What is the effect of larval therapy on the debridement of venous leg ulcers? A systematic review

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Abstract

Aim: To determine the impact of larval therapy on the debridement of venous leg ulcers, in comparison to other debridement methods or no debridement.

Method: Using systematic review methodology, published quantitative studies focusing on the effect of larval therapy on the debridement of venous leg ulcers were included. The search was conducted in January 2020 and updated in May 2021 using CINAHL, PubMed, Embase, and the Cochrane library, and returned 357 records, of which six studies met the inclusion criteria. Data were extracted using a predesigned extraction tool and all studies were quality appraised using the RevMan risk of bias assessment tool.

Results: Larval therapy was found to debride at a faster rate than hydrogel ($p= 0.011$, $p<0.001$, $p= 0.0039$), have a similar effect to sharp debridement ($p=0.12$, $p=0.62$), and was a resource-effective method of debridement ($p<0.05$, $p<0.001$, $p<0.001$). When larval therapy in combination with compression therapy was compared to compression alone, larvae had a greater effect on debridement ($p<0.05$), however, it did not improve overall wound healing rates ($p=0.54$, $p=0.664$, $p=0.02$). Pain levels increased during larval therapy and reduced after treatment, when compared to other standard debridement techniques.

Conclusion: Larval therapy promotes rapid debridement of venous leg ulcers. However, further high quality randomised controlled trials, comparing larval therapy to other debridement methods for venous leg ulcers, incorporating the use of compression is required to determine the long term effects of larval therapy.

Keywords: debridement, larva, larval therapy, venous leg ulcers

1 Introduction

Venous leg ulcers (VLUs) are the most common type of lower limb ulceration (1). They are identified as a defect to the dermis of the lower limb, most commonly located between the knee and ankle joint (2). VLUs can be singular or multiple and vary in size (3). This is a chronic condition which often results in a prolonged period of wound healing and is synonymous with recurrence (4).

The prevalence of VLUs is high, affecting approximately 1% of the population in western countries (5). This significantly impacts healthcare resources, consuming approximately 23-50% of community nurses' time (6) . Currently there are no global studies representing the health-related burden of VLUs. However, the annual UK expenditure for VLU management is estimated at £5.3 billion (7), which may well reflect the situation among other countries. VLUs dramatically impact the lives of patients due to issues including frequent nurse visits, pain, odour and in some cases social isolation (8). It is widely accepted that compression therapy is the most effective treatment method for VLUs (9). However, VLUs remain difficult to heal, therefore it is necessary for clinicians to explore additional treatment options.

Debridement is the process of removing devitalised tissue from a wound (10). There are various debridement options available, including; mechanical, surgical, autolytic, enzymatic, and biological (11). Many factors impact the choice of debridement including; patient characteristics and preferences, resources available, and the skill of the practitioner (12). Biological debridement is also known as maggot debridement therapy (MDT) or larval therapy. This involves the use of live medical-grade larvae that have the ability to debride, promote cellular activity, and act as an anti-microbial agent (13). The most common form of larvae used is ‘Lucilia sericata’, used due to its ability to feed exclusively on non-viable tissues (14). Larval therapy can be applied in two forms; loose larvae, placed directly onto the wound or bagged larvae, contained in a pouch placed on the wound bed (15). Bagged larvae have been utilised effectively alongside compression therapy. Larvae debride by loosening non-viable tissue with their mandibles and secreting strong proteolytic enzymes, this liquefies devitalised tissue into a ‘soup’ which the maggots can easily ingest (16).

The condition of the wound bed must be considered in order to identify any potential barriers to healing (17, 18). One of these potential barriers is the presence of non-viable tissue (12), including necrotic or sloughy tissue (19). The presence of this type of tissue can lead to infection, or a prolonged inflammatory stage of wound healing, further, it can mechanically obstruct wound contraction and impede re-epithelialization (20).

Larval therapy, as a choice of debridement method, boasts many advantages. Firstly, it is a natural form of debridement that does not harm any healthy tissue (21). Conventional forms of debridement, such as surgical debridement can cause greater trauma by harming healthy tissue while debriding non-viable tissue (16). Larval therapy is a cost-effective form of debridement which is easy to apply (22). Larvae also have antimicrobial properties and have been found to be effective against resistant bacterial strains (23). The use of larvae in the treatment of chronic wounds has been found to promote wound healing and significantly reduce costs in wound care (24). Currently there is no systematic review (SR) exploring the effect that larvae have on debridement specifically for VLUs. At present, larvae are often regarded as a final resort in the management of VLUs or are not considered at all (25), therefore this SR aims to address an important gap in the evidence relating to the management of VLUs.

2 Methods

2.1 Objectives

The objective of this SR was to determine the effect that larval therapy has on wound debridement of VLUs.

2.2 Primary and Secondary Outcomes

The primary outcome of this review is the measurement of the effect that larval therapy has on the debridement of VLUs. This will involve assessing how quickly larval therapy can debride VLUs and how efficient they are at removing non-viable tissue. The secondary outcome measures are wound healing, pain, and resource impact.

2.3 Inclusion Criteria

The papers included for review were determined by the inclusion and exclusion criteria.

2.3.1 Types of Studies

All types of studies were considered for inclusion in this SR. There was no limitation on language or year of publication.

2.3.2 Types of participants

All included papers were required to focus on participants with VLUs. Studies including both venous leg ulcers or mixed-venous arterial leg ulcers, where both aetiologies were undergoing the same managaement were also included. Studies focusing on all other aetiologies of ulcers were excluded.

2.3.3 Types of larval interventions

Studies were required to explore larvae as a debridement method. Thus, all studies that did not measure the effects that larvae have on debridement specifically were excluded. Studies utilising both loose and bagged larvae were included. There was no limitation applied to studies including compression therapy alongside larval application. The length of larval application is usually determined by the success of treatment therefore there was no limitation to the length of larval application.

2.3.2 Types of Outcome Measures

All studies were required to determine the primary outcome which was the effect of larval debridement. This could be determined by the rate of debridement or measured by the reduction of non-viable tissue from the wound bed. Secondary outcomes were the rate of wound healing, pain caused by larval therapy and post-larval debridement and the impact that larvae has on resources.

2.4 Search Strategy

An extensive search of the literature was undertaken in January 2020 and updated in May 2021 to identify all relevant available studies for consideration in the review. The keywords derived from the research question were searched (see table I), utilising indexing terms or subject headings, alongside Boolean operators and truncation, to further ensure the sensitivity of the search (26). These terms were searched across four databases; CINAHL, PubMed, Embase, and the Cochrane Library (see figure 1). Additionally, hand searching was employed, this involved screening the reference lists of included studies to identify any further studies.

-Insert Table I here-

2.5 Data Collection and Extraction

Data collection involved two stages; the first stage involved screening the title and abstracts for their relevance. The relevant studies were then brought forward to the second stage of screening where the full text was examined to determine the final articles for inclusion. This was determined by two reviewers independently (EG, DP). Consensus between the two reviewers in relation to the studies and the data to be included was obtained through a discussion when discrepancies were identified. PRISMA was adopted as a framework for reporting the systematic review, a PRISMA flow chart provides a visual display of literature flow, and the final corpus of citations included (27). All relevant data from the included studies was inserted into a data extraction table. The data extraction table was devised by the reviewers using predefined headings as seen in table III.

2.6 Quality assessment

The quality appraisal determines the strength of the selected studies, in terms of accuracy, relevance, and reliability (28). The quality of each of the selected studies was appraised using the RevMan software (version 5.3) risk of bias tool. This tool was used to appraise the evidence under six domains of bias as follows; selection, performance, detection, attrition, reporting, and other bias (29).

2.7 Data Analysis

The data derived from the review could not be meta-analysed due to the heterogeneity of the included studies. This was due to the varying methods across the studies used to measure the success of larval debridement. For this reason, a narrative analysis was adopted to combine and summarize the results of the six included studies. The results were aggregated thematically using narration, summary tables, and charts to present the results of the review.

3 Results

3.1 Search Process

The literature search resulted in 357 potentially relevant studies with two other studies retrieved through hand searching of reference lists. When duplicates were removed using the Endnote referencing manager, 251 articles remained. The title and abstract of these studies were screened, resulting in the removal of 239 articles as not meeting the inclusion criteria. The full text of these 12 studies was read and six studies met the inclusion criteria (figure 1).

-Insert Figure 1-

3.2 Excluded articles

The excluded studies and reasons for exclusion can be seen in table II. In summary, six studies were excluded, debridement was not measured in two studies (30, 31). One study included just those with arterial disease (32) and one did not outline the aetiology of those within the study (33). One study provided no results (34) and the final study reported on a separate outcome of a study already included in this review (35).

-Insert Table II here-

3.3 Study Characteristics

3.3.1 Participants and Settings

The mean sample size was 88 (total 531 participants), with the largest study including 267 participants (36) and the smallest including 12 participants (37). The studies were predominately conducted in the UK; three in England (36-38) and one in Wales (39). The remaining two studies were undertaken in France (40) and Mexico (41). Two studies were conducted in the community (38, 41). One study recruited solely inpatients (40). The remaining studies included participants in both the community and hospital settings (36-39). Details of the participant characteristics can be seen in table III.

3.3.2 Study Designs

All of the included studies were randomized controlled trials (RCTs).

3.3.3 Interventions and Follow-up

Each of the studies examined larvae as a debridement method, but, the method of application of larvae varied between the studies. Three studies explored the use of larvae in the form of bagged larvae (38-40). Two used free-range larvae in their studies (37, 41). The remaining study explored the effect of both bagged and loose larvae (36). Another element that varied between studies was incorporating compression into the trial. Two of the studies applied compression therapy to all participants (38, 39). Three studies did not use compression therapy during the trial period (37, 40, 41). In one study, some of the participants received compression in the control group but no participants received compression whilst receiving larval therapy (36). The comparison group also varied amongst the studies. Three studies compared larvae to a standard method of encouraging autolytic debridement; hydrogel (36, 37, 39), whereas two studies compared larvae to surgical debridement (40, 41). One study did not use a debridement method in the control group (38).

The method of measurement for the effectiveness of debridement varied between each of the studies. Two of the studies measuring larvae by giving a percentage of slough reduction (38, 40). One study measured the time to debridement (36). Another study measured the increase in granulation tissue (41). Finally two studies measured whether debridement was fully successful or not at the end of the trial (37, 39).

The time to follow-up varied in each group, therefore it was reported upon as described by the study authors. One trial assessed the percentage of the slough at day four, wound healing rates were assessed bi-weekly for up to a maximum of 12 weeks (38). Another trial assessed all outcomes at day 21, participants were reassessed 7-14 days after their last study visit to determine if slough had reoccurred (39). One study followed up participants after a period of 1 month (37). Participants studied in another trial were evaluated weekly for four weeks (41). The next study assessed wound debridement until successful debridement was achieved, the maximum length of follow up in this trial was 12 months (36). The final trial reassessed the wounds at days 8, 15, and 30 (40). Notably, with the exception of two trials (39, 40), the researchers did not reassess the wound bed after the trial has been completed to determine the long term effects of larval debridement.

3.5 Primary Outcome: Debridement

3.5.1 Comparison 1: Larvae compared to Hydrogel

Three studies compared larvae to hydrogel, (36, 37, 39). The first study considered successful debridement to be a *"clean wound bed that no longer required a debridement agent"*(39). At the end of the 21 day trial period 67.4% (n=46) of ulcers in the larvae group were successfully debrided, whereas 26% (n=42) of the ulcers in the hydrogel group had achieved total debridement (p=0.001). However, when the ulcers were reassessed 7-14 days after completion of the study only nine (29%) of the 31 ulcers that achieved successful debridement during the trial period remained debrided. This compared to seven (73%) of the

11 successfully debrided ulcers in the hydrogel group remaining debrided, this was statistically significantly different (p=0.011).

The next RCT conducted defined debridement as "*a cosmetically clean wound"*(36). In the loose larvae group, the median time to debridement was 14 days (95% CI 10 -17), in the bagged larvae group the median time to achieve debridement was 28 days (95% CI 13 - 55) and in the hydrogel group median debridement time was 72 days (95% CI 56 -131). The risk ratio for debridement 2.31 (95% CI 1.65 - 3.24, p<0.001), in favour of the larvae group.

The third study deemed successful debridement to be when less than 5% of the ulcer surface area covered in slough (37). All six participants in the larvae group were successfully debrided at the end of the one month trial, whereas two participants in the hydrogel group were deemed to be successfully debrided. The authors conclude that debridement was statistically better in the larvae group (p=0.0039).

3.5.2 Comparison 2: Larvae compared to sharp debridement

Two studies compared larvae to sharp debridement (40, 41). The first measured debridement as being the increase of healthy granulation tissue (41). The larvae group had a median granulation percentage of 90% (n=10) and in the control group this was 60% (n=9) at the end of the four-week trial (p=0.12).

The second study measured slough percentage using digital software prior to the commencement of the trial and after 2 weeks of treatment (40). The mean slough reduction from day 1 to day 15 was 24.3% (n=51) in the larvae group and 24.9% (n=54) in the control group (*p*=0.78). The participants were then followed up 15 days after the trial was completed.

The number of participants fully debrided remained the same in the larvae group, but there was a mean increase of 6.2% slough in the control group (*p*=0.62).

3.5.3 Comparison 3: Larvae combined with compression compared to compression alone

One study compared larvae alongside compression therapy to a control group of compression therapy alone (38). The control group did not receive a debridement method. On day four, the larvae group showed a median slough reduction of 4.2 cm^2, which was an 84% median reduction of the slough. The median slough reduction in the standard treatment group was 3.7 cm^2, a 50% median slough reduction. The findings were statistically significant, favouring larvae alongside compression therapy ($p < 0.05$).

3.6 Secondary Outcomes

3.6.1 Wound Healing

Four studies explored the effect of larvae on wound healing of VLUs (36, 38, 40, 41). The first study assessed the participants until the wound was healed, up to a maximum of one year (36). Ulcer healing was defined as *'complete epithelial cover in the absence of a scab'*. The median time to healing for the larvae groups was 236 days (95% CI 147 to 292) and for the hydrogel group was 245 days (166 to upper limit not estimable). The risk ratio of healing was 1.13 (95% confidence interval 0.76 to 1.68 *p*=0.54), indicating no difference in healing between the study groups.

The second study measured wound dimensions on day one and again at the end of four weeks of treatment (41). The median reduction in wound dimensions in the larvae group was

8.31cm², and 8.82cm² in the sharp debridement group, indicating no difference in the rate of wound healing between the two groups.

The third study compared wound dimensions from day zero to day 10 (38). The median wound size reduction in the larvae group and compression therapy was 1.5cm² and in the control group this was 3.2cm² (p=0.664), indicating no difference in wound healing between the study groups.

The fourth study also compared wound dimensions at the beginning and end of the trial period (40). At day 15 where the mean wound surface area increased by 14.6% in the larvae group and decreased by 8.2% in the control group (p=0.02). At day 30 there was a mean 5.3% increase in the wound surface area in the larvae group and a 12.9% decrease in the control group (p=0.32).

3.6.2 Pain

Three studies explored the impact of larvae on pain (36, 39, 40). One study assessed pain using a visual analog scale (VAS)(39). This scale ranged from 0 (no pain) to 100 (worst pain). The mean baseline VAS score was 36.11 (SD=28.13) in the larvae group which reduced to 19.26 (SD 21.48) after treatment. In the control group the mean VAS score at baseline was 30.17 (SD=26.44), which reduced to 21.80 (SD= 27.98) after treatment. Notably, nine participants withdrew from the study due to pain or discomfort, one of these participants were in the hydrogel group and eight in the larvae group. The authors (43) conclude that the larvae group experienced increased pain during treatment and less pain after treatment when compared to the hydrogel.

A further study also assessed pain using a VAS score, however, this scale ranged from 0 (no pain) to 10 (worst pain) (40). Participants who received larvae had an overall mean VAS score of 2.3 (SD=2.6), while participants in the hydrogel group had an overall mean VAS score of 2.7 (SD=2.6) (p=0.8).

The third study assessed pain during the 24 hour period before the first removal of the debridement treatment, using a VAS score (0-100)(36). The loose larvae group had a mean VAS score which was 46.74 higher than the hydrogel group ($p<0.001$) and the bagged larvae group had a mean VAS score which was 38.58 higher than the hydrogel group ($p<0.001$).

Overall, the studies here show that there is evidence of higher pain levels during larval application with a reduction in pain after the completion of treatment.

3.6.3 Resource Impact

Three studies reported on the healthcare resource impact of larval therapy, such as time, money, and dressings (37, 39, 40). One study measured the cost of treatment for both larvae and hydrogel as a primary outcome, and explored the impact that larval therapy had on nursing time(37). The median cost of treatment in the larvae group was £78.64 and £136.23 for the control group over a period of one month ($p<0.05$). Nursing time was measured as the median number of visits required over the trial period. The control group required a median of 19 visits, versus three visits in the larvae group ($p<0.05$) over the one month trial period.

A further study also examined the impact of larval therapy on resources, focusing on the resource of nursing time (39). The subjects in the larvae group required a mean number of

2.83 dressing changes (SD=1.102), whereas the control group required a mean number of 5.40 (1.795) dressing changes ($p < 0.001$).

The final study explored the impact of larval therapy on nursing time by measuring time per visit (40). The mean time of care required at each visit was 10.1 minutes (SD=9.7) for the larvae group and 40.1 minutes (SD=8.8) for the control group ($p<0.001$).

3.7 Risk of bias

The RevMan (42) risk of bias tool was used to assess the included studies (see figure 3). In two of the included studies, random sequence generation and allocation concealment are unclear (39, 41) as the authors did not provide details on how participants were allocated to each group. All of the included studies demonstrated a high risk of performance bias as nurses and participants were not blinded during the trials, with one exception (40), where participants were unaware of the group they were allocated to, as they were blinded during dressing changes. One study was judged at a high risk of detection bias because the results of debridement were determined by the nurse's opinion (37). Attrition bias refers to the number of participants that fell out of the studies. All studies reported results on all included participants, therefore attrition bias was reported as low. Reporting bias was also low as all pre-specified outcomes were reported in the studies. Evidence of other bias detected involved the low number of participants in two studies (37, 40), this may have affected the external validity of these studies.

- *Please Insert Figure 2,3 here-*

4 Discussion

4.1 Summary of the Evidence

The results of this review show that larval therapy is an effective method of debridement for VLUs. Although extensive research has been carried out on larval debridement, no single systematic review exists specifically related to the effect of larval debridement for venous leg ulcers. However, some parallels can be drawn with previous reviews conducted to explore the effect of larvae on the debridement of other wound aetiologies, such as diabetic foot ulcers, pressure ulcers, and burn wounds (14, 43). Research suggests that larval therapy promotes faster debridement than hydrogel for VLUs. This also reflects the results of a previous review which found that larvae were a significantly more effective debridement agent than hydrogel (44). The evidence suggests that there are savings in cost and nursing time when choosing larvae over hydrogel (37, 39). Thus, there may be of greater value in considering larvae therapy than simply debridement alone. Although, one study suggests that the long term effects of larval therapy are not as effective as a hydrogel (39). There is limited research investigating the lasting effects of larval debridement for VLUs. Further research is required in this area to understand the lasting effects of larval debridement.

The results indicate that larvae and sharp debridement have a similar effect on the debridement of VLUs. Sharp debridement is a quicker form of debridement therapy which boasts instant results. However, larvae may be more appropriate in cases where sharp debridement is unsuitable due to a high risk of bleeding, proximity to other bodily structures, or a patient's comorbidities (16, 41). Additionally, sharp debridement is more time consuming than larvae (40), therefore the use of larvae may be more appropriate when nurses are under time pressure or where they are not competent in the skill of sharp debridement.

There have been a number of previous reviews exploring the effect of larvae on various chronic wounds which found that larvae can improve wound healing rates (43, 45, 46).

However, the results of this review indicate that larvae do not have a significant impact on improving the rate of wound healing for VLUs when compared to standard treatment methods (36, 38, 40, 41). It is important however, to note that the majority of trials omitted compression therapy alongside larvae, with the exception of one study (38). This is despite the fact that it has been shown that larvae survive under compression bandages (38). Given the fact that compression therapy is the gold standard in healing VLUs (47, 48), future research is required to explore the effect of larvae on the healing rate of VLUs alongside compression therapy to determine its true effect.

A secondary outcome of this review was to explore the effect that larvae have on pain. Maggots can induce or intensify pain in ulcers or surrounding tissue, especially for patients with superficial wounds, or those who are in pain prior to initiation of larval therapy (49). However, there is a common misconception that larval therapy is a painful experience due to a sensation of biting, however, they do not have teeth and work to debride tissue by secreting enzymes to dissolve the nonviable tissue (50). One of the trials in this review found that the participants in the larval therapy group were in more pain during the treatment phase of larvae than the treatment phase of the hydrogel (36). However, the use of larvae resulted in a greater reduction in pain after treatment when compared to pain levels after hydrogel debridement was completed (39, 40). Therefore, a patient may experience more pain during the treatment phase of larvae, however, the long term effects show decreased levels of pain.

Larvae are still seen as a final resort for treating VLUs when conventional treatments have failed (14). The difficulty researchers had in recruiting participants displays the general resistance that patients and practitioners have towards larval debridement (38-40). However, with the evidence emerging from this review and that of recent studies, alongside an increased public and medical awareness (43), the use of larvae as a debridement method in the treatment of VLUs should be considered more frequently and promptly.

The quality of evidence was assessed according to six domains of bias for all studies: random sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other biases. All included studies displayed a risk of bias in one or more domains. Therefore one must consider the impact that bias has on a study when interpreting the effect of an intervention. Selection bias was unclear in two studies (39, 41) and trial results may be impacted by systematic differences between participants who are chosen or excluded in a study, or systematic differences in those allocated to the experimental or control groups (51). As the participants and nurses providing the treatments were not blinded, it is possible that the effect of the intervention was overestimated (52). However, it is not possible for a nurse to provide this treatment without being aware of which group they are caring for. An example could be taken from the 'single-blinded' study where participants are blinded during dressing changes and were unaware of which treatment group they were allocated to (40). In one of the trials, the nurse determined the effect of the intervention using her own judgment and was aware of which intervention each group received (37). This provided a margin for detection bias as preconceived ideas may impact the nurse's perception of the effect of the intervention. Attrition bias was low in all of the studies. Although some participants dropped out amongst the studies, for example in one study eight participants who received larval therapy withdrew due to pain (39), these participants were all accounted for in the final assessment. As seen in the risk of bias summary, one of the six studies is at a high risk of bias (37). Due to the low number of studies available for this review it was included, however, its findings should be interpreted with caution.

4.2 Limitations

A limitation of this review was the high heterogeneity amongst the included studies. Although all of these studies were RCTs, the method in which larvae were delivered varied in terms of application and treatment time. Additionally, the measure of larval effectiveness varied across the studies. For this reason, a meta-analysis could not be completed. Another limitation of this review was the number of studies focusing specifically on the effect of larvae on the debridement of VLUs. Only six studies have been identified and some of the studies had a small number of participants. These factors limit the strength of the results. Even though it is not possible to blind assessors and patients, there is a need for more RCTs with a larger number of participants considering power calculation, and definitively outlining inclusion and exclusion criteria, following a strict regime of larval application alongside compression therapy in order to establish the outcome of larvae on the debridement of VLUs in order to develop an informative meta-analysis.

5 Conclusion

Due to the hetrogentity of the studies a meta-analysis could not be conducted, therefore, the evidence for larval therapy on the debridement of VLU remains unclear. However, from this narrative review it was identified that larval therapy promotes rapid debridement of non-viable tissue in VLUs and it was seen to be a resource-effective debridement method. The evidence emerging from this review does not indicate that larvae have the ability to improve the rate of wound healing. Further, pain levels may marginally increase during the treatment phase, however they were shown to reduce from baseline after treatment was completed. There are some elements of bias that impact the believability of the evidence, thus, further larger scale research, incorporating the use of compression therapy is required, with a particular focus on the long term effects of larval therapy.

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Table I: Keywords and Expansion Terms

Keywords	Expansion
Larvae	'Larvae' OR 'Larval' OR 'Biosurgery' OR 'Biodebridement' OR 'maggot*' OR 'MDT' OR 'wound myiasis' OR 'Lucilia sericata'
Venous Leg Ulcer	'Venous leg ulcer*' OR 'Venous ulcer*' OR 'VLU*' OR 'leg ulcer*' OR 'stasis ulcer*' OR 'varicose ulcer*' OR 'stasis dermatitis'
Debridement	'Debridement'

Table II: Excluded Studies

Author & Year	Reason for Exclusion
McInnes et al. (2013)(30)	Debridement not measured
Evans (2002)(31)	Debridement not measured.
Campbell and Campbell (2014)(32)	Leg ulcer aetiology only arterial.
Munro et al. (2017)(34)	No results available.
Soares et al. (2009) (35)	This RCT was carried out alongside the study by Dumville et al. (2009) to focus on the cost of treatment. No new or additional data provided on wound debridement results.
Wootton (2013)(33)	Aetiology of leg ulcer not specified. No specific results on reduction in slough.

Table III: Data Extraction Table

Author & Year	**Type of Study**	**Location**	**Setting**	**Population**	**Larvae Group**	**Control Group**	**Debridement Measurement**	**Debridement Results**	**Secondary Outcomes**	**Validity**
Contreras-Ruiz et al. (2016) (41)	RCT	Mexico	Community	19 Patients with sloughy VLUS	10 Participants Loose larvae, hydrocolloid dressing, gauze and adhesive tape for 48 hour period, followed by 'non-stick dressing' and compression bandage for 5 days. This cycle was repeated 5 times for each patient.	9 Participants Sharp Debridement and Silver Dressing for 48 hour period, followed by 'non-stick dressing' and compression bandage for 5 days. This cycle was repeated 5 times for each patient.	Median increase of Percentage of granulation tissue in wound over 4 week trial period	Larvae: median area of granulation increased from 25% to 90%. Control group-median area of granulation increased from 30% to 60%.	Wound healing Median reduction in wound dimensions after 4 weeks Larvae: 8.31 cm² Control: 8.82 cm²	Primarily low/ unclear risk
Davies et al. (2015) (38)	RCT	Cheltenham, England	Community Leg ulcer Service	40 Participants with VLUs that have >20% of their surface area covered in slough. ABPI between 0.85 and 1.25	20 Participants-Bagged larvae and compression bandaging for 4 days. Larvae removed and continued in compression thereafter.	20 Participants -N-A Dressing and compression bandaging	Percentage area of slough reduction at day 4 assessed by digital planimetry measurements	Median Slough reduction at day 4: Larvae group:84% reduction Control group: 50% reduction	Wound Healing Median wound size reduction at day 4 Larvae group: 1.5 cm² Control Group:3.2 cm² 12 week healing rate Larvae Group: 68% Control Group: 73%	Primarily low risk

Mudge et al. (2014) (39)	RCT	Cardiff, Wales	Community, Inpatients &Outpatients	88 Participants with VLUs/ mixed aetiology leg ulcers- containing over 25% slough/necrosis. ABPI ≥ 0.5	46 Participants- Bagged Larvae plus compression therapy. Reviewed every 3-4 days until debridement was complete	42 Participants- Hydrogel plus compression therapy	Whether fully debrided within 21 days. Final review 7-14 days post last study visit to determine if resloughing had occurred.	At day 21: 67.4% of Patients treated with larvae fully debrided 26.2% of Patients treated with Hydrogel fully debrided	<u>Resource Impact</u> Mean number of dressing changes required over 21 days. Larvae group: 2.83 Control group: 5.40 <u>Pain</u> Measured as mean reduction in VAS score before and after treatment. Larvae group: 36.11 reduced to 19.26 Control group: 30.17 reduced to 21.80	Primarily low/ unclear risk
Opletalová et al. (2012) (40)	RCT	Caen and Lyon France	Two hospitals	105 Patients with sloughy VLUs of 40cm² or less ABPI ≥0.8	51 Participants Bagged larvae for 2 week period. No compression	54 Participants Sharp Debridement plus hydrogel, plus appropriate secondary dressing for 2 week period No compression	Mean Percentage of slough reduction at day 15	Mean slough percentage reduction Larvae group: 24.3% Control group: 24.9%	<u>Wound Healing</u> Mean wound size increase/decrease: Larvae: 5.3% increase day 30 Control:12.9% decrease day 30 <u>Resource Impact</u> Mean time per treatment Larvae: 10.1 Minutes Control: 40.1 Minutes <u>Pain</u> Mild in both Groups	Primarily low risk

Dumville et al. (2009) (36)	RCT	York, England	22 centres Community, Inpatients & Outpatients	267 Patients with at least one VLU/ mixed venous arterial ulcer with minimum 25% coverage of slough or necrotic tissue and ABPI ≥ 0.6	Loose larvae group: 94 participants, loose larvae and no compression Bagged larvae group: 86 participants, bagged larvae and no compression Both groups had larvae applied for 3-4 day periods, if further larvae required hydrogel and usual bandaging applied while more larvae were ordered. This cycle was continued until successful debridement	87 participants Hydrogel plus knitted viscose dressing plus compression	Time to debridement	Median time to debridement Loose larvae: 14 days Bagged larvae: 28 days Hydrogel: 72 days	Wound healing Median time to heal Combined larvae groups: 236 days Hydrogel group: 245 days	Primarily low risk
Wayman et al. (2000) (37)	RCT	Whitehaven, England	4 Participants in community leg ulcer service remaining 8 hospital inpatients.	12 Participants with sloughy venous leg ulcers	6 Participants loose Larvae for 72-hour periods until complete debridement	6 participants Hydrogel and Telfa Dressing changed every 72 hours	Whether Debridement was successful within one-month trial period	Larvae- 6/6 patients fully debrided Control- 2/6 patients fully debrided	Resource Impact Median Cost of treatment Larvae: £78.64 Control: £136.23	High risk

Figure 1: PRISMA Flow Diagram: Combined Search

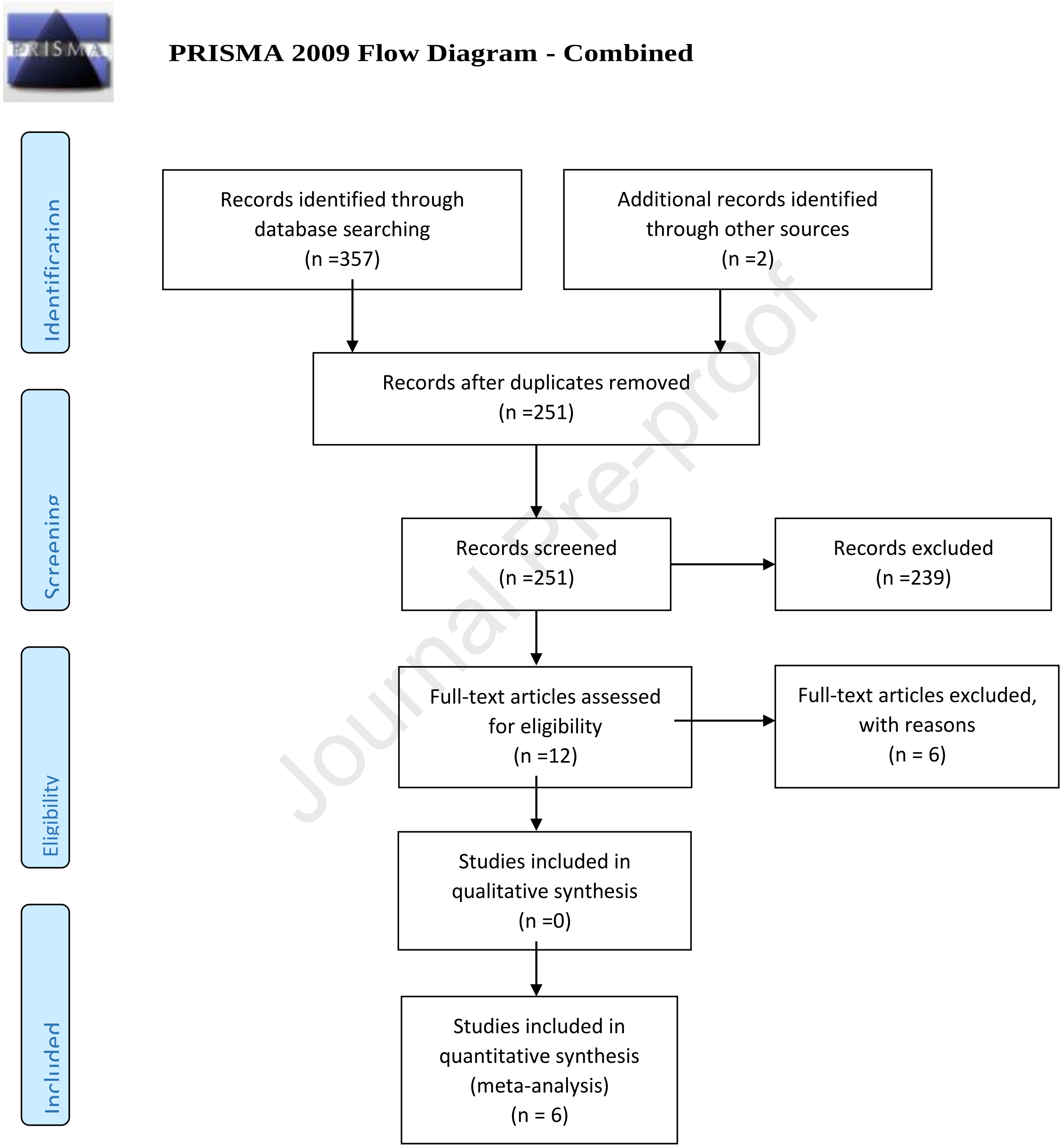


Figure 2: Risk of Bias Graph

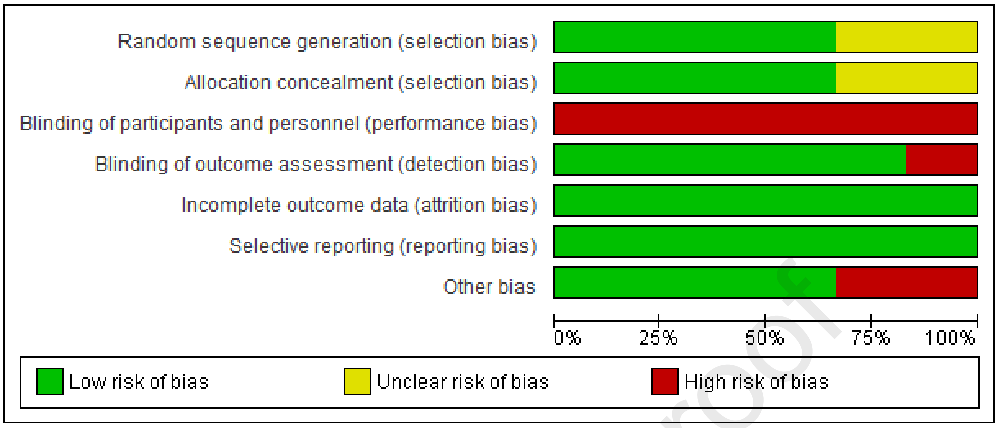
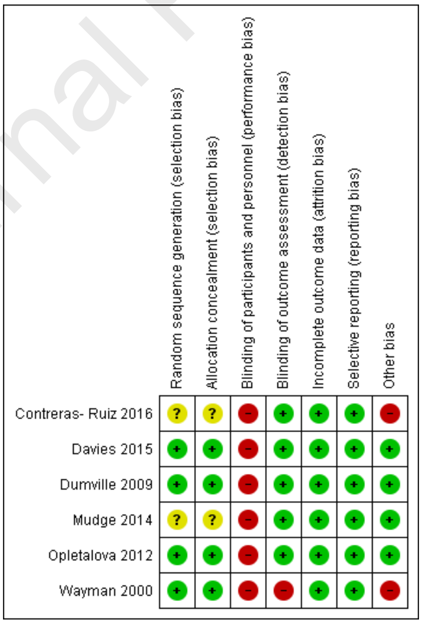


Figure 3: Risk of Bias Summary



Highlights

- Larval debridement was found to debride venous ulcers at a fast and effective rate.
- Further high quality RCTs, incorporating compression therapy are required to provide more conclusive evidence of venous leg ulcer debridement and its long term effects.

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