound surface area of leg ulcers and other chronic wounds reduced by 64% and 44%, respectively. 19/20 burns healed in 5–19 days. For all wound types, the dressing was very easy/easy to apply and remove in &gt;80% of dressing changes, with no pain at removal in &gt;73%. Safety was good</td>
</tr>
<tr>
<td>Coudert et al.60</td>
<td>305 patients</td>
<td>Mainly traumatic</td>
<td>UrgoTul Duo versus UrgoTul</td>
<td>Compare resource utilisation between the two dressings</td>
<td>Wounds treated with UrgoTul were significantly more likely to require a secondary dressing (p&lt;0.001). A large majority of nurses considered that it saved them time (88%) and made care easier to deliver (98%). Cost savings were produced by avoiding the need for secondary dressings</td>
</tr>
<tr>
<td>Ma et al.43</td>
<td>28 patients</td>
<td>Full-thickness traumatic</td>
<td>UrgoTul versus gauze</td>
<td>Healing time and wound size</td>
<td>Wounds treated with UrgoTul healed significantly faster (p=0.024). Fewer dressing changes were required</td>
</tr>
<tr>
<td>Tan et al.44</td>
<td>25 patients</td>
<td>Partial-thickness burns and skin graft donor sites</td>
<td>UrgoTul versus tulle gras</td>
<td>Efficacy and acceptability</td>
<td>Mean healing time was significantly faster for UrgoTul (p&lt;0.05). 100% of the nurses considered it very easy to use/change and remove versus 0% for tulle gras. Bleeding at first dressing change was observed in twice as many tulle-gras sites as UrgoTul: 100% vs 52% (p&lt;0.05)</td>
</tr>
<tr>
<td>Letouze et al.16</td>
<td>100 children</td>
<td>Burns and other wounds (principally traumatic and postoperative)</td>
<td>UrgoTul</td>
<td>Reduction in pain levels</td>
<td>Faces scale and and visual analogue scale (VAS) results indicate there was limited pain at dressing change. Objective pain scale results suggest that at most dressing changes (50–65%) children did not cry, move or become restless, regardless of wound type</td>
</tr>
<tr>
<td>Meaume et al.79</td>
<td>91 patients</td>
<td>Venous leg ulcers plus compression bandaging</td>
<td>UrgoTul versus DuoDERM E (also known as Granuflex)</td>
<td>Efficacy, tolerability and acceptability</td>
<td>Efficacy of the two dressings was similar but there was a significant difference in favour of UrgoTul for ease of removal, reduction in malodour, maceration and pain at removal (p&lt;0.001)</td>
</tr>
<tr>
<td>Dereure et al.81</td>
<td>2532 patients</td>
<td>Venous leg ulcers plus compression bandaging</td>
<td>UrgoTul Absorb</td>
<td>Adherence with compression therapy and acceptability</td>
<td>64% of respondents self-reported that they wore their compression bandages each day. 82% of patients considered that their wounds either healed or improved. High scores for tolerability and acceptability</td>
</tr>
<tr>
<td>Moller et al.48</td>
<td>2125 patients</td>
<td>Acute and chronic wounds</td>
<td>UrgoTul Absorb Border</td>
<td>Efficacy, tolerability, acceptability and pain at dressing change</td>
<td>54.7% healing rate over 8 weeks. 99.3% of patients rated the tolerability as very good/good. 84.2% of patients rated dressings changes as ‘painless’ and 48.5% considered that UrgoTul Absorb Border caused less pain than similar foam dressings</td>
</tr>
<tr>
<td>Hessam et al.48</td>
<td>42 patients</td>
<td>Surgical excision of a single skin lesion</td>
<td>UrgoTul versus Bactigras</td>
<td>Tolerability and pain at dressing change</td>
<td>There was significantly less adherence to the wound bed with UrgoTul than Bactigras (p&lt;0.001), less bleeding at dressing removal (p=0.001) and lower VAS pain scores (p=0.022)</td>
</tr>
</tbody>
</table>
Dressings with hydro-desloughing fibres and TLC healing matrix

At the start of the healing trajectory, many chronic wounds contain necrotic or sloughy tissue. This non-viable tissue encourages the multiplication of aerobic and anaerobic bacteria within the wound bed, and so must be removed.\textsuperscript{28,99–101}

Necrotic tissue or eschar develops as a result of an inadequate local blood supply. It is composed of dead cells and debris that accumulates as a result of cell death; the longer it remains in the wound bed, the more dehydrated and darker it becomes. Its presence causes the inflammatory phase to be prolonged, and the wound is unable to contract or re-epithelialise.\textsuperscript{25}

Slough is yellow or grey fibrinous tissue of a generally soft and moist consistency. It is composed of fibrin, pus and protein-rich material\textsuperscript{102} and may develop on the surface of a previously clean wound bed. It is thought to be linked to increased bacterial activity within the wound.\textsuperscript{25,103}

Both necrotic tissue and slough must be removed as they are linked to increased bacterial burden and delayed wound closure.\textsuperscript{103} Necrotic tissue may require a combination of debridement methods and tends to respond to the more aggressive forms, such as surgical or biosurgery.\textsuperscript{200} In clinical practice, autolytic debridement, facilitated by the use of dressings, is the most common method of debriding slough as it achieves this through a naturally occurring process.\textsuperscript{302} This occurs when enzymes present in highly exuding wounds degrade the slough. Dressings can be used to create an environment that supports this process. This chapter summarises the evidence on UrgoClean, which contains hydro-desloughing fibres designed to absorb exudate and trap slough.

**Venous leg ulcers**

A randomised controlled trial (the EARTH RCT)\textsuperscript{30} studied 159 patients with venous or mixed aetiology leg ulcers across 37 European centres spanning France, Germany and UK. It found that UrgoClean was superior to Aquacel in terms of its ability to facilitate desloughing, despite being comparable in terms of efficacy and safety.

Patients with wounds at least 3 months old covered with $\geq 70\%$ slough were randomised to either the UrgoClean test group (n=83) or the Aquacel control group (n=76). At baseline, patient demographics and wound characteristics were comparable in the two groups, with the exception of gender distribution and status of the surrounding skin. All patients wore compression therapy.

Patients were assessed weekly during the 6-week treatment period. Eighty-four per cent (n=134) completed this follow-up period. The percentage reduction in wound surface area was similar in both groups: 34.1\% for UrgoClean versus 34.4\% for the control group (intention-to-treat analysis). In contrast, the reduction in the percentage of the wound covered with slough was significantly higher in the UrgoClean group than in the control group (65.3\% vs. 42.6\%; $p=0.013$). The UrgoClean group also had a significantly higher percentage of debrided wounds (defined as 30\% of the wound surface area covered with slough) compared with the controls (52.5\% vs. 35.1\%; $p=0.033$) (Fig 21).
Table 6. Summary of main outcomes of studies involving the use of dressings with hydro-desloughing fibres and TLC

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Wound types</th>
<th>Product used</th>
<th>Outcome measures</th>
<th>Key results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meaume et al.</td>
<td>159 patients</td>
<td>Chronic leg ulcers</td>
<td>UrgoClean vs. Aquacel</td>
<td>Efficacy, safety and acceptability</td>
<td>The two dressings had similar results for reduction in wound surface area and safety. UrgoClean resulted in a higher reduction of sloughy tissue (p=0.013), produced a higher percentage of debrided wounds (p=0.033) and scored higher on subjective parameters such as patient comfort, pain at removal, handling and condition of the surrounding skin, compared with Aquacel.</td>
</tr>
<tr>
<td>Meaume et al.</td>
<td>44 patients</td>
<td>Chronic venous leg and pressure ulcers</td>
<td>UrgoClean</td>
<td>Efficacy, tolerability and acceptability</td>
<td>The median decrease of sloughy tissue observed was 75% for venous leg ulcers and 89% for pressure ulcers. Six wounds healed completely over 6 weeks. Dressing was rated as ‘very easy’ to use, with ‘very good’ conformability, and was widely reported as ‘painless’ on removal. Good tolerability and acceptability.</td>
</tr>
<tr>
<td>Moller</td>
<td>1558 patients</td>
<td>Acute and chronic wounds</td>
<td>UrgoClean</td>
<td>Efficacy, tolerability and acceptability</td>
<td>There was a 54% decrease in slough over the treatment period. Overall, 32% of the wounds healed (57% of the acute wounds and 27% of the chronic wounds). The most commonly cited problem, spontaneous pain, decreased by 40%. Almost all patients (≥97%) rated the treatment as tolerable, acceptable and easy to use.</td>
</tr>
<tr>
<td>Allaert</td>
<td>1410 patients</td>
<td>Acute and chronic wounds</td>
<td>UrgoClean</td>
<td>Efficacy, tolerability and acceptability</td>
<td>Mean wound surface area reduced from 30.8cm² to 15.8cm² (49.1%) over 6 weeks. A significant decrease in sloughy tissue was seen (from 63.7% to 29.7%), as well as a significant increase in granulation (from 31.8% to 49.6%) and epithelialisation tissues (from 10.1% to 50.5%) (p&lt;0.0001 in all cases). High tolerability and acceptability.</td>
</tr>
</tbody>
</table>

The tolerability results showed that both dressings had a similar safety profile. In terms of acceptability, the subjective global performance score was higher for UrgoClean than for the control (30.1±3.9 vs. 27.4±5.8; p=0.002), with the investigators giving significantly higher scores for six of nine parameters measured (efficacy, safety and condition of the peri-wound skin, ‘respect of’ granulation tissue, pain at removal, handling and patient comfort) (p<0.05). There were 14 withdrawals in the UrgoClean group and 11 withdrawals in the control group.
Acute and chronic wounds

Prior to this, a published multicentre non-controlled open-label pilot study found that UrgoClean markedly reduced slough in a sample of 44 patients with either venous leg ulcers or category III or IV pressure ulcers.

At baseline, the mean wound duration was 8.3 ± 6.4 months for the venous leg ulcers and 2.9 ± 3.0 months for the pressure ulcers. The mean wound surface areas for the two groups were 11.9 ± 11.3cm² and 12.5 ± 10.7cm² respectively. The mean percentage of sloughy tissue covering the wound bed was >70% in all patients.

Following 6 weeks of treatment with UrgoClean, the amount of sloughy tissue present had decreased by a mean of 75% in the venous leg ulcers and by a mean of 89% in the pressure ulcers. Six wounds healed over the treatment period (five venous leg ulcers and one pressure ulcer). After a mean treatment time of 37.1 ± 9.3 days in the venous leg ulcer group and 37.8 ± 11.8 days in the pressure ulcer group, the mean surface area reductions were 23.7% ± 53.4% and 29.2% ± 72.5%, respectively.

In terms of tolerability, the clinicians noted an improvement in the condition of the surrounding skin, which was rated as healthy in 64% and 75% of venous leg ulcer and pressure ulcer patients, respectively, compared with a baseline of 37% and 40%. The dressing was also rated highly in terms of acceptability, with 81% considering it very easy to remove, 84% considering it very easy to apply, and 77% regarding it as highly conformable. In addition, 91% observed pain-free dressing removals.

Four patients in the venous leg ulcer group switched to another dressing following local adverse events considered to be potentially related to the test dressing: two eczema, one pain and one erythema.

These results were supported by an unpublished multicentre observational study involving 1558 patients with sloughy acute or chronic wounds. The majority of wounds (61%) were chronic, most commonly venous leg ulcers and diabetic foot ulcers. The acute wounds (32%) mostly comprised postoperative wounds and dermabrasions. At baseline, the mean wound duration was 73.3 ± 244.2 days (median: 14 days), and the mean surface area for chronic wounds and acute wounds was 13.6cm² ± 30.8cm² and 17.7cm² ± 30.8cm², respectively. The most common problem identified was ‘spontaneous pain’. A total of 1444 patients (92%) completed the evaluation.

Fig 22. A 64-year-old male with a pretibial laceration (a); after 6 weeks of treatment with UrgoClean, the slough has been completely eliminated (b). Exudate was well managed and the wound surface area reduced by 47%

Fig 23. An 83-year-old female with a 4-week-old traumatic wound to her lower left leg. On presentation, the wound was very wet with 90% slough and 10% granulation tissue (a); the wound after 1 week (b); after 4 weeks of treatment with UrgoClean, the slough has been eradicated and the wound has healed (c)
At inclusion, the wounds were covered with a mean of 69% slough. Following 6 weeks of treatment with UrgoClean, this reduced to 15.2%. Just over half of the acute wounds (57%, n=257) and approximately a quarter (27%, n=240) of the chronic wounds had healed by the final visit, when the mean surface areas were 3.9 ± 22.0 cm² and 4.7 ± 12.9 cm² respectively.

By the end of the 6-week treatment period, the median pressure ulcer scale for healing (PUSH) score (Table 5), which assesses the overall condition of the wound, had decreased by 6 points and spontaneous pain had decreased by 40% (50.7% at baseline versus 11% at the final visit). Almost all physicians rated UrgoClean as very good/good in terms of tolerability (99%) and acceptability (98%).

Another unpublished evaluation, this time involving 1410 patients, found that UrgoClean reduced slough, with the investigators showing that the reduction was statistically significant. Wound types comprised venous and mixed aetiology ulcers (41%), postoperative and post-traumatic wounds (26%), pressure ulcers (11%) and diabetic foot ulcers (5%). On entry, the mean wound duration was 29.9 ± 70.7 weeks (median 6.4 weeks) and the mean surface area was 30.8 cm² ± 46.1 (median 16.0 cm²).

Over the course of the 6-week treatment period, there was a significant reduction in the percentage of sloughy tissue present: 63.7% at inclusion vs. 29.7% after 6 weeks (p<0.0001). The wounds were also progressing towards healing, with the mean surface area reducing from 30.8 cm² at baseline to 15.8 cm² at week 6 (p<0.0001). The mean percentage reduction in wound size after 6 weeks of treatment was 49.1% (±61.1%).

Almost all patients rated UrgoClean as very good/good (97%) in terms of its acceptability and tolerability (99.3%). In over 95% of cases, the clinicians judged UrgoClean to be better or similar to alginates and Hydrofiber dressings in terms of ease of application, conformability and handling.

Table 6 summarises the main outcomes of the studies on the use of UrgoClean. In addition, the desloughing properties of UrgoClean are illustrated in Figs 22–25.

Fig 24. A 57-year-old female patient with a chronic wound of 8 months’ duration (a); after 2 weeks of treatment with UrgoClean, the percentage of slough present reduced from 75–80% to 10–15% (b)

Fig 25. Sloughy pressure ulcer before (a) and after 6 weeks of treatment with UrgoClean (b)
The role played by matrix metalloproteinases (MMPs) in perpetuating wound chronicity is described earlier in this supplement. To summarise, the increased levels of MMPs (along with pro-inflammatory cytokines and reactive oxygen species) observed in chronic wound exudate results in the degradation of the extracellular matrix and inactivation of growth factors. In this way, the wound is maintained in an uncontrolled inflammatory state, which delays or stalls tissue repair, cellular proliferation and angiogenesis. A dressing that is capable of sequestering excess MMPs from chronic wound exudate may therefore help to produce an anti-inflammatory effect and thus benefit healing.

To achieve this, Urgo has produced a range of dressings that incorporate the MMP inhibitor nano-oligosaccharide factor (NOSF) into the TLC healing matrix; the resulting combination is termed TLC-NOSF. According to the manufacturer, when in contact with wound exudate, the TLC-NOSF healing matrix forms a gel that binds onto all surfaces of the wound. The TLC-NOSF then interacts with the MMPs in the wound exudate, inhibiting and neutralising their activity. Urgo proposes that controlling excess MMP activity in this way helps to accelerate the healing process and avoids wounds becoming longstanding.

Dressings in the TLC-NOSF range comprise UrgoStart Contact (a contact layer with TLC-NOSF), UrgoStart (a soft-adherent foam dressing with TLC-NOSF) and UrgoStart Border (silicone adhesive foam version). Like all TLC dressings, they are non-adherent and promote a moist wound environment.

By accelerating the healing process and avoiding wounds from becoming longstanding, TLC-NOSF improves quality of life. This was illustrated in a French observational study involving 1005 outpatients with non-healing venous leg ulcers, which showed that patients experienced less pain/discomfort and anxiety/depression, as well as greater mobility, following treatment with TLC dressings including TLC-NOSF; the patients were also better able to perform their usual day-to-day activities.

The efficacy and safety of TLC-NOSF dressings have been demonstrated in various laboratory and clinical trials, described below.

**In vitro evidence**

The effectiveness of TLC-NOSF in reducing MMP activity has been demonstrated *in vitro*. A laboratory study, reported in a poster, used a normal human dermal fibroblast culture to compare the effect of the TLC-NOSF dressing (UrgoStart Contact) on overall MMP activity at 24 hours. Results (based on chemiluminescent staining) show that the TLC-NOSF dressing significantly reduced overall MMP activity when compared with a control.

The investigators then used the ELISA assay kit to measure the effect of the TLC-NOSF dressing (UrgoStart Contact) on MMP-1, MMP-2 and MMP-9 levels in supernatants of U937 human macrophages and normal human epidermal keratinocytes following 24 hours’ exposure. (Keratinocytes and macrophages express MMP-2, MMP-1 and MMP-9, respectively.) Again, there was a significant reduction in levels of all three MMPs when compared with the control. As stated above, MMP levels, particularly MMP-2 and MMP-9, are raised in chronic wounds, while MMP-1, MMP-2 and MMP-9 all degrade collagen.

These results are supported by another *in vitro* study in which a TLC-NOSF dressing (UrgoStart) was placed over a three-dimensional dermal equivalent that had formed following the incorporation of normal human dermal fibroblasts into a collagen matrix. The culture media were analysed on days 2, 4 and 8. Results showed that the TLC-NOSF dressing had inhibited the enzymatic activity of MMP-2 and MMP-9 (gelatinases) and MMP-1 and MMP-8 (collagenases) on day 4 (MMPs can be either collagenases or gelatinases, and both degrade collagen). This effect was maintained until day 8 in the gelatinases but not in the collagenases. As stated above, gelatinase (MMP-2 and MMP-9) levels are particularly high in chronic wounds. The investigators propose that the effects demonstrated in this dermal equivalent model are likely to be similar to those occurring in an *in vivo* dressing application.

Finally, comparative *in vitro* experiments involving human umbilical venous endothelial cells, reported in a poster, demonstrated that NOSF enhanced the proliferation and migration of these cells at 24 hours, following the creation with a
pipette of a ‘continuous lesion’ across the monolayer, when compared with a control. These three studies suggest that TLC-NOSF has the potential to neutralise MMP activity, stimulate the proliferation and migration of endothelial cells and thus allow the wound to progress through the healing process.

**Chronic wounds**

Evidence is emerging of the clinical efficacy of TLC-NOSF dressings in promoting healing in chronic wounds. Large-scale clinical studies involving patients with a wide range of wound types, and which therefore reflect the real-life clinical environment, give a good insight into the benefits the dressing can offer patients and practitioners.

The largest observational study on the use of UrgoStart, which cites data from 2052 patients attending 483 wound centres across Germany, found that it helped to accelerate healing, with a median 75% reduction in wound surface area across the entire sample, and was acceptable to patients. Wounds comprised venous leg ulcers (58%), pressure ulcers (9%), arterial leg ulcers (8%), diabetic foot ulcers (5%), fungating wounds (1%) and other (19%). All patients with venous leg ulceration wore some form of compression therapy. Dressings used prior to entry into the study were gauze, dry compress, alginate, TLC dressings, foam, hydrocolloid, silver dressings and other. Patients were followed up for a maximum of 8 weeks.

Combining all wound types, the median baseline wound surface area of 10 cm² had reduced to 2 cm² by the study end — a median reduction of 75% (Fig 26). This effect was most marked in pressure ulcers. Twenty-eight per cent of ulcers healed. Fifty-nine per cent of the sample completed a questionnaire enquiring about the acceptability of the dressing. Of these, 58% stated that they never/rarely and 23% that they occasionally experienced pain at dressing removal, while 96% reported that the dressing was very comfortable/comfortable. Ninety-four per cent of patients were very satisfied/satisfied with the dressing. Of the entire sample, 30 patients (2%) reported adverse events, most of which were dressing related: primarily oedema, erythema and itching.

Another large observational study, this time involving 1185 patients, found that use of UrgoStart was associated with a progression towards healing in chronic wounds of varying aetiologies. The investigators used an assessment tool, which allocates individual scores for the wound surface area, wound healing stage, exudate level and presence of spontaneous pain, to produce an overall score. Wounds comprised venous leg ulcers (68%), diabetic foot ulcers (10%), pressure ulcers (9%), angiodermatitis (2%) and other (11%). Of the wounds, 21% had been present for over 6 months, and 64% were recurrent. The average follow-up time was 44 ± 25 days. The overall scores reduced by an average of approximately 50% for all wound types, with an improvement noted as soon as 2 weeks. The benefit was most marked for non-arterial wounds of less than 6 months’ duration.

These results are supported by a smaller multicentre observational study involving 78 inpatients (mean age 39.5 years) from 17 hospitals, which found that UrgoStart accelerated healing in patients with chronic wounds with risk factors including arteriopathy of the lower limb, immobility, diabetes, malnutrition and general corticotherapy. Wound types included leg ulcers (41%), pressure ulcers (27%), surgical wounds and chronic traumatic wounds (16%), diabetic foot ulcers (14%) and other (2%). Previous dressings used included wound contact layers, alginites and foams. The mean baseline wound surface area was 34.3 cm². Following treatment with UrgoStart, the clinicians considered the reduction in wound surface area to be very satisfactory/satisfactory in 86% of cases. Similarly, dressing absorption, ease of application, conformability and non-adherence to the wound were considered to be very satisfactory/satisfactory in 97%, 99% and 98% of cases, respectively.

Since 2011, five large non-controlled observational evaluations have been completed, but as yet all are unpublished. They are described below.

The first, a German evaluation conducted by Lue-
Tzendorf in 2011–2012, showed that UrgoStart promoted healing and improved quality of life. The participating patients (n=1528) had a total of 1513 chronic wounds, which comprised venous leg ulcers (31%), diabetic foot ulcers (20%), pressure ulcers (10%), mixed aetiology leg ulcers (8%), lymphatic ulcers (3%), arterial leg ulcers (2%) and ‘other’ (26%).

On entry, the mean wound duration was 4.1 ± 15.7 months (median 0.8 months), and the mean wound surface area was 16.6 ± 35.5 cm² (median 6 cm²). By the end of the 8-week follow-up period, 43% of the wounds had healed. In the remainder, the wounds had decreased from a median of 9 cm² to 2.5 cm².

Just under one-third of the sample (30%) filled out a EQ-5D quality-of-life questionnaire, in which they reported decreased pain and discomfort when using the dressing and increased ability to engage in daily activities. They also reported improved mobility, autonomy and overall health, as well as less anxiety and depression.

Almost all physicians (≥98%) rated the tolerability and acceptability of UrgoStart as very good/good, and nearly 94% rated it as extremely useful/useful. More than 95% of the physicians rated its handling as very good/good. Most physicians rated UrgoStart as better than a standard foam dressing in terms of the speed of healing (84%), pain experienced (72%), conformability (70%), ease of application (66%), acceptability (66%) and handling (64%). The remaining physicians rated it as comparable, with less than 1% rating it as worse.

The OPUS evaluation set out to determine the number of chronic wounds treated with UrgoStart that healed in 20–24 weeks. A total of 2622 patients entered the evaluation, with the investigators assessing one ulcer per patient. Wound types comprised leg ulcers (venous aetiology, mixed aetiology, post-phlebitis, arterial or not specified) (57%), ‘other’ (21%), diabetic foot ulcers (10%), pressure ulcers (8%), angiodermatitis (2%), malignant wounds (1%) and ‘not known’ (1%). All wounds were at least one month old, with just over one third (34%) being over 6 months. Approximately half of the wounds (49%) were recurrent. Baseline data collected included the Pressure Ulcer Scale for Healing (PUSH) score (Table 7), regardless of aetiology.

Of the 2622 wounds, 1280 had healed (48.8%) at the end of the median follow-up period of 59 days. Wounds for which data were missing were classified as non-healing. The sample included 1505 leg ulcers, of which 84% had healed at the end of a median follow-up period of 64 days. However, 910 of the leg ulcers (n=910) were followed up for a median of over 90 days. For these ulcers, the healing rate was 78.4% (61% of the complex wounds treated at specialist hospital units healed, as did 81% of the less complex wounds treated in the community). This figure is close to that (84%) for the entire leg ulcer subgroup.

The findings of the OPUS evaluation confirm the benefits of using UrgoStart until wound closure.

The investigators also sought to determine which factors were predictors of healing. Binary logistics regression showed that a higher baseline PUSH score, an ulcer duration of >6 months and an arterial component were statistically significant predictors of non-healing within 24 weeks.

The SPEED evaluation investigated whether wounds treated with UrgoStart as a first-line treatment healed more quickly than when it was used as a second-line treatment. The evaluation involved 968 adult hospital inpatients and outpatients, who were assessed at baseline and then at their follow-up visit 4–8 weeks after inclusion. Thirty-one per cent of the sample received UrgoStart as a first-line treatment.

More than half of the wounds (55%) were venous leg ulcers, followed by ‘other’ wound types (17%), pressure ulcers (11%), longstanding acute wounds (9%) and diabetic foot ulcers (8%).

Baseline wound durations ranged from less than 1 month to >6 months. PUSH scores were calculated for all wounds, regardless of aetiology. Patients given UrgoStart as a second-line treatment had higher baseline PUSH scores, although this difference was not significant.

The median follow-up period for the entire sample was 29 days. In patients given UrgoStart as a first-line treatment, the mean PUSH score, after adjusting for wound duration, wound type and length of follow-up period, reduced by a mean -5.3 ± 0.5 compared with -3.8 ± 0.2 when UrgoStart was used as a second-line treatment (p=0.006; Fig 27). The author concluded that use of UrgoStart as a first-line treatment had the impact of UrgoStart on the wound bed characteristics of a variety of chronic wounds. Wounds were assessed for 12 weeks using the START-PC scale, which was purposefully devised for this evaluation. This produced individual scores for wound surface area, exudate level, colour and quality of wound bed tissue, and levels of spontaneous pain, to produce a total score ranging from 0 (wound closure) to 21.
A total of 1185 patients with wounds of varying aetiologies (67% venous leg ulcers, 12% traumatic wounds, 10% diabetic foot ulcers, 9% pressure ulcers and 1% other) were recruited into the evaluation. Baseline wound durations ranged from less than one month to >6 months, with just under half of the sample (48%) having a duration of >3 months. Ninety percent of the wounds had a mean START-PC score of 12.7 ± 3.8.

At least one complete baseline and one complete final START-PC score were available for 1016 patients. At the end of the follow-up period, scores had reduced by a mean 56% ± 30%. The reduction, which was similar for all wound types, was already evident at week 2 (Fig 28). The biggest reduction was observed in wounds with a baseline duration of <6 months, for whom the mean START-PC score was 12.7 ± 3.8 at baseline vs. 5.9 ± 4.4 at the final evaluation.

Overall, in a global assessment of the efficacy, tolerability and conformability of UrgoStart, as well as its ability to manage exudate and minimise pain at dressing change, over 75% of respondents gave it a score of ≥4, where 1 = ‘very bad’ and 5 = ‘very good’.

Finally, an observational evaluation involving 1248 patients with chronic wounds of varying aetiologies also showed that UrgoStart Contact helped accelerate healing. The two most common wound types were venous leg ulcers (36%) and arterial leg ulcers (27%) (data are missing for 13 wounds). The mean baseline wound duration was 109.5 ± 277 days (median 61 days) and the mean baseline surface area was 13.3cm² ± 27.5cm² (median 5cm²).

Nearly half of the wounds (45%) treated with UrgoStart Contact healed by week 8, and another 49% had improved significantly (36%) or slightly (13%) by this time. The highest healing rate was noted in diabetic foot ulcers, of which 116 (61%) healed. There was also an improvement in pain at dressing change, the problem most commonly cited by patients on entry into the evaluation. At the final follow-up visit on week 8, 72% of the sample experienced no pain at dressing change compared with a baseline of 51%.

In terms of acceptability and tolerability, 99% of physicians rated the therapy as very good/good. They also rated its handling as very good/good (96%).

**Venous leg ulcers**

The gold standard treatment for venous and mixed aetiology leg ulcers is compression bandaging, but adjuvant therapy with a dressing that can rebalance MMPs levels can also aid healing.

Confirmation of the efficacy of UrgoStart Contact first comes in the form of a randomised controlled trial (RCT) in which the control was the protease-inhibitor, Promogran (Systagenix Wound Management); both products were used under compression. The study was conducted in 22 French hospitals and five UK wound specialist centres. Fifty-seven patients with non-healing venous leg ulcers were randomised to receive the TLC-NOSF (UrgoStart Contact) dressing and 60 to the control. Both groups were comparable for ulcer severity parameters at baseline. Wounds were regularly measured by planimetry and photography. Twenty-four patients in the control group and 17 in the UrgoStart Contact group withdrew, mainly because of withdrawal of consent, ulcer aggravation and local adverse events. All randomised patients were included in the intention-to-treat analysis (ie, all those allocated to a treatment were...
Fig 29. Acceptability of TLC-NOSF dressing (UrgoStart Contact)\textsuperscript{37}

Fig 30. An 87-year-old patient presented with two leg ulcers of 12 months’ duration on her left leg (a); complete healing was achieved after 16 weeks (b)
Urgo has risen to the challenge and has conducted an unique double-blind RCT comparing the efficacy of UrgoStart (foam dressing with NOSF) with that of a ‘neutral’ foam (UrgoTul Absorb) in the management of chronic venous leg ulcers under compression. Efficacy was based on the reduction in wound surface area, measured by planimetry, after 8 weeks of treatment. Secondary outcomes were the percentage of ulcers whose surface area reduced by 40% after 8 weeks, tolerability, acceptability, and the effects of the dressings on quality of life. The study population, which comprised 187 patients (inpatients and outpatients) from 45 centres, was randomised to receive one of the two foam dressings.

Results show that both groups were comparable at baseline. The average baseline wound surface area was 16.8cm$^2$ ± 15.7cm$^2$; 54.5% of ulcers had a surface area larger than 10cm$^2$. After 8 weeks, there was a highly significant difference between the two groups in the median percentage reduction in ulcer area: 58.3% for UrgoStart versus 31.6% for UrgoTul Absorb group (p=0.0021). The difference in median absolute values after 8 weeks was also highly significant in favour UrgoStart: 6.13cm$^2$ versus 3.26cm$^2$ (p=0.0038). Furthermore, significantly more of the ulcers in the UrgoStart group had reduced by 40% in surface area by then: 65.6% versus 39.4% (p=0.0003), which as stated is highly predictive of wound closure at 20–24 weeks. Rate of healing was more than twice as fast with UrgoStart: 10.83mm$^2$/day versus 5.15mm$^2$/day (p=0.0056).

No significant differences were observed in tolerability and acceptability. However, there was a significant difference in favour of Urgostart in two of the five quality-of-life parameters assessed (using the EQ-5D questionnaire): pain (p=0.022) and anxiety-depression (p=0.037). For the first time, a foam dressing (UrgoStart) has demonstrated a superior efficacy over another foam dressing.

An example of a healing outcome achieved following use of UrgoStart on a leg ulcer is shown in Fig 30.

**Pressure ulcers**

Pressure ulcers are caused by unrelieved pressure, shear, or friction. Increased age, reduced mobility, impaired nutrition, vascular disease, incontinence and the skin condition at baseline consistently emerge as risk factors, although no one factor can be identified as having more weight over another. Given these risk factors, patients are often elderly and have impaired mobility and comorbidities. While the gold standard treatment is pressure redistribution, wound dressings also play a central role as they can be used to maintain a moist environment, prevent critical colonisation or infection and, as in the case of UrgoStart dressings, maintain a healthy balance of proteases within the wound.

As yet, only one study (unpublished) has assessed the efficacy and tolerability of UrgoStart on pressure ulcers. It found that the foam dressing helped to promote healing in wounds with a poor prognosis, in this case category 3 pressure ulcers (EPUAP classification). This 6-week open multicentre study involved 25 patients with pressure ulcers, which were mainly located on the heels and sacrum. Patients underwent standardised weekly clinical, planimetric (area tracings) and photographic assessments. The mean baseline surface area of 6.56cm$^2$ reduced to 4.19cm$^2$ at week 6, a mean reduction of 43.8%. Three ulcers healed completely in a mean of 27 days. Two adverse events (overgranulation) occurred in the same patient. Clearly, wound dressings need to be used as part of pressure ulcer management strategy including pressure redistribution to be effective.

Fig 31 illustrates the clinical benefits achieved following use of UrgoStart on a chronic pressure ulcer.

**Diabetic foot ulcers**

Diabetic foot ulcers are the most common cause of non-traumatic lower limb amputation in the western world, with the risk being 15–46 times higher in patients with diabetes than in those without the disease. Amputation is normally a result of complications following ulceration. Aetiology can be multifactorial, including peripheral arterial disease, sensory and autonomic neuropathy, structural deformity and limited joint mobility. Treatment centres on offloading to avoid further trauma, but again dressings are required to promote an environment.
that promotes healing. Indeed, biopsies have shown that the concentration of MMPs is up to 65-fold higher in diabetic foot ulcers than in traumatic wounds, with MMP-2 and MMP-9 being six- and 14-fold higher respectively.

A dressing that can inhibit MMPs, and thus rebalance the relationship between MMPs and tissue inhibitors of metalloproteinases (TIMPs) will therefore be a useful adjunct to offloading.

A multicentre clinical study involving 34 patients with University of Texas classification grade 1A (i.e., non-infected, non-ischaemic, superficial) neuropathic plantar wounds ulcers showed that TLC-NOSF (UrgoStart Contact) promoted healing and was well accepted by both practitioners and patients. Baseline surface area was 2.7 ± 2.4cm² (range 0.46–8.63, median 1.85). Planimetric data (for 32 patients) showed that 10 wounds had healed after 12 weeks of treatment, while the mean reduction in wound surface area for the entire group was 62.7 ± 49.8% (median 82.7). The above 10 wounds healed in a mean of 61.7 days ± 21.4 (range 31–91, median 57.5). Final evaluation showed that a large majority of wounds either healed (31%) or improved (50%). Of the remainder, 13% stagnated and 6% deteriorated. Three local adverse events were recorded (aggravation of wound [n=1] and maceration [n=2]), but none led to discontinuation with treatment.

High scores were reported for the acceptability parameters, with the dressing being regarded as easy/very easy to remove at 99.7% of dressing changes, with hardly any reports of adherence or bleeding. Application was considered easy/very easy in 96% and conformability very good/good in 85% of dressing changes, respectively. Dressing conformity is an important consideration for diabetic foot ulcers as the dressing will need to stay in place under footwear while also being exposed to pressure when the patient is walking.

Fig 32 shows the healing outcome achieved following 10 weeks’ treatment with UrgoStart on a diabetic foot ulcer.

Arterial ulcers
Prolonged peripheral arterial occlusive disease leads to poorly nourished skin, increasing its vulnerability to trauma and infection. The poor supply of oxygen and nutrients can severely impair healing. Treatments include medication to promote arterial perfusion, angioplasty or reconstructive surgery.

TLC-NOSF healing matrix has been shown to promote healing in arterial leg ulcers that have not responded to revascularisation procedures including angioplasty and stenting. This case series, which as yet is available as a poster, involved 15 patients with stage IV peripheral arterial disease who had 17 wounds that had not healed for a mean of 9.8 months (range 2–34) after the revascularisation procedure. Sixteen wounds had been treated with at least two different dressings before the TLC-NOSF regimen (UrgoStart) was started. The average baseline wound size was 22.5cm² (range 3–74.6) All wounds were treated with UrgoStart for an average of 6.5 weeks (range 2–14). Thirteen wounds either healed (n=7) or improved (n=6), with a mean surface area reduction of 72% (range 49–91). One wound remained static and three wounds deteriorated: two because of local infection and one because of maceration following cutting of the dressing.

Acute wounds that have become chronic
These wounds are often traumatic in origin, and so are particularly prone to infection due to the presence of devitalised tissue, foreign bodies and bacteria. Risk factors for delayed healing include old age, poor vascular supply and comorbidities such as diabetes.
NOSF dressings have been studied and proved to be effective in a number of such wounds, including:

- Dehisced abdominal wounds\(^{136–138}\)
- Pretibial laceration.\(^{139}\) Fig 33 shows an example of a healing outcome achieved following use of the TLC-NOSF dressing on this wound type
- Post-traumatic or post-surgical wounds\(^{140–144}\)
- Pilonidal sinus\(^{144}\)

Table 7 summarises the main outcomes of studies on the use of TLC-NOSF dressings.

Table 7. Summary of main outcomes of clinical studies involving the use of TLC-NOSF dressings

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Wound types</th>
<th>Product used</th>
<th>Outcome measures</th>
<th>Key results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Munter(^{112})</td>
<td>2052 patients</td>
<td>Chronic wounds of various aetiologies</td>
<td>UrgoStart</td>
<td>Efficacy, acceptability and tolerability</td>
<td>Median surface area reduced from 10cm(^2) to 2cm(^2) (75%) over 8 weeks. 81% never/rarely/occasionally experienced pain at dressing removal. 94% of patients were very satisfied/satisfied with the dressing. Only 2% of patients experienced adverse events</td>
</tr>
<tr>
<td>Schmutz et al.(^{37})</td>
<td>117 patients</td>
<td>Chronic venous leg ulcers</td>
<td>UrgoStart Contact versus Promogran</td>
<td>Efficacy, tolerability and acceptability</td>
<td>Median wound area reduced by 54.4% and 12.9% at 12 weeks in the UrgoStart Contact and Promogran groups, respectively (p=0.0286). 56% of ulcers in the UrgoStart Contact group achieved a 40% reduction in surface area versus 35% for Promogran (p=0.022). Mean healing rate was also significantly higher in the UrgoStart Contact group (p=0.029). Pain and infection occurred more frequently in the control group: 18 versus 5 patients. Acceptability results were better in the UrgoStart Contact group</td>
</tr>
<tr>
<td>Meaume et al.(^{44})</td>
<td>1248 patients</td>
<td>Chronic wounds of various aetiologies</td>
<td>UrgoStart versus Urgotul Absorb</td>
<td>Efficacy, tolerability and acceptability</td>
<td>There was a highly significant difference between the two groups in the median percentage reduction in ulcer area after 8 weeks: 58.3% for UrgoStart versus 31.6% for Urgotul Absorb (p=0.0021). The median ulcer size at week 8 in wounds treated with UrgoStart was half that of those treated with the comparator: 3.26cm(^2) versus 6.13cm(^2) (p=0.0038). Significantly more ulcers in the UrgoStart group reduced by 40% in surface area: 65.6% versus 39.4% (p=0.0003). The healing rate was twice as fast with UrgoStart: 10.83mm(^2)/day versus 5.15mm(^2)/day (p=0.0056). There were no significant differences between the groups in terms of tolerability and acceptability</td>
</tr>
<tr>
<td>Allain(^{116})</td>
<td>2622 patients</td>
<td>Chronic wounds of various aetiologies</td>
<td>UrgoStart</td>
<td>Efficacy and predictive factors of healing</td>
<td>48.8% had healed by the end of the median follow-up of 59 days. A higher baseline PUSH score, an ulcer duration greater than 6 months and an arterial component were significant predictors of non-healing within 24 weeks</td>
</tr>
<tr>
<td>Kerihuel(^{117})</td>
<td>968 patients</td>
<td>Chronic and longstanding acute wounds</td>
<td>UrgoStart</td>
<td>Efficacy</td>
<td>Use of UrgoStart as a first-line treatment resulted in a significant improvement in the condition of the wound and its progression towards healing compared with those in which it was used as second-line treatment (p=0.006)</td>
</tr>
<tr>
<td>Kerihuel(^{118})</td>
<td>1185 patients</td>
<td>Chronic wounds of various aetiologies</td>
<td>UrgoStart</td>
<td>Efficacy, tolerability and pain</td>
<td>Favourable healing outcomes were achieved, based on overall scores of a purposefully devised assessment tool that assessed the following parameters: wound surface area, exudate levels, colour/quality of wound tissue and ongoing pain experienced by patient. The mean overall score reduced by approximately 50% for all wound types. Results showed high tolerability and a marked reduction in pain</td>
</tr>
<tr>
<td>Tsantilas et al.(^{119})</td>
<td>1248 patients</td>
<td>Chronic wounds of various aetiologies</td>
<td>UrgoStart Contact</td>
<td>Efficacy, tolerability, acceptability and quality of life</td>
<td>Use of UrgoStart either resulted in healing (45%) or a significant reduction in wound size (49%). Almost all physicians (99%) rated UrgoStart as ‘very good’ or ‘good’, while results of a quality-of-life questionnaire revealed improvements in health</td>
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</table>
Dressings with TLC-Ag and TLC-SSD healing matrix

All wounds — acute and chronic — contain microorganisms, but this does not mean that they are infected. In chronic wounds, the presence of devitalised tissue can result in colonisation by a variety of microorganisms, but this is only regarded as problematic if there is a host reaction (characterised by the clinical symptoms of critical colonisation or infection), which will delay healing. While the number of bacterial species present in the wound is not necessarily an indicator of infection, the presence of four or more groups increases the risk, as does, of course, host susceptibility and the presence of certain pathogens, such as Staphylococcus aureus, Streptococcus species, anaerobes and Pseudomonas aeruginosa.

The concepts of critical colonisation and infection are based on the level of host response to the pathogens present in the wound. While there is no universally agreed definition of critical colonisation, it is proposed that a wound is critically colonised when the bacteria delay healing with subtle signs of a host reaction or inflammation but no overt signs of infection — for example, when the wound margins fail to contract, exudate levels increase, the wound bed is predominantly sloughy and, possibly, granulation is friable and bleeds easily at dressing change. In contrast, infection is associated with damage to the host, with the classic signs including pain, erythema, heat, oedema, malodour, cellulitis, delayed healing and wound breakdown.

More recently, it has been proposed that all chronic wounds contain biofilms. Most bacteria grow when attached to a surface, such as the host tissue, and the numbers and species of bacteria multiply to become a stable, self-sustaining, polymicrobial community (the biofilm) that is encased within a matrix of extracellular polymers. A host inflammatory response then occurs, resulting in the recruitment of excess neutrophils, pro-inflammatory cytokines and excess host-derived proteases, which provide the biofilm with a constant source of nutrients. The biofilm has an evolutionary ability to adapt to its environment, avoid the immune system and resist antibiotics, thereby ensuring its survival. As time passes, the aerobic and anaerobic bacteria in the biofilm increase their pathogenic effect, potentially causing infection and delaying healing still further.

Topical antimicrobials can be used to prevent and treat local infection in high-risk patients. In addition, the various antiseptics contained within most of these dressings will reduce the bioburden, thereby helping the host to regain control. Topical antimicrobials have an advantage over systemic antibiotics in that they are not associated with resistance, and have a broader antimicrobial spectrum and much lower sensitisation rates. While best practice guidelines are still in development, it is prudent to restrict use to a maximum of 3–4 weeks before re-assessing the patient, depending on local protocols. Topical antimicrobials should only be used while the signs of critical colonisation or local infection are resolving. If the infection becomes systemic, then antibiotics must be applied.

Silver has a broad antimicrobial effect against both Gram-positive and Gram-negative bacteria, including Pseudomonas aeruginosa, meticillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE), as well as some fungi, viruses and protozoa. It is thought to bind to and damage microbial cell walls, inhibit replication and reduce metabolism and growth.

The safety and tolerability profile of silver is good. The potential for bacterial resistance to silver has also been raised, but recorded occurrences are very rare. Silver has therefore been incorporated into the TLC healing matrix to give it antimicrobial properties. Silver sulphadiazine (3.75%) has been added to UrgoTul to produce UrgoTul SSD, and silver sulphate (3.5%) to UrgoTul to produce UrgoTul Ag/Silver. Both are indicated for the treatment of non-low exuding acute wounds (burns, skin abrasions, traumatic injuries, second-degree burns) and chronic wounds showing signs of infection or critical colonisation. They can also be used on more heavily exuding wounds when in combination with an absorbent dressing.
Three unpublished large-scale observational studies demonstrate that clinicians have used these TLC-Ag dressings on over 8000 patients with critically colonised and/or locally infected acute and chronic wounds, with the results indicating that they were well accepted by both practitioners and patients.

Despite the widespread acceptance of silver dressing in clinical settings, the lack of multiple, large-scale, high-quality trials on silver dressings — and thus robust efficacy data — has raised concern among commissioners that the expense incurred by their routine use may not be justified. Such concern was fuelled by the VULCAN RCT, which reported that silver dressings are no more effective than low-adherent dressings in healing venous leg ulcers, even though there is nothing to indicate in the study that the dressings were applied to critically colonised or infected ulcers, indicating that its methodology was flawed. Clearly, a more considered approach to the literature is warranted.

This chapter provides substantial evidence from the laboratory trials and clinical studies that dressings with TLC-Ag or TLC-SSD healing matrix can help improve wounds with signs of critical colonisation or infection.

**In vitro evidence**

Following the launch of UrgoTul SSD, *in vitro* research, presented in a poster, investigated the bactericidal properties (based on minimal inhibitory concentration, MIC) of silver sulphadiazine against 117 strains of bacteria, including meticillin-resistant *Staphylococcus aureus* (MRSA). (The MIC test determines the degree of antimicrobial activity of a material against a specific bacterium.) Results revealed it produced low MIC values, demonstrating that silver sulphadiazine is bactericidal against a large amount of the strains tested, including those with known antibiotic resistance.

Further *in vitro* studies showed that UrgoTul SSD has minimal cytotoxic effects on human dermal cells. In a comparative, independent, laboratory study involving five silver dressings — Acticoat (Smith & Nephew), Aquacel Ag (ConvaTec), Contreet Foam (Coloplast), PolyMem Silver (Aspen Medical) and UrgoTul SSD (Urgo) — PolyMem Silver and UrgoTul SSD had the least cytotoxic effects on human keratinocyte and fibroblast monolayer cultures (Fig 34). The cultured skin cells were ‘relatively safe’ in the presence of these two dressings, but died when exposed to the other three. In fact, the biological activity of UrgoTul SSD was comparable to that of a non-silver dressing control (Aquacel) on the keratinocyte monolayer.

Silver has been shown to inhibit biofilm formation *in vitro*. *In vitro* research, as yet available only as posters, demonstrated the efficacy of TLC healing matrix containing silver (TLC-Ag) in destroying *Staphylococcus aureus* and *Pseudomonas aeruginosa* biofilms. Based on bacterial counts, one study showed that TLC-Ag killed 98% of *Pseudomonas aeruginosa* biofilms and 99.9% of *Staphylococcus aureus* biofilms, with a maximum effect after 1 and 2 days respectively. These results were confirmed by scanning electron microscopy (SEM).

A second laboratory study, which focused on UrgoCell Ag/Silver, confirmed these results, finding that it destroyed 99.98% and 99.97% of *Pseudomonas aeruginosa* and *Staphylococcus aureus* biofilms, respectively, within 24 hours. Dressing samples were also exposed to the biofilms for 2, 4 and 7 days. Results show that changing the dressing after 2 days (as indicated in the manufacturer’s instructions for use) sustained the antimicrobial effect. Again, these antimicrobial effects were confirmed by SEM.

A more recent *in vivo* study demonstrated the significant anti-inflammatory effects of UrgoTul Ag/Silver on chronic skin inflammation induced on the backs of hairless female mice. A total of 30 mice were randomised to five groups (n=6), whereby UrgoTul Ag/Silver was compared with a nanocrystalline silver dressing (Acticoat, Smith & Nephew), UrgoTul, desonide corticoid cream 0.05% (positive control) and sterile gauze (negative control). During the 7-day treatment period, the
degree of skin inflammation was assessed. After this, histological evaluations were performed to gather a global microscopic score for skin inflammation, ranging from 0 (no or no further skin inflammation) to 44 (hyper-inflammatory skin). The results show that UrgoTul Ag/Silver reduced skin inflammation on the third day of treatment slightly faster than did Acticoat and much faster than did UrgoTul or the negative control, neither of which produced any observable reductions in inflammation by the end of the treatment period (UrgoTul: 5.7 ± 0.5; gauze: 6.3 ± 0.3).

**Burns**

Burns are traumatic wounds that may be caused by exposure to thermal extremes, caustic chemicals, electricity, radiation or direct heat. Pain can be severe, particularly in superficial burns. Infection is the main cause of morbidity and death. The main aims of management are therefore to reduce pain between and during dressing change, prevent infection and restore form, function, and feeling.173

Traditionally, silver sulphadiazine cream was used to prevent or treat infection in burns, but its use prolongs healing,174 inactivates enzyme debrid- ing agents 175 and has cytotoxic effects. 176 It also requires daily dressing changes. To counter these effects, silver sulphadiazine has been incorporated into dressings, with a view to facilitating a slow, but sustained, release of silver sulphadiazine.

UrgoTul SSD is a silver sulphadiazine-impregnated TLC contact layer that delivers a known dose of silver sulphadiazine to the wound and reduces dressing-change frequency compared with the cream. Its efficacy in burn injuries has been largely proven.

In a multicentre clinical study, Carsin et al. found that its use either resulted in healing or enabled skin grafting in hospitalised patients with recent (<24 hours) partial-thickness burns.177 Mean baseline surface area was 192.7cm² (± 151.1, range 30–629). Of the 41 patients included, 24 healed in a mean of 10.8 ± 4.3 days (range 5–21) and 13 had a skin graft within a mean of 11.5 days (range 4–24). None developed a secondary infection during the 4-week study period, even though swabs results identified *Staphylococcus aureus* in eight patients. It is noteworthy that seven of these eight patients healed; the eighth patient was withdrawn due to the development of eschar on the treated wound. The mean dressing change frequency was 1.73 days (range 1–5).

Nurses scored the dressing highly in terms of acceptability, and it was almost always considered easy/very easy to remove with no/slight bleeding. There was no or slight adherence at 82% of dressing changes. Conformability was considered very good/good at approximately two-thirds of dressing changes (73%). Only one adverse event was reported: pain on the third day of treatment but this did not warrant discontinuation.177

An independent randomised controlled trial (RCT) that compared UrgoTul SSD with 1% silver sulphadiazine not only confirmed the dressing’s efficacy but also showed it was associated with lower pain scores than the comparator treatment.178 Sixty-eight patients with partial-thickness burns of less than 15% total body surface area were randomised to receive either UrgoTul SSD (n=34) or 1% silver sulphadiazine (n=34). Both groups had comparable demographic data and wound characteristics at baseline. Statistically significant differences in favour of UrgoTul SSD were reported in terms of mean healing times (10 ± 4 days versus 12 ± 6 days respectively, p<0.05) and pain scores (recorded 30 minutes after each dressing change using a 0–10 visual analogue scale) (3 ± 1 versus 6 ± 2, p<0.05). Fewer patients treated with UrgoTul SSD required analgesia (p=0.04). The mean follow-up times at the outpatient burn clinic were significantly shorter for the UrgoTul SSD patients (p=0.03). The authors state that the UrgoTul SSD group required less frequent dressing changes.

Good results have also been reported in paediatric burns. An independent, retrospective cohort...
study that compared UrgoTul SSD with Contreet Ag (also known as Biatain Ag) (Coloplast) reported that it provided near-painless wound management and was highly acceptable to children with partial- or full-thickness burns. Two comparable groups of 20 children were evaluated. Analgesia was administered only before dressing change in accordance with the physician’s preference. Pain results slightly favoured UrgoTul SSD, with pain being absent or slight in 92% of dressing changes compared with 85% for Contreet Ag, while the results for acceptability were comparable for the two dressings. However, UrgoTul SSD was considered ‘very easy’ to apply and remove in 49% and 73% of dressing changes respectively, versus 35% and 56% for the control group. Examples of the efficacy of UrgoTul SSD on partial-thickness burns are given in Figs 35 and 36.

**Grafts**

When removing a dressing to determine graft take, care must be taken to avoid adherence as this will traumatisate the new vascularity of the graft. A non-adherent dressing is therefore advised. UrgoTul SSD has been shown to avoid adherence and thus painful dressing changes in ulcers following grafting. According to a poster presentation, 10 patients whose post-necrotic angiodermatitis skin grafts were dressed with UrgoTul SSD experienced less pain at dressing change. Dressing change frequency was every 2 days for the first 8 days and then twice weekly, thereby reducing the risk of mechanical trauma to the graft and aiding healing. Necrotic angiodermatitis is a painful, lower extremity, ischaemic ulcer associated with poorly controlled hypertension. Treatment comprises excision and grafting, while management includes infection control. None of the graft sites developed an infection.

**Venous leg ulcers**

UrgoTul Ag/Silver is impregnated with silver ions. These are not released into the wound, but are instead maintained within the lipidocolloid gel. The antibacterial effect only occurs when the gel comes into contact with the wound. UrgoCell Ag/Silver is a foam version of UrgoTul Ag/Silver, and is indicated for low to moderate exudate levels. The clinical studies outlined below show that TLC-Ag dressings aid healing in chronic wounds with signs of infection or critical colonisation.

A multicentre, open-label RCT found that UrgoTul Ag/Silver, worn under compression bandaging, promoted healing of critically colonised venous leg ulcers, when compared with a non-silver control (UrgoTul). A total of 102 patients from 24 centres with at least three of the following signs of critical colonisation — pain between two consecutive dressing changes, peri-wound erythema, oedema, malodour and heavy exudation — were included in the efficacy analysis. The treatment period lasted 8 weeks, with patients in the treatment group (n=52) receiving UrgoTul Ag/Silver for the first 4 weeks and then UrgoTul for the
following 4 weeks. The control group (n=50) received UrgoTul for 8 weeks. Wound surface area was measured objectively by planimetry and photography. The mean baseline wound areas were 22.3cm² (± 20.4, median 16.3) and 17.5cm² (± 14.4, median 12.6) for the treatment and control groups respectively. The two groups were comparable at baseline. In the investigators’ opinion, a large majority of all ulcers (79%) were ‘stagnating or aggravating’. Three patients dropped out before the first week following withdrawal of consent, aggravation of the ulcer and an intercurrent event, so the intention-to-treat (ITT) analysis was performed on 99 patients. Twenty-eight patients dropped out of the study, primarily due to ulcer aggravation (n=11) and local adverse events (n=13). Most of these (n=20) were in the control group, and five were possibly dressing related.

Results show greater efficacy for UrgoTul Ag/Silver throughout the study period. At week 4, wound area in the UrgoTul Ag/Silver group reduced on average by 6.5 ± 13.4cm² (median 4.2cm²) compared with 1.3 ± 9.0cm² (median 1.1cm²) for the control (p=0.023). The same trends were observed when surface area evolutions were expressed as a percentage reduction from baseline (Fig 37). By week 8, median ulcer area regression was 47.9% in the UrgoTul Ag/Silver group versus 5.6% in the controls (p=0.036). Interestingly, after week 4, when UrgoTul Ag/Silver was replaced with UrgoTul, the mean ulcer area in this group continued to decrease, whereas no clinically relevant change was noted in the control group, which used UrgoTul throughout the study period. By week 8, the mean ulcer size reduction was 5.9cm² for the treatment group compared with 0.8cm² for the control group, representing a marked statistically significant difference (p=0.002). Results also showed that ulcers treated with this dressing were less likely to be still critically colonised at week 4 than the controls (61% versus 83%). Indeed, compared with baseline, there was a significant reduction in the number of clinical signs of infection in the wounds dressed with UrgoTul Ag/Silver versus the control (-2.5 ± 1.5 versus -1.0 ± 1.4; p<0.001).

There was no difference in the number of adverse events (n=11) in each group, and the authors were unable to determine whether or not they were dressing related. Four patients from the treatment group and five from the control group discontinued treatment because of them. These results are
particularly interesting in the light of the VULCAN debate as they provide clear evidence that UrgoTul Ag/Silver promotes healing when compared with a non-adherent neutral control when used on the appropriate wound types.183

In 2006, a multicentre clinical study assessed the efficacy of UrgoCell Ag/Silver under compression bandaging in venous leg ulcers, although here efficacy was defined not only as the reduction in the wound size but also as a reduction in the clinical signs of critical colonisation.184 The results showed that this dressing performed well for both outcomes. Forty-five patients with 3–5 signs of critical colonisation (spontaneous pain between dressing changes, peri-wound erythema, malodour, oedema and heavy exudation) and a mean venous ulcer surface area of 12.6cm² (± 10.0) (range 2.6–48) were included in the study. Wound size was determined by tracing and photography. By week 4, only 10 patients still had three or more of these symptoms — a highly significant reduction (p<0.001). Similarly, at week 4 the mean percentage reduction in ulcer size was 35% (± 58%, median 33%), which was also highly significant (p<0.001). Of the 45 ulcers, five healed and 30 improved. The dressing was left in place for 2.6 days on average, and even up to 13 days in one case. Results for acceptability are given in Fig 38.

Fig 39 illustrates the full healing achieved following application of UrgoTul Ag/Silver on a chronic venous leg ulcer.

Acute and chronic wounds
Schäfer et al.185 conducted a binational evaluation undertaken in France (n=2820 patients) and Germany (n=2140 patients) in which either UrgoTul Ag/Silver (Germany) or UrgoTul SSD (France) or UrgoCell Ag/Silver (France and Germany) was used for 8 weeks on locally infected wounds. The most common wound types were venous leg ulcers (44%) and traumatic wounds (25%). The median baseline wound duration was 60 days for France and 45 days for Germany.

Following treatment with a TLC-Ag dressing, 30% of the wounds had healed, while the mean number of signs of local infection reduced from a baseline of 4.0 to 0.54. 97% of the participating physicians rated dressing tolerability as ‘good’ or ‘very good’.

Other wounds
The antimicrobial properties of TLC healing matrix with silver dressings have also been demonstrated on other wound types, including diabetic foot ulcers,186 malignant wounds,187 complex wounds,187 abdominal wounds,186,187 frostbite wounds,186 post-traumatic wounds186,187 and rhinophyma.182

Table 8 summarises the main outcomes of clinical studies involving the use of TLC-Ag or TLC-SSD dressings.

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample size</th>
<th>Wound types</th>
<th>Product used</th>
<th>Outcome measures</th>
<th>Key results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muangman et al.</td>
<td>68 patients</td>
<td>Partial-thickness burns</td>
<td>UrgoTul SSD versus 1% silver sulphadiazine</td>
<td>Efficacy</td>
<td>Healing times and pain scores significantly favoured UrgoTul SSD (p&lt;0.05)</td>
</tr>
<tr>
<td>Lazareth et al.</td>
<td>102 patients</td>
<td>Critically colonised venous leg ulcers</td>
<td>UrgoTul Ag/Silver versus UrgoTul</td>
<td>Efficacy, tolerability and acceptability</td>
<td>At week 8, there was a significantly greater reduction in wound size in the UrgoTul Ag/Silver group (p=0.002), as well as fewer clinical signs of critical colonisation (p&lt;0.001). There was no difference in terms of local adverse events and tolerability</td>
</tr>
<tr>
<td>Schäfer et al.</td>
<td>4960 patients (2820 in France and 2140 in Germany)</td>
<td>Locally infected wounds</td>
<td>UrgoTul Ag/Silver, or UrgoTul SSD, or UrgoCell Ag/Silver</td>
<td>Efficacy and tolerability</td>
<td>At 8 weeks, 30% of the wounds had healed and the mean number of signs of local infection reduced from a baseline of 4.0 to 0.54. 97% of the participating physicians rated dressing tolerability as ‘good’ or ‘very good’</td>
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**Benefits of sequential treatment with TLC healing matrix**

One of the initial aims of treatment is to clean the wound bed by removing any devitalised tissue present and to manage signs of local infection. Once the wound bed has been prepared, a moist environment needs to be promoted and maintained in order to facilitate healing. However, it may also be necessary to neutralise harmful matrix metalloproteinase activity. Dressings in the TLC healing matrix range can be used sequentially to achieve these objectives, as is illustrated in the following evidence.

Allaert et al. described the outcomes of an observational study involving patients with chronic wounds of various aetiologies who received sequential treatment with UrgoCell Ag/Silver and UrgoStart. The sample comprised 279 patients, of whom 38% had a venous leg ulcer, 22% a mixed aetiology leg ulcer, 13% a traumatic wound that had become chronic, 10% a diabetic foot ulcer, 10% a pressure ulcer and 7% an arterial leg ulcer. The wounds were chronic, with a median baseline duration of 2 months, and had signs of local infection. Patients received UrgoCell Ag/Silver for 4 weeks followed by UrgoStart for 4 weeks.

Signs of clinical infection practically disappeared following use of UrgoCell Ag/Silver. Results showed that the mean wound surface area reduced from 27.5 ± 39.3 cm² to 17.9 ± 32.6 cm² (p<0.0001) after the initial 4 weeks’ treatment with UrgoCell Ag/Silver, and then to 8.9 ± 28.8 cm² (p<0.0001) after 4 weeks with UrgoStart. This represents surface area reductions of 34.9% and 67.6% for the two dressings respectively. Thirty-eight per cent of the wounds healed.

The authors commented that these results compared favourably with those of the Lazareth RCT, where the sequential use of UrgoTul Ag/Silver and UrgoTul resulted in an overall median reduction in wound surface area of 47.9% (36.6 ± 48.8%).

The investigators also found that the sequential use of the two dressings resulted in a significant reduction in pain levels assessed using a 0–100mm visual analogue scale (ranging from none to intolerable). The baseline pain scores of 50.5 ± 24.3mm (ongoing pain) and 59.0 ± 23.8mm (pain at dressing change) reduced to 22.4 ± 22.5mm and 22.5 ± 23.2mm, respectively, during the course of the evaluation.

Finally, Alexandra Whalley reported on a series of case studies describing the successful sequential use of UrgoClean and UrgoStart in patients with chronic wounds (diabetic foot ulcers, leg ulcers, pressure ulcers and traumatic injuries). One case described how treatment with UrgoClean followed by UrgoStart resulted in a marked decrease in wound size in a diabetic foot ulcer over an 8-month period. The patient, who was 63 years old, had neuropathy which had resulted in bilateral Charcot feet. Previously, he had been non-adherent with treatment and instead had lived with his wounds, which remained static. UrgoClean was used to deslough the wound bed and UrgoStart to promote healing. During the course of treatment, neither of the two TLC dressings adhered to the wound, and both were easy to remove. As the wound progress through the various stages of the healing trajectory, there was a concomitant improvement in the patient’s quality of life. Similar results were reported for a large and deep PU which had almost healed after 80 day, and a chronic VLU, which healed within 3 weeks. Fig 40 shows the diabetic foot ulcer before and after 8 months of treatment. Outcomes for the leg ulcer and pressure are shown in Figs 41 and 42.
Conclusion
There is extensive evidence, from in vitro to double-blind RCTs, to support the TLC healing matrix range of dressings. The pre-clinical scientific data clearly shows that TLC dressings promote fibroblast proliferation and collagen production, two of the prerequisites for healing. This is supported by clinical studies, much of which reflect the challenges of real-life practice, showing that use of TLC healing matrix either achieves full wound closure or promotes healing in a broad range of wound types. In addition, the tolerability and acceptability data consistently show that the dressing scored highly in terms comfort and ease of use, with the minimal pain and bleeding experienced at dressing removal, reflecting its non-adherent properties.

This review also provides evidence that dressings in the TLC healing matrix range meet the needs of wounds at all stages of the healing trajectory. For example, it clearly demonstrates that TLC-Ag dressings resolve signs of local infection, and that TLC with hydro-desloughing fibres promotes safe, effective and atraumatic desloughing, thereby fulfilling the requirements of the TIME paradigm. In chronic wounds, use of UrgoStart dressings effectively accelerated healing while TLC was shown to promote the moist environment required for healing. Much of the supporting evidence is new and is cited here for the first time, with many of the evaluations having sample sizes of over 100 patients.

Taken as a whole, the evidence on the TLC dressing range shows it meets the twin objectives of promoting healing and improving quality of life.

Fig 41. The leg ulcer before (a) and after (b) 3 weeks’ sequential treatment with UrgoClean followed by UrgoStart

Fig 42. The pressure ulcer before (a) and after (b) 80 days’ sequential treatment with UrgoClean followed by UrgoStart
polyurethane foam: similar early effects on wound dressing. Br J Nurs 2005; 14: (Suppl. 82)
Ulcers reported as ‘difficult to heal’ and their impact on patient QoL, results of the TRAJECTOIRE Survey JPC 2008; 8: 6, 34–37.


174 Thomas, K. Clinical case report illustrating the benefits in treatment with an antibacterial lipido-colloid contact layer and an absorbing dressing Poster presented at EWMA, Lisbon, May 2008.


188 Aliers, F.A. Use of UrgoTul Border in the local management of wounds with various aetiology. Poster presented at CPR Piccadilly, dry day. Poster presented at CPR Piccadilly, dry day.


