Developing Clinical Practice Guidelines for the Prevention and Management of Venous Leg Ulcers

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An inaugural Venous Leg Ulcer Consensus meeting was held in Perth, Western Australia, on 6 September 2005. It was attended by a large number of Australia’s wound care leaders who endorsed the need for, and support of, a proposal to develop Clinical Practice Guidelines for the Prevention and Management of Venous Leg Ulcers under the auspices of the Australian Wound Management Association (AWMA). The guidelines will not duplicate existing resources, but develop an innovative Australian framework for care. The key aim in developing the proposed guidelines is to improve health outcomes for the Australian community by preventing venous leg ulcers and their recurrence and provide an evidence-based framework for their management.

Since this meeting a Venous Leg Ulcer Guidelines Development Committee (VLUGDC) has been formed, with a multidisciplinary membership of wound care leaders from around Australia and New Zealand. In 2007, the committee applied to the National Health and Medical Research Council (NHMRC) to develop external guidelines and was successful in its application. The VLUGDC has commenced the process with the guidance of the NHMRC Guideline Assessment Register (GAR) Consultant. This article will highlight the rigorous process of developing the guidelines and include the Scoping Document 2009–2010 and the evidence appraisal progress to date.

Scoping document 2009–2010

1. Aim of the guidelines

The aim is to develop multidisciplinary, evidence-based guidelines for the diagnosis, prevention and management of venous leg ulcers in Australia.

2. Objectives of the guidelines

The guidelines will focus on patient-centred outcomes. The guidelines seek to assist primary healthcare professionals to:

- minimise incidence and prevalence of venous leg ulcers in Australia
- improve the knowledge of healthcare professionals and the public in relation to venous leg ulcers
- provide the best available evidence for prevention, assessment and management of venous leg ulcers
- facilitate benchmarking
- support future research and quality activities
- encourage healthcare providers to incorporate venous leg ulcer incidence and prevalence as a key indicator of healthcare quality
- prevent recurrence
- optimise self-management
- optimise health-related quality of life (QoL)
- address barriers to treatment implementation.

3. Background

Venous leg ulceration is a debilitating, chronic condition that affects people of all ages. The most common causes of lower extremity ulcers are venous insufficiency, arterial insufficiency, neuropathy (usually due to diabetes), prolonged pressure and ischemia. Venous insufficiency accounts for nearly 80% of all leg ulcers 1. The pathophysiology of venous ulceration is controversial 2; however, it is believed that ulcers result from venous occlusion or valvular incompetence and subsequent, superficial venous hypertension 3. Risk factors for development of venous ulcers include venous disease, obesity, immobility, phlebitis, family history of varicose veins, deep vein thrombosis, previous surgery for varicose veins and congestive cardiac failure 4. Up to 50% of patients with chronic venous insufficiency have a history of leg injury 1.

Currently venous leg ulcer management is a significant burden on the healthcare system. Venous leg ulcers are the most common clinical wound problem seen in general practice and community nurses spend some 50% of their time treating leg ulcers 5-7. Viewed in the context of an ageing Australian population, the management of venous ulcers will continue to cause considerable strain on the health
system into the future. Strategies to prevent and improve management options must, therefore, be seen as a national health priority.

Australian data indicates that 99.1% of patients with a venous leg ulcer are aged 60 years or over. Treatment costs average at $2300 per patient. In 1996 the private hospital cost for a mean stay of 23.9 days for management of chronic ulceration was estimated to be $8734. In the Silver Chain study conducted in 1996–97, the mean cost of treating a venous leg ulcer in the community was $2300. In 2000–01 a similar survey found the mean cost to heal any leg ulcer was $1436 when comprehensive assessment was implemented. This survey demonstrated that implementation of comprehensive assessment and management strategies has the potential to significantly reduce the cost of leg ulcer treatment to the healthcare system.

4. Need for guidelines – degree of urgency

The following points indicate there is a high degree of urgency for a guideline on management of venous leg ulcers:

- There is a high incidence of venous leg ulcers and recurrence within the Australian community.
- Many rural patients are disadvantaged due to inadequate access to vascular specialist services, diagnostic investigations and management options.
- Currently no national clinical guidelines exist for the Australian healthcare context, although guidelines have been developed in other regions including Scotland, New Zealand, Europe, Canada and the UK.
- There is a lack of awareness in the broader community regarding venous leg ulcers and their prevention.
- There is a need to address existing inequities in professional knowledge and implementation of best practice in the management of leg ulcers.
- Venous leg ulcer research is underfunded.
- An anticipated increase in venous leg ulcers amongst ageing Australians will result in a substantial increase in health costs.

Significance of the problem

Chronic leg ulcers affect 1% at any one time of the general population and 3.6% of people older than 65 years. Venous leg ulcers are difficult to heal and approximately 56% will recur within the first three months after healing. The impact of leg ulcers is felt both in physical suffering and reduced QoL of those affected and in financial costs to the community. Analysis performed more than 10 years ago in Australia estimated that venous ulcers were responsible for about $400 million annually in healthcare costs. The projected cost of management of venous ulcers is significant. Currently one in eight Australians are aged over 65 years. By 2044 those aged over 65 years will account for one in four of the Australian population. Over the next 20 years the ageing population will lead to a tripling of demand for government-funded care provision for those aged over 80 years.

Consistency with Australian health priority

The Council of Australian Governments (COAG) recognises the desire of Australians to maintain and, where possible, improve the quality of their lives as they age. There is significant growth in the population of adults aged over 65 years and this is projected to increase almost threefold over the next four decades. COAG recognises the implications of an ageing Australia, including demands on infrastructure and community support; the impact of ageing in regional areas; and the availability of accessible, appropriate health and aged care services. The significance of venous leg ulcers has already been discussed in relation to the ageing person. Explicit costs include hospital admissions, domiciliary nursing services, medical consumables, pathology and radiology investigations, general practitioner (GP) and specialist consultations, pharmaceutical costs, and additional adjunct therapies. The financial cost to both the patient and the community is enormous. However, the implicit costs to patients and their families are difficult to measure. Access to appropriate services for diagnosis and management of venous leg ulcers for all Australians will significantly improve health outcomes and QoL.

Variations in practice to be addressed

The AWMA aims to increase awareness of leg ulcers within the community. A priority is to minimise incidence and prevalence of venous leg ulcers via the dissemination of best available evidence and to simplify clinical decision-making processes for healthcare professionals.

Clinical practice variations

In most instances, diagnosis of venous ulceration can be made using clinical criteria alone. Approximately 25% of patients will have mixed venous and arterial disease and diagnosis will require more specific diagnostic investigations. The gold standard for diagnosing venous disease is colour duplex ultrasonography. However, hand-held Doppler ultrasound is used more commonly to record an ankle-brachial pressure index and this facilitates assessment of arterial disease and possibly superficial venous reflux.

Once confirmed, the treatment for venous leg ulcers is sustained, graduated high compression therapy using either bandages or surgical stockings. Healing can also
be expedited through activities such as elevation of the affected limb, improvement in mobility, weight reduction, and improved nutritional status. Compression bandages and surgical stockings vary in composition and evidence for use. A recent meta-analysis of bandaging systems found that multi-layer compression bandages delivered as three or four layers appeared to be superior to single-layer bandages in promoting ulcer healing. However, it was noted that many of the studies had small sample sizes and the quality of research in the area was poor. To prevent capillary exudation in legs affected by venous disease, an external pressure of 35 to 40 mmHg at the ankle is recommended. If applied correctly, three- and four-layer bandage systems should provide sustained pressure of 40 to 45 mmHg at the ankle, graduating to 17 mmHg below the knee. The proposed guideline would correlate and present the best available evidence for compression therapy in the treatment of venous ulceration.

Barriers to compression bandaging systems implementation

The use of compression bandaging has been demonstrated to improve wound healing and reduce costs compared to conventional treatment. Despite best available evidence, which indicates that compression-bandaging systems improve wound healing more than dressing alone and non-compressive bandages, uptake by GPs is inconsistent. Barriers to the use of compression bandaging systems by GPs include lack of confidence regarding management of ulcers and lack of awareness that compression is an effective treatment. For those patients who do receive compression bandaging, major determinants of successful wound healing include the extent to which the patient complies with the compression bandaging regime and the skill in which the bandaging is applied. There is a perceived lack of skill in bandage technique amongst health professionals. Lack of concordance with the use of compression bandages is also reported to be a major problem amongst some patients.

5. Care providers for whom the guidelines are intended

The guidelines are intended for use in primary care settings by healthcare professionals including GPs, allied health professionals, nurses, pharmacists, and community-based health workers. The guidelines could also be used as an informative source for consumers.

6. Consumers for whom the guidelines are intended

Guidelines are intended to refer to people of all ages. The guidelines are intended for use in primary care settings in metropolitan, regional, rural and remote areas of Australia. The guidelines will seek to address issues specific to special populations including:

- people living in rural and remote areas
- people from an Aboriginal and Torres Strait Islander background
- people from culturally and linguistically diverse backgrounds.

7. Consumers and interventions NOT covered by the guidelines

The guidelines will seek to cover all consumers. The guidelines will not include surgical interventions for managing venous leg ulcers.

8. Evidence to be evaluated

An extensive review of the literature will be attended and evidence that will assist in answering the following questions will be evaluated.

Aetiology

What factors are associated with the development of venous insufficiency/venous ulceration?

Prevention

What are the most effective interventions to prevent the occurrence and/or reoccurrence of venous leg ulcers?

Diagnosis, assessment and referral

1. What is the most reliable and valid diagnostic criteria?
2. What is the most reliable and valid method of assessing patients for venous insufficiency/venous ulceration?
3. When should a person be referred to a specialist?

Management

1. What are the most effective pharmacological and non-pharmacological interventions to manage venous insufficiency/venous ulceration?
2. What are effective pharmacological and non-pharmacological interventions to manage pain associated with venous leg ulcers?
3. What strategies are most effective for promoting compliance with treatment in patients with venous insufficiency/venous ulceration?

9. Process – criteria for considering studies for the review

Types of studies

Studies that provide Level I or Level II evidence on the NHMRC Levels of evidence scale will be considered for inclusion. For intervention studies, RCTs (or systematic reviews – SRs – of RCTs) that compare a single or combination intervention to placebo, sham-intervention, no treatment
or another active intervention will be included. If there is a sparsity of Level I or Level II evidence, the review will be expanded to consider lower levels of evidence including, but not limited to, cohort trials, case-control studies, consensus-based guidelines and expert opinion. For questions related to aetiology, diagnosis and assessment of leg ulcers, it is anticipated that there will be limited level I or II evidence available. All forms of evidence, including case reports, expert opinion and consensus guidelines will be included.

**Types of participants**

The review will include research conducted in participants with venous leg ulcers and participants at risk of developing venous leg ulcers.

**Types of evidence**

Evidence will be defined as falling within, but not limited to, the following categories:

**Aetiological factors**: arterial, venous, lymphatic, socio-economic, gender, lifestyle, comorbidities.

**Interventions**: compression therapy, nutrition, education, health professional training and competency, exercise, elevation, pharmacological management, complementary and/or alternative treatments, environmental barriers, wound management products, specialised leg ulcer clinics, hyperbaric oxygen, foot pump, leg clubs.

**Assessment**: Doppler studies – measurements of ankle brachial pressure index, palpation of lower limb pulses, assessment tools, health professional training and competency, specialised leg ulcer clinics.

**Types of outcomes to be measured**

Outcome measures of interest will include:

- Assessing wound response to the intervention such as time to complete wound healing, changes in ulcer size, proportion of ulcers healed in trial period, prevention of recurrence (e.g. number of new ulcers developed in trial period).
- Other outcomes related to the intervention such as QoL and global assessments, functional outcomes, venous ulcer specific QoL (e.g. Cardiff Wound Impact Schedule), pain, compliance with therapy.
- Adverse events.

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### Table 1. NHMRC levels of evidence for intervention studies

<table>
<thead>
<tr>
<th>Level</th>
<th>Intervention</th>
<th>Aetiology</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant RCTs</td>
<td>A systematic review of level II studies</td>
<td>A systematic review of level II studies</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least one properly designed RCT</td>
<td>A prospective cohort study</td>
<td>A study of test accuracy with independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation</td>
</tr>
<tr>
<td>III-1</td>
<td>Evidence obtained from well-designed, pseudo-randomised, controlled trials (alternative allocation or some other method)</td>
<td>All or none</td>
<td>A study of test accuracy with independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation</td>
</tr>
<tr>
<td>III-2</td>
<td>Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group</td>
<td>A retrospective cohort study</td>
<td>A comparison with reference standard that does not meet the criteria for Level II or Level III-1 evidence</td>
</tr>
<tr>
<td>III-3</td>
<td>Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group</td>
<td>A case-control study</td>
<td>Diagnostic case-control evidence</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from case series, either post-test or pre-test and post-test</td>
<td>A cross-sectional study</td>
<td>Study of diagnostic yield (no reference standard)</td>
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Search strategy for identification of studies
The following databases and sources will be searched in order to identify studies:

- MEDLINE (OVID).
- EMBASE (OVID).
- CINAHL.
- Cochrane Library, including CENTRAL Cochrane Controlled Trial Register (CCTR).
- The WHO International Clinical Trials Registry Platform Search Portal.
- Hand searching of the AWMA journal.
- Reference lists in review articles and trials retrieved.

The database search of MEDLINE, EMBASE and CINAHL will combine search terms describing venous ulceration. The initial search will not be restricted by terms describing interventions for venous ulceration as this would narrow the search. Papers published after 1984 in the English language literature will be included. The following search strategy applies to the MEDLINE database and will be adapted to apply to the other databases.

**Medline search**

1. *Leg Ulcer/*
2. *Varicose Ulcer/*
3. *Venous Insufficiency/*
4. Venous ulceration.mp
5. Varicose eczema.mp
6. 1 OR 2 OR 3 OR 4 OR 5
7. limit 6 to (English language and humans).

If insufficient Level 1 and 2 evidence relevant to the review is located, this search will be expanded by combining the above search terms with terms specific to interventions for venous ulceration as this would narrow the search. Papers published after 1984 in the English language literature will be included. The following search strategy applies to the MEDLINE database and will be adapted to apply to the other databases.

**Study selection**

One reviewer will assess the titles and available abstracts of all studies identified by the initial searches and exclude any clearly irrelevant studies. Two reviewers will independently assess papers identified as potentially eligible studies using the inclusion criteria and resolve disagreements on inclusion by consensus, with reference to a third reviewer if necessary. Papers that are retrieved based on the title and abstract and then assessed as not meeting inclusion criteria will be cited, along with the reason for exclusion.

**Methodological quality assessment**

Two reviewers will independently assess the methodological quality of each included trial and resolve disagreements by consensus, with reference to a third reviewer if necessary.

**Methodological quality of systematic reviews**

Methodological quality of included SRs will be assessed using the Scottish Intercollegiate Guidelines Network (SIGN) Methodology checklist for systematic reviews and meta-analyses. Assessment will be against key methodological criteria listed below:

- appropriate focused clinical question
- appropriate criteria to select studies for inclusion
- unlikely that relevant studies were missed (i.e. thorough and transparent search strategy)
- validity of included studies is appraised
- assessments of studies is reproducible (e.g. two or more people independently assessed studies for inclusion and quality of included studies)
- results similar from study to study or discrepancies can be explained
- appropriate strategies are used for pooling and analysing results
- potential conflicts of interest are clearly reported.

**Methodological quality of RCTs**

Methodological quality of included RCTs will be assessed using the SIGN Methodological Checklist for randomised controlled trials. Assessment of RCTs will be against key methodological criteria listed below:

- eligibility criteria for participants is specified
- appropriate randomisation methods used
- allocation concealment
- the study groups were similar at baseline regarding the most important prognostic indicators
- blinding of subjects
- blinding of therapists/researchers who administered the intervention
- blinding of assessors who measured at least one key outcome
- measures of at least one key outcome were obtained from more than 80% of the subjects initially allocated to groups
- relevant outcomes were measured in a standard, valid and reliable manner
- all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by “intention to treat”
- where the study is conducted at different sites, results are comparable between sites
- potential conflicts of interest are clearly reported.

**Methodological quality of cohort studies**

Methodological quality of included cohort studies will be assessed using the SIGN Methodology checklist for cohort studies.
Assessment will be against key criteria listed below:

- appropriate focused clinical question
- cohorts are selected from comparable source populations
- participation rate is reported and comparable between cohorts
- likelihood of outcome existing at commencement of trial is investigated
- measures of at least one key outcome were obtained from more than 80% of the subjects initially enrolled
- comparison is made between full enrolment populations by exposure status (e.g. consideration of participants lost to follow up)
- clearly defined outcomes measured using reliable and valid methods
- blinding of assessors, therapists and researchers who measured at least one key outcome
- confidence intervals are reported
- potential conflicts of interest are clearly reported.

**Methodological quality of case-control studies**

Methodological quality of included cohort studies will be assessed using the SIGN Methodology checklist for cohort studies. Assessment will be against key criteria listed below:

- appropriate focused clinical question
- cases and controls are selected from comparable source populations an subjected to the same exclusion criteria
- participation rate is reported and comparable between groups
- comparison between participants and non-participants to establish representation
- cases and controls clearly defined and differentiated from one another
- exposure status is concealed
- exposure status is measured using a reliable and valid method
- potential confounders are identified and considered in trial design

**Methodological quality of guidelines**

Methodological quality of existing guidelines will be assessed using the Appraisal of Guidelines Research and Evaluation Collaboration (AGREE) Agree instrument. The AGREE instrument provides a method of assessing six different aspects of guideline development to establish an overall quality score. The instrument assesses the following domains:

- scope and purpose
- stakeholder involvement
- rigour of development
- clarity and presentation
- applicability
- editorial independence.

Table 2. Identified systematic reviews.

Table 3. Identified RCTs.

Table 4. Evidence appraisal progress.
Quality of other evidence sources

Other sources of evidence may be relevant and used in the development of the venous leg ulcer guideline, particularly in domains where high-level sources of evidence are sparse.

If appropriate diagnostic studies are identified, the SIGN Methodological checklist for diagnostic studies will be utilised. However, it is anticipated that the reports on types of diagnosis and assessment used for venous leg ulcers are unlikely to be appropriate for assessment with this tool. Methods of diagnosis, interpretation of diagnostic results, expert opinion and where possible, comparison to the gold standard for diagnosing venous disease will be reported (colour duplex ultrasonography).

For papers describing leg ulcer assessment tools the methods used for ulcer assessment, reproducibility of assessments, training required by tool users, expert opinion and, where possible, comparison to other leg ulcer assessment tools will be used.

For textual papers, opinion papers, literature reviews and case reports, a tool developed specifically for this project will be used to collate information and report on signs of quality including search strategies, expert standing and support from references.

Evidence appraisal progress

Identified literature

Eighty-four SRs and 508 RCTs covering aetiology, diagnosis and assessment, interventions to manage VLUs and prognosis have been identified (Tables 2, 3 & 4).

The appraisal process initially used two reviewers for 100% of the SRs and due to the high level of inter-rater reliability only 30% of RCTs are now required to be reviewed by two reviewers.

Compression therapy

Reviewing the literature for compression therapy has identified 11 SRs and 69 RCTs. Six SRs and five RCTs met the inclusion criteria. Three recommendation statements related to compression therapy have been developed in the following three areas.

- primary prevention of VLUs
- treatment of VLUs
- prevention of VLU recurrence.

The guidelines will include practice tips for compression therapy

They will address issues such as:

- factors in selecting a compression therapy system
- duration of compression
- minimum pressure of compression
- training of clinicians
- patient education
- compliance.

Review and appraisal of the literature will continue over the next 12 months and further recommendations and practice tips will be developed. This information will be available on the AWMA website. Consumers and health professionals will be asked to comment and provide feedback. The guidelines will then be submitted for NHMRC approval. The completion of this project is due in 2011.

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References
