

VenUS II: a randomised controlled trial of larval therapy in the management of leg ulcers

JC Dumville,¹ G Worthy,¹ MO Soares,¹
JM Bland,¹ N Cullum,^{1*} C Dowson,²
C Iglesias,¹ D McCaughan,¹ JL Mitchell,³
EA Nelson⁴ and DJ Torgerson¹ on behalf of
the VenUS II team

¹Department of Health Sciences, University of York, UK

²Biological Sciences, University of Warwick, UK

³Micropathology Ltd, Coventry, UK

⁴School of Healthcare, University of Leeds, UK

*Corresponding author

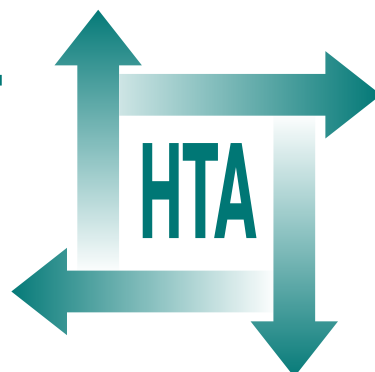


Executive summary

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Executive summary

Objectives

The objectives of the trial were to compare the clinical effectiveness and cost-effectiveness of larval therapy with those of a standard debridement technique (hydrogel).

Design

This was a pragmatic, three-arm, randomised controlled trial with an economic evaluation.

Setting

The setting was in community nursing services, community leg ulcer clinics and hospital outpatient leg ulcer clinics in a range of urban and rural settings.

Participants

Patients with venous or mixed venous/arterial ulcers (minimum ankle brachial pressure index of 0.6) where a minimum 25% of ulcer area was covered by slough and/or necrotic material.

Interventions

The treatments comprised loose larval therapy and bagged larval therapy in comparison with hydrogel.

Main outcome measures

The primary end point was complete healing of the largest eligible (the reference) ulcer and the primary outcome was time to complete healing of the reference ulcer. Secondary outcomes were: time to debridement, treatment costs, health-related quality of life (including ulcer-related pain), bacterial load, presence of methicillin-resistant *Staphylococcus aureus* (MRSA) and staff and patient attitudes to and beliefs about larval therapy.

Results

Between July 2004 and May 2007 the trial recruited 267 people aged 20–94 years at trial entry. There were more female than male participants (59.2% compared with 40.8%) and most ulcers (75.7%) were classified by the nurses as having an area greater than 5 cm². Using the log rank test, there was no evidence of a difference between the three treatment arms in the time to healing of venous leg ulcers ($p = 0.62$). Using a Cox proportional hazards model to adjust for stratification and prespecified prognostic factors (centre, baseline ulcer area, ulcer duration and type of ulcer) there was no evidence of a difference between bagged and loose larvae in terms of healing [chi-squared test statistic 0.194, degrees of freedom (df) = 1, $p = 0.66$]. When results for loose and bagged larvae were pooled and compared with hydrogel there was no evidence of a difference in time to healing. The hazard ratio for healing was 1.13 [95% confidence interval (CI) 0.76 to 1.68], which indicated a slightly increased risk of healing for the larvae group although this was not statistically significant ($p = 0.54$). The difference in time to debridement between loose and bagged larvae was not significant when compared in the Cox proportional hazards model ($p = 0.22$). The hazard of debriding at any time for both loose and bagged larvae was approximately twice that for hydrogel (hazard ratio for loose larvae relative to hydrogel was 2.56 (95% CI 1.76 to 3.71) and 2.06 (95% CI 1.39 to 3.03) for bagged larvae relative to hydrogel).

There was no statistically significant difference between the larvae and hydrogel with respect to scores on the Physical Component Summary ($p = 0.81$) and Mental Component Summary ($p = 0.97$) scores of the Short Form-12 health-related quality of life assessment. There was no evidence of a difference between larvae and hydrogel in terms of bacterial load over time ($p = 0.75$). When swab data were analysed up to the point of debridement only, there was also no evidence of a difference between the larvae and hydrogel groups ($p = 0.86$). Only 6.7% of participants had MRSA detected, using molecular

techniques, in their ulcers at baseline. There was no statistically significant difference between the larval and hydrogel therapy groups in the proportions of people who experienced eradication of MRSA by the end of the debridement treatment phase ($p = 0.34$) although this analysis has low statistical power because of the small numbers. People treated with larval therapy reported significantly more pain ($p < 0.001$) in the previous 24 hours when asked at the removal of the first debridement treatment compared with patients in the hydrogel arm; mean pain scores for both loose and bagged larvae were approximately twice those of the hydrogel participants.

Our base-case economic evaluation suggested a large decision uncertainty associated with the cost-effectiveness of larval therapy when compared with hydrogel with a 50% probability of larval therapy being cost-effective. The nature of the uncertainty associated with our estimates of difference in costs and health benefit suggests that larval therapy and hydrogel are likely to have similar costs and effects in the treatment of sloughy leg ulcers.

Conclusions

Larval therapy significantly reduced the time to debridement of sloughy and/or necrotic chronic venous and mixed venous/arterial leg ulcers compared with hydrogel. However, larval therapy did not increase the rate of healing of the ulcers and was associated with significantly more ulcer pain. It was impossible on the basis of this evidence to distinguish between larval therapy and hydrogel in terms of cost-effectiveness.

Implications for health care

There is no evidence from this trial that larval therapy should be used routinely on sloughy or necrotic leg ulcers with the aim of speeding healing or reducing bacterial load.

If debridement *per se* is a treatment goal, e.g. before skin grafting or other surgery, then larval

therapy should be considered; however, it is associated with significantly more pain than hydrogel.

Recommendations for future research

In the context of sloughy or necrotic venous and mixed aetiology leg ulcers, The Venous Ulcer Study II (VenUS II) did not find that use of an active debridement treatment resulted in more rapid wound healing. Further robust exploration of the relationship between debridement and healing is required, including in wounds of different aetiologies, to inform clinical wound-care practice, where debridement is commonly undertaken.

Relatively little is known about the outcomes that matter most to people with chronic wounds. Further research is required to explore the value of debridement to patients and clinicians.

There are several wound debridement methods available. When making debridement treatment choices, decision-makers are faced with a more complex decision than that represented by a single trial. To ensure the most cost-effective treatments are used, decision analytic modelling of all alternative debridement treatments should be undertaken. Modelling should aim to resolve decision uncertainty where debridement is the treatment goal and where treatments aim to promote ulcer healing.

Trial registration

This trial is registered as ISRCTN55114812.

Publication

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NIHR Health Technology Assessment programme

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The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

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