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## Chronic Venous Leg Ulcers: Is Topical Zinc the Answer? A Review of the Literature



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2.9 Contact Hours

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This continuing educational activity will expire for physicians on January 31, 2015.

**PURPOSE:**

**To enhance the learner's competence with knowledge of research data on topical zinc for treatment of chronic leg ulcers.**

**TARGET AUDIENCE:**

**This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.**

**OBJECTIVES:**

**After participating in this educational activity, the participant should be better able to:**

- 1. Analyze the findings of the topical zinc dressing literature search to assess its role in healing venous leg ulcers (VLUs).**
- 2. Apply results of study findings in case scenarios for VLU treatment regimens.**
- 3. Recognize the limitations of the research studies in the literature review on topical zinc dressings.**

## ABSTRACT

Venous leg ulcers (VLUs) are chronic leg wounds that can have a debilitating effect on the physical and psychological health of patients. Older patients, who are a vulnerable group, suffer from VLUs more frequently, and the prevalence of these ulcers increases as the population ages. Venous leg ulcers also pose a serious cost to the healthcare industry. Zinc, in the form of topical creams and lotions, has been used in wound care for more than 3,000 years and is now contained in a variety of wound care products that are used in the treatment of chronic VLUs.

**OBJECTIVE:** The aim of this review was to examine the current empirical evidence to assess if topical zinc-based wound products are effective in promoting the healing of VLUs.

**METHODS:** Following a systematic search and review of the literature, based on selected keywords, 11 studies were identified as being relevant, and data were extracted using content analysis.

**RESULTS:** The results show that there is currently very poor-quality evidence to suggest that topical zinc-based wound products are effective in healing VLUs, either in conjunction with compression therapy, as compression bandages themselves, or as a topical skin protectant. Some of the studies were sponsored by industry, which challenges the validity and reliability of their results.

**CONCLUSIONS:** It is apparent that not only was much of the literature conducted on a small scale, it is also outdated and methodologically inconsistent. There is scant high-quality evidence to suggest that topical zinc-based wound products are effective in promoting the healing of VLUs. New studies are urgently needed that are larger, scientifically rigorous, and without bias from industry. This will enable clinicians to implement evidenced-based practice and choose the most appropriate wound management product to improve patient care and reduce the costs of healthcare.

**KEYWORDS:** venous leg ulcer, topical zinc, zinc oxide wound care

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## INTRODUCTION

Venous leg ulcers (VLUs) are the most common type of leg ulcer. They are wounds that occur on the leg or foot in the presence of venous disease and remain unhealed for at least 4 weeks.<sup>1</sup> They are mainly caused by incompetence valves in the blood vessels in the leg leading to venous stasis and hypertension.<sup>2</sup> Venous leg ulcers are a chronic condition that can cause pain, exudate and odor, poor sleep, loss of mobility, and social isolation for those

who suffer from them, which can seriously affect patients' morbidity and quality of life.<sup>3</sup> The prevalence rates of VLUs have been reported to vary between 0.12<sup>4</sup> and 2.4%,<sup>5,6</sup> with an average rate of 1.7% reported for those 60 years or older.<sup>7,8</sup> These incidence rates could more than double by 2050 as the global population ages.<sup>9</sup>

In addition, the cost of treating just 1 venous VLU in the United Kingdom<sup>10</sup> was estimated at £1300 (US \$2100), and the overall cost to the National Health Service is thought to be in the region of £400 (US \$646) million annually.<sup>11</sup> Similar figures from the United States reveal the average cost per month of care for a patient with VLUs is \$2400 (£1483).<sup>12</sup> This places a large burden of approximately \$1 billion (£618 million) on the US national healthcare budget each year.<sup>13</sup> If VLUs are poorly managed and treated, they will not only cause a series of debilitating physical and psychological problems for a vulnerable age group, but also create a serious financial and resource burden on national health services.

Topical zinc, in the form of zinc oxide or calamine lotion, has been used medicinally in wound care for more than 3000 years and is still widely used in wound care products today.<sup>14</sup> Zinc is the second most abundant trace element in the human body after iron and is an essential mineral in human nutrition. It is required for catalyzing more than 100 enzymes,<sup>15</sup> and it is necessary for antibody production and immune cell function,<sup>16</sup> as well as protein and DNA synthesis.<sup>17</sup>

A seminal study by Henzel et al<sup>18</sup> in the 1970s noted that postoperative wounds of some patients after major surgery were very slow to heal. On investigation, the researchers found that these patients had decreased serum zinc levels in their blood, and split-thickness skin biopsies revealed they also had up to 50% less zinc in the granulation tissue and wound margin compared with other postoperative patients. The authors attributed the deficit in serum zinc levels to the poor wound healing process, which along with other research prompted the use of topical zinc in wound care.

Many wound care products contain topical zinc, such as zinc pastes; zinc paste and calamine products; zinc paste, calamine, and clioquinol; zinc paste and coal tar; and zinc paste and ichthammol products.<sup>19</sup> These have been marketed as anti-inflammatory, antimicrobial, and overall as contributing to the wound healing process. As such, these products have been used to treat a variety of wounds such as chronic VLUs.

Despite the widespread use of topical zinc in wound dressings that are used in the management of chronic VLUs, however, no in-depth review has ever been undertaken to assess its efficacy. Given that clinical practice should be grounded on high-quality

and rigorous scientific and social science research, this article examines the literature to determine if the use of various zinc-based wound products is effective in promoting the healing of VLUs and the implications this can have for patients, clinical practice, and healthcare services. This information will help clinicians select the most appropriate dressing for patients, helping to minimize pain, exudate and odor, stress and anxiety, and healing time.

## METHODS

An electronic literature search was conducted by searching the databases CINAHL, MEDLINE/PubMed, and the Cochrane Library, using a combination of key search terms such as “topical zinc,” “zinc oxide,” “zinc paste,” “wound healing,” “zinc dressing,” “zinc bandage,” “zinc stocking,” “leg ulcer,” and “venous leg ulcer.” A manual search of textbooks was also conducted to provide background information that supplemented the literature review. Included in the search were English-written, peer-reviewed journals, between January 1980 and December 2013, to ensure results were comprehensive and of the highest quality. Exclusion criteria consisted of studies that focused exclusively on leg ulcers whose etiology stemmed from nonvenous origins and wound care products that did not contain zinc as one of the primary ingredients.

Eleven articles were identified describing a range of studies of zinc dressings used to heal chronic VLUs. Eight were randomized clinical studies of varying sizes; there was 1 longitudinal study, 1 case study, and 1 systematic review. Each study was analyzed in detail, and a matrix model was used to summarize and categorize the results under the following headings: clinical setting and sample size, study design, methodological approach, data analysis, and key findings.<sup>20</sup> The literature revealed topical zinc is used in 4 main ways to promote the healing of VLUs. First, zinc paste bandages are used in conjunction with compression therapy; second, zinc-impregnated bandages are used as compression therapy; third, topical zinc ointment is used as a skin protectant; and finally, zinc oxide can be used for debridement. The findings of this review are shown in Tables 1 and 2 and are summarized in the following sections.

## ZINC PASTE BANDAGES WITH COMPRESSION THERAPY

Research has highlighted that zinc-impregnated bandages have been in use since 1854, and their modern-day equivalents are still one of the main treatments for VLUs in conjunction with

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compression therapy.<sup>21</sup> They are made with open-weave bleached cotton and are impregnated with a zinc oxide paste ranging in concentration from 6% to 15%. An early study examined the effect

of a zinc oxide dressing on the healing of 18 VLUs and 19 arterial ulcers.<sup>22</sup> The randomized double-blind study compared 2 groups: one that used gauze impregnated with zinc oxide and the second that used identical gauze without any topical ointment, on their leg ulcer. In both groups, the size of the ulcer, granulation, and debridement based on 2 treatments over 8 weeks were examined. Patients with venous wounds received additional compression therapy. Although the results showed a better healing rate among the patients who received zinc oxide (83%) compared with the control group (42%), the study's sample size, short time frame, and mixed wound type limit the generalizability of the results. Also, the study is nearly 30 years old, and newer, more effective wound care products have been developed since the 1980s.

A later randomized controlled study looked at the effectiveness of 2 types of occlusive bandages in treating 34 VLUs.<sup>23</sup> This concluded that over 10 weeks there was no difference in the healing rate between an aluminium foil dressing with compression bandaging and an inner stocking impregnated with zinc oxide paste and an outer elastic bandage. Other research compared a zinc oxide–medicated dressing with a hydrocolloid dressing in a prospective, randomized trial over 8 weeks.<sup>24</sup> It investigated the effects of both dressing types on the healing rate and pain in both venous and arterial leg ulcers. Compression therapy was applied over the dressings on VLUs only. The study reported a 65% reduction in wound area under adhesive zinc oxide tape compared with a 48% reduction in the size of ulcer when the hydrocolloid dressing was applied. Both wound dressings had similar analgesic effects, but several patients had to withdraw from the study because of a sensitivity reaction to the zinc oxide–medicated dressing treatment. Overall, it concluded that there were insufficient data for the results to be significant as only 31 patients in total participated.

Stacey et al<sup>25</sup> examined the effect of 3 different wound dressings on 133 VLUs caused by venous disease. The randomized controlled trial revealed patients treated with a zinc paste bandage had far higher healing rates (79%) than did those who had zinc oxide stockingettes (59%) or a calcium alginate fiber dressing (56%) applied under compression bandaging. However, the authors concluded that healing was mainly attributed to the extra compression that improved venous return and not because of the dressing applied. Others argue that compression bandaging may

**Table 1.****LITERATURE REVIEWED ON TOPICAL ZINC TO TREAT VENOUS LEG ULCERS WITH COMPRESSION THERAPY**

Author	Clinical Setting	Sample Size	Study Design	Methodology Approach	Data Analysis	Key Findings
Brandrup et al (1990) <sup>24</sup>	Odense University Hospital, Denmark	N = 61 Patients with venous and arterial leg ulcers	Prospective randomized trial over 8 wk	Comparison of zinc oxide-impregnated dressing, and a hydrocolloid dressing. Patch test done, colophony allergy was an exclusion criteria.	SPSS predictive analytics software	Both dressings were well tolerated by patients—similar analgesia effects. No major difference in the efficacy of the 2 occlusive dressings.
Cordts et al (1992) <sup>28</sup>	Dressing clinic at Boston City Hospital, Massachusetts	N = 30 Patients with Grade III VLU	Randomized controlled trial 12-wk study	Comparison of a hydrocolloid dressing combined with a compression bandage against Unna boot. Weekly wound dressings, photograph and measurements. Poststudy patient and nurse survey on treatment provided	SPSS software, Student <i>t</i> test, Wilcoxon rank sum test, $\chi^2$ test, linear regression analysis, analysis of variance, correlation analysis	Ulcers with the hydrocolloid dressing combined with a compression bandage healed more quickly than those treated with Unna boot within a 12-wk period, although the results were not statistically significant
Eriksson (1986) <sup>23</sup>	Wound clinic, Danderyd Hospital, Sweden	N = 34 Patients with VLUs	Randomized controlled study, 10 wk	Comparison of a hydrocolloid dressing (aluminium foil) and a double-layered bandage consisting of an inner zinc and outer elastic bandage. Evaluated against stereophotogrammetric measurement of ulcer area and volume, and bacterial counts	SPSS predictive analytics software	No difference was found in the healing rate between the dressings
Hendricks and Swallow (1985) <sup>27</sup>	Asheboro Dermatology Clinic, North Carolina	N = 21 Patients with stasis leg ulcers	Randomly assigned to 2 groups	Comparison of Unna boot versus an elastic support stocking with graded compression	SPSS software—Wilcoxon rank sum test, Cox regression analysis	No statistically significant difference between their success rate ( $P = .9394$ ). Healing time was shorter for patients treated with Unna boot.
Kerstein and Gahtan (2000) <sup>29</sup>	Mount Sinai Medical Center, New York	N = 81 Patients with venous ulcers	Longitudinal study	Explore the outcomes and cost of wound in a home healthcare setting and an outpatient setting. Ulcers managed with saline gauze, or a hydrocolloid dressing and compression therapy, or an Unna boot	No specific technique stated	Patients preferred home care, but the costs were higher. Data suggests hydrocolloid dressings are the most cost-effective. Lower recurrence of ulcers in hydrocolloid (13%) and Unna boot (21%) group

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**Table 1.****LITERATURE REVIEWED ON TOPICAL ZINC TO TREAT VENOUS LEG ULCERS WITH COMPRESSION THERAPY, CONTINUED**

Author	Clinical Setting	Sample Size	Study Design	Methodology Approach	Data Analysis	Key Findings
Parboteeah and Brown (2008) <sup>21</sup>	Vascular clinic, Leicester Hospital, United Kingdom	N = 3 Patients with VLU	3 case studies	Clinical case studies of zinc oxide paste bandage applied to VLUs under 4-layered compression bandaging ranging from 4 mo to 1 y	Clinical observations and analysis.	Zinc oxide paste therapy in conjunction with compression bandaging can be effective in healing VLUs that are proving difficult to treat by other methods
Polignano et al (2004) <sup>30</sup>	Camerata Hospital, Florence, Italy	N = 68 Patients with VLUs	Prospective randomized trial over 24 wk	Comparison of healing rates, handling properties, and patient comfort in a 4-layer compression bandage system versus Unna boot	No difference in time to closure ( $P = .13$ ). 4-layer compression bandage system was easier to apply ( $P = .013$ )	4-layer compression bandage system is as effective as Unna boot in treating VLUs, it was easier to apply
Stacey et al (1997) <sup>25</sup>	Leg ulcer clinic, Fremantle Hospital, Australia	N = 133 Patients with VLUs	Prospective randomized clinical trial	Comparison of a zinc oxide-impregnated paste bandage with a zinc oxide stockingette and a calcium alginate fiber dressing. Weekly dressings for 9 mo. Rate of reduction of ulcer size in $\text{cm}^2$ was measured weekly	$\chi^2$ Analysis, Kruskal-Wallis 1-way analysis of variance, Wilcoxon rank sum test, Cox regression analysis, Bonferroni test	Improved healing with the zinc oxide-impregnated paste bandage under compression compared with the other dressings
Strömberg and Agren (1984) <sup>22</sup>	Dressing clinic, Stockholm University Hospital, Sweden	N = 37 Patients with arterial and VLUs	Randomized double-blind study over 8 wk	Comparison of gauze compress medicated with zinc oxide compared with identical gauze without zinc oxide. Weekly measurements of ulcer size, presence of granulation, and ulcer debridement	$\chi^2$ Analysis and Wilcoxon test using SPSS	The zinc-treated patients responded significantly better ( $P < .05$ ) than the control group. Healing of leg ulcers can be improved after the addition of topical zinc

have masked any beneficial effect that zinc oxide and the other dressings had during healing and recommended more in-depth, explicit research.

Three single-case studies involving the use of zinc paste bandage, in conjunction with K4 compression bandaging, on VLUs demonstrated that zinc paste bandages can be effective in treating VLUs that are difficult to heal.<sup>21</sup> Although helpful, this type of clinical practice-based research is low-quality evidence compared with other more rigorously conducted research. The current body of literature points toward the efficacy of zinc paste bandages; however, when applied in conjunction with

compression therapy to promote the healing of VLUs, the evidence remains inconclusive.

## ZINC-IMPREGNATED BANDAGES AS COMPRESSION THERAPY

Unna boot is a zinc paste-containing bandage, wrapped around the patient's leg from above the toes to below the knee, which is used to treat VLUs mainly in the United States.<sup>26</sup> The first study to examine whether Unna boot, as a form of compression therapy, was as effective as other interventions in promoting the healing of VLUs used a randomized trial.<sup>27</sup> It treated 10 patients

**Table 2.****LITERATURE REVIEWED ON TOPICAL ZINC AS A PERIWOUND SKIN PROTECTANT TO TREAT VENOUS LEG ULCERS**

Author	Clinical Setting	Sample Size	Study Design	Methodology Approach	Data Analysis	Key Findings
Cameron et al (2005) <sup>33</sup>	Weekly dressing clinic, Whitney Community Hospital, Oxfordshire	N = 35 Patients with VLU	12-wk randomized controlled trial	Observational study comparing alcohol-free liquid barrier film against zinc paste compound. Weekly wound measurements and poststudy questionnaire for nursing staff	SPSS predictive analytics software	Minimal difference between the 2 products in terms of healing rate. Time required to remove and reapply the products was significantly shorter for the alcohol-free liquid barrier film
Schuren et al (2005) <sup>34</sup>	3M Germany Laboratory, Carl-Schurz-Strasse, Neuss, Germany	N = 9 Studies	Systematic review	Evaluate the clinical performance and cost-effectiveness of a film-forming liquid acrylate in the protection of the chronic ulcer periwound	Meta-analysis	There is no difference between the protective properties of different barrier methods to protect the periwound skin around chronic ulcers

who had VLUs with Unna boot, whereas 14 patients, also with VLUs, received elastic support stockings. Unfortunately, both treatment groups were small, and the results showed no statistically significant difference between their success in healing the leg ulcers ( $P = .9394$ ). The average healing time was much shorter for patients who received Unna boot (7.3 weeks), whereas it took on average 18.4 weeks for VLUs to heal for patients who were treated with support stockings.

A subsequent study compared a gel formula dressing plus compression to Unna boot.<sup>28</sup> It reported that during the first 4 weeks of therapy healing rates for 30 patients with chronic VLUs were faster with the gel formula dressing plus compression ( $0.384 \pm 0.059 \text{ cm}^2/\text{wk}$  per centimeter perimeter) than for patients using Unna boot ( $0.135 \pm 0.043 \text{ cm}^2/\text{wk}$  per centimeter perimeter). Again at 12 weeks, the results showed the cohort using the gel formula dressing plus compression had better healing rates; however, the results at that stage were not statistically significant ( $P = .11$ ). Overall, the study concluded that a gel formula dressing with compression may be more effective for promoting the healing of chronic VLUs than Unna boot.

A longitudinal study by Kerstein and Gahtan in 2000<sup>29</sup> looked at the outcomes of treating VLUs in a home-care versus an outpatient setting. It used 3 types of treatments: (1) a saline gauze dressing, (2) a hydrocolloid dressing, both in conjunction with compression therapy, and (3) Unna boot. Patients with the hydrocolloid dressing had the best results as they had the lowest rates of ulcers, which failed to heal or that recurred at 13%. This

was followed closely by Unna boot with a recurrence or failed healing rate of 21%, whereas the saline dressing was the least effective with a rate of 88%.

In 2004, research by Polignano et al<sup>30</sup> compared a 4-layer compression bandaging system against Unna boot. This prospective, randomized, parallel-group trial followed 68 patients over 24 weeks. Although the results showed that the ease of applying the 4-layer compression bandaging dressing was rated more highly than Unna boot, there was no significant difference in the time taken for the VLUs to heal. Furthermore, the research was funded by a manufacturer of the compression products, which could have biased the study design and skewed the results in favor of its wound care product. The use of Unna boot is becoming less common as it is being replaced by elastic compression bandaging, which provides sustained pressure, is easier to use, is better shaped for the leg, and does not have to be changed as frequently.<sup>31</sup> It is impossible to say if zinc bandages as a form of compression therapy alone are effective in promoting the healing of VLUs, yet it is unlikely given the major advancements in wound dressings and compression bandaging over the last few years.

## TOPICAL ZINC OINTMENT AS A SKIN PROTECTANT

Zinc oxide ointment is also used as a barrier film on skin to protect it from wound exudate, reduce inflammation, and stimulate wound healing.<sup>32</sup> One study examined the effects of different



types of periwound skin protectants on VLUs.<sup>33</sup> It compared the effectiveness of using a no-sting barrier film as opposed to a zinc paste compound, as they both help create a barrier film to protect skin surrounding VLUs from irritation and maceration. The randomized controlled trial revealed that there was very little difference, in terms of the decrease in wound size or the healing rate of the ulcers, between the 2 products. The authors did report that nurses found the no-sting barrier film was much faster and easier to apply than the zinc oxide paste, and the no-sting barrier film was preferred from a patient comfort point of view. However, the results are overshadowed by the fact that the research was sponsored by a manufacturer of a no-sting barrier film product, which could have biased the results.

Other research has identified issues with using topical zinc paste as a barrier film. A systematic review and meta-analysis of periwound skin protectants warned that zinc paste can actually obscure the wound margin and make it more difficult to observe.<sup>34</sup> In essence, it found no difference between different barrier methods to protect the skin surrounding chronic VLUs. Research has also highlighted the possibility of sensitivity reactions to zinc paste and recommends doing a patch test on patients' skin first.<sup>35</sup> It suggests applying a small amount of zinc paste to normal skin for 3 days, then removing it and doing a follow-up examination of the patients' skin on day 5 to ensure there is no reaction. Others have stressed that many nurses do not leave the patch test for a long enough period to enable them to accurately determine if the patient has a reaction.<sup>36</sup> In conclusion, there is insufficient evidence to suggest that topical zinc ointment improves the healing of VLUs or better protects the skin surrounding these types of wounds over other products.

## DISCUSSION

Recommendations to improve the quality of evidence in wound management have highlighted the flaws inherent in today's clinical studies in wound care such as inadequate sample sizes, the lack of randomization or blinding, and poor-quality control groups, to name a few.<sup>37</sup> This review has found similar issues with the current empirical evidence on the effectiveness of zinc-based wound products for promoting the healing of VLUs.

The most concerning issue is that the majority of literature on this topic is out of date; only 3 of the 12 research studies re-

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viewed were published within the last decade. Even the most recent evidence from 2008 is already 5 years old and consisted of very low-quality evidence from 3 case studies. Furthermore, newer wound care products and procedures are continuously being

developed and tested as is evident from the introduction of 4-layer compression bandaging to manage chronic VLUs. For example, in 2013, a Cochrane review of compression for VLUs found that VLUs heal faster with compression than without and that multicomponent compression systems that include elastic bandages appear to be more effective than single-component systems.<sup>38</sup> More up-to-date research is therefore necessary to ensure newer products are taken into account so the effects of a variety of contemporary zinc-based wound products on the healing of VLUs can be investigated. This is essential to ensure healthcare practitioners select the most appropriate dressing for patients that minimizes pain, exudate and odor, and stress and anxiety and shortens the time it takes for them to heal. These improvements will then not only help reduce the cost of treating VLUs but also free up time for clinicians to concentrate on other activities. However, the challenges in conducting clinical studies, such as the high cost and lack of funding, the length of time involved, regulatory and administrative burdens, and a lack of researchers with the necessary expertise, could help explain some of the reasons for the dearth of contemporary research and need to be addressed if high-quality wound management research that will have an impact on practice is to be conducted.<sup>39</sup>

Another issue is that most of the research is on a small scale, typically with fewer than 42 participants. Although some of the larger studies were able to undertake statistical analysis and produce results with some significance, the majority of them were too small to draw a generalizable conclusion. This is compounded by the fact that the research also applied a variety of design types from randomized clinical trials, to longitudinal studies and case studies, which represents varying levels of quality on the hierarchy of evidence and makes the results of 1 study difficult to assess against another. A further complication is that the literature also examined a diverse range of dressings, such as zinc oxide-impregnated dressings, double-layer elastic adhesive bandages, and zinc oxide stockingettes.

In parallel, the studies also examined several different criteria to rate the effect of the wound dressings, from healing times and rates using various measurements, to the size of the ulcerated area, the presence or absence of granulation, handling properties, patient

comfort, and pain levels, to name a few, which makes comparison difficult. The European Wound Management Association has stressed the importance of agreeing on a consistent way to define, measure, and evaluate appropriate interventions and outcomes to improve the quality of clinical studies in wound care.<sup>37</sup> Their patient outcome group has designated a set of outcome criteria to help ensure studies are reliable and reproducible. These will help future investigators to design more robust clinical studies that are consistent and comparable.

The inconsistency of the methodological approaches used in the studies makes it impossible to assess the real impact of zinc-based wound products in promoting the healing of chronic VLUs, as no definitive conclusion can be drawn as to their efficacy. Therefore, healthcare professionals are often left to apply their best clinical judgement, as well as anecdotal evidence. And this could delay the wound healing process, causing excess pain and burden to the patient and additional cost and time constraints to healthcare. A review of barriers to implementing evidence-based practice in relation to wound care confirms this and highlights additional factors. These include the practice and experience of individual clinicians being valued over evidence from wound care theory and research, and the lack of training and expertise in research methodologies and techniques among practicing clinicians makes it difficult for them to interpret the evidence and apply it to practice.<sup>40</sup>

A final point to note is the involvement and sponsorship of industry in some of the research. Although the authors state no such conflict of interest, it is always questionable whether the research was conducted with adequate scientific rigor. Industrial sponsorship has been associated with choosing unsuitable comparators, reporting more favorable analysis, and overall skewed results that favor industry-driven research as opposed to evidence based.<sup>41</sup> Others highlight that commercial support for research is also associated with restrictions on publication and data sharing.<sup>42</sup> Furthermore, a comparison of industry-sponsored meta-analyses versus Cochrane reviews concluded that research produced with industry support was less transparent, played down the significance of any methodological restrictions, and overall was more favorable than the equivalent Cochrane review.<sup>43</sup> Given that the US wound care market was estimated to be worth \$820 million in 2012, it is hard not to be skeptical of research backed by industry as they have a vested interest in promoting the widespread use of their wound care products.<sup>44</sup> However, there are benefits of research collaboration between

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academia and industry, such as financial sponsorship to conduct research, a higher number of publications and more evidence for practice,<sup>45</sup> new innovations, more patents, and commercially viable products.<sup>46</sup>

## CONCLUSIONS

It is clear from the literature reviewed that evidence is insufficient to determine if topical zinc-based wound products are effective in healing VLUs and that more research is needed. Anecdotal evidence from historical practices, small-scale limited research that is outdated, and incorrect assumptions about wound care products based on advertising should not form the knowledge base of healthcare professionals. It must be grounded on high-quality, rigorous scientific, and social science research. Therefore, new research is urgently needed to determine the effect, if any, of topical zinc in healing VLUs.

Future research in this area should focus on larger, high-quality trials to determine the effectiveness of wound dressings on VLUs and should include a priori sample size calculation, have a time to total healing as their primary outcome measure, and include cost-effectiveness and quality-of-life data.<sup>3</sup> This would give healthcare professionals more definitive guidance as to what wound products, zinc based or otherwise, to apply to help heal VLUs, reduce patient morbidity, improve quality of life and reduce the costs of healthcare.

In addition, further research should also reconsider the traditional view that compression therapy, whether it is used in conjunction with zinc or not, is the mainstay treatment for VLUs. Contemporary research has shed fresh light on alternative therapies such as pentoxifylline, a drug that improves blood flow. A recent Cochrane systematic review found that it is an effective adjunct to compression bandaging to treat VLUs and may even be effective in the absence of compression therapy.<sup>47</sup>

Although zinc in all its forms will no doubt continue to be used in the treatment of VLUs, the rationale for this needs to be questioned and investigated through high-quality research. Only wound care practices that are based on sound evidence will make a meaningful long-term impact on the health of patients with VLUs and the healthcare profession.

## PRACTICE PEARLS

- Treatment of VLUs currently has a significant impact on US healthcare budgets (\$1 billion annually), but this is set to rise because of graying population trends. Thus, attention to cost-effective VLU wound treatment products is important.



- Zinc-based wound products are marketed as anti-inflammatory and antimicrobial, and they contribute to the wound healing process. However, the implication of their use on patients within clinical practice and health services is unknown.
- Despite the modern drive toward evidence-based practice, the routine use of products such as zinc, which has been in use for over 3,000 years, still prevails.
- More contemporary research, that is methodologically sound, is required on the efficacy of zinc-based wound products to inform clinical wound care practices.
- The benefits of industry sponsorship in wound care research should be compared with the potential bias it could introduce into research based on commercial wound care products.
- Despite the modern drive toward evidence-based practice, the routine use of products such as zinc, which has been in use for over 3,000 years, still prevails.
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