

SYSTEMATIC REVIEW PROTOCOL

Economic evaluation of compression therapies in the treatment of venous leg ulcers: a systematic review protocol

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Abstract

Background Venous leg ulcers (VLU) are an important public health issue, impacting individuals' lives and representing a societal economic burden. Compression therapy is considered the best treatment for VLU, but there is no conclusive evidence whether the health benefits outweigh the costs.

Objectives To identify and describe economic evaluations relating to compression therapy for the treatment of VLU and to evaluate the quality of these studies.

Method We will conduct a systematic review of the MEDLINE, EMBASE, Cochrane Central, CINAHL, Scopus, Web of Science and LILACS databases and Google Scholar. We will include randomised controlled trials, pragmatic clinical trials, cohort studies, case-control studies and quasi-experimental studies which also describe an economic evaluation of compression therapy for VLU, published in English, Portuguese or Spanish. No time restriction will be applied. The screening and assessment will be done by two independent reviewers, supported by Covidence Software. ROB-2 and ROBINS-I tools will be used to assess risk of bias, and the CHEERS tool will support the assessment of the quality of economic evaluations.

Discussion This systematic review will contribute to expand the knowledge about the topic. In addition, it may support health professionals' clinic decision making, assist managers regarding the allocation of resources, and improve the quality of life of individuals with VLU.

Registration PROSPERO CRD42023393289.

Keywords health economics, cost-benefit analysis, compression bandage, venous ulcer, systematic review

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Introduction

Venous leg ulcers (VLU) are an important public health issue. They greatly impact an individual's life, causing discomfort, social isolation and disability. They also represent a societal economic burden, as they can lead to loss of productivity, frequent visits to healthcare services and recurrent hospitalisations^{1,2}. Systematic reviews have demonstrated varied approaches to VLU management in developed countries (Australia, France, Germany, Italy, Spain, the UK, and the USA), but all treatments have high costs³. Countries

are spending 3–6% of their total health costs treating chronic wounds⁴. Furthermore, the average recurrence rate for VLU is 70%⁵, meaning they have an important impact on the quality of life of these individuals.

Compression therapy is considered the gold standard treatment for VLU management^{3,6} and there is evidence of moderate certainty that compression therapy is better than no compression on VLU healing^{6,7}. A systematic review comparing compression systems to no compression

published in 2021 included 14 studies (with 32 publications) and a total of 1391 participants with VLU⁷. It concluded that using compression systems rather than non-compression resulted in a shorter time to complete healing and a greater number of VLU which completely healed⁷. A more recent meta-review included 12 published systematic reviews with a total of 71 trials and 7,141 participants with VLU. The comparison of compression vs no compression included 10 trials and 768 participants, and the superiority of compression was identified as moderate certainty evidence (RR:1.5; 95% CI 1.43–1.78, $p < .00001$), where 61% ($n=236/385$) of the participants in the compression group healed while only 39% ($n=151/383$) of VLU healed in the no compression group⁶.

Different types of compression systems are available – inelastic and elastic compression bandages, simple layer and multilayer bandages, compression hosiery, and intermittent pneumatic compression systems^{3,6}. The compression systems can be classified according to the pressure applied – light (14–17mmHg), moderate (18–24mmHg), high (25–35mmHg) and extra-high (up to 60mmHg). In the same way, hosiery can be classified as light-support (14–17mmHg), medium-support (18–24mmHg) and strong-support (25–35mmHg)⁷. Among the different forms of compression therapy, the recent meta-review suggested no conclusion as to the best approach from the available studies, largely due to missing information about parameters of elasticity/inelasticity of the compression bandages used in the studies⁶.

Furthermore, the majority of compression therapy studies indicate the clinical effectiveness of these treatments on VLU healing – time-to-complete wound healing (HR:2.17; 95% CI 1.52–3.10) and proportion of wounds completely healed (RR:1.77; 95% CI 1.41–2.21), pain improvement (mean difference (MD) –1.39; 95% CI –1.79 to –0.98), and better patients' health-related quality of life (MD –6.87; 95% CI –13.10 to –0.64) – but there is no evidence whether the health benefits outweigh the costs⁷. Evidence about cost and effectiveness of different compression systems are important to inform the allocation of scarce resources and to expand knowledge. Thus, the following question will guide our systematic review: what is the evidence in the literature on the economic evaluation of compression therapies in the treatment of VLU?

Objective

This protocol aims to provide a detailed overview of the process of developing the systematic review, promoting a transparent process. The systematic review aims to identify and describe economic evaluations relating to compression therapies for the treatment of VLU and to analyse the quality of these studies.

Methods

This protocol was registered with The International Prospective Register of Systematic Reviews (PROSPERO) – CRD42023393289 and was developed according to the

Preferred Reporting Items for Systematic review and Meta-Analysis Protocol (PRISMA-P) recommendations⁸.

Eligibility criteria

The inclusion criteria are framed by PICO strategy, as presented in Table 1.

Regarding study design, we will include randomised controlled trials (RCTs), pragmatic clinical trials, cohort studies, case-control studies and quasi-experimental studies which describe a cost-effectiveness analysis and/or a cost-utility analysis. Other designs, such as systematic reviews, will be excluded. Besides that, no restriction will be adopted on timeframe. We will consider available studies published in English, Portuguese and Spanish.

Information sources

Searches will be conducted in the following electronic databases: Ovid MEDLINE, EMBASE, Cochrane Central, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Scopus, Web of Science, the Latin American and Caribbean of Health Sciences Information System (LILACS) and Google Scholar.

Search strategy

Search terms will include controlled vocabulary such as medical subject headings (MeSH terms) and free text terms

Table 1. Inclusion criteria framed by PICO strategy

PICO	Description
Participants/ Population	<i>Inclusion criteria:</i> adults (aged 18 years or older) with VLU <i>Exclusion criteria:</i> any other chronic wound (arterial, mixed, pressure, diabetic foot ulcer or atypical wounds)
Intervention	Studies that evaluate compression therapy to treatment of VLU. Will consider all types of compression therapy (elastic, inelastic, single or multilayer)
Comparators	All comparators (other compression therapies, placebo, usual care, non-compression or other wound treatment)
Outcomes	<i>Inclusion criteria:</i> cost-effectiveness analysis, cost-utility analysis – cost, cost-effectiveness, Incremental Cost-Effectiveness Ratios (ICER), healing rate, reduction of the size (wound area), mean time to healing, Quality-Adjusted Life Year (QALY), and Health-Related Quality of Life (HRQoL) <i>Exclusion criteria:</i> description of costs or effectiveness with no cost-effectiveness/cost-utility analysis

related to compression therapy to treat VLU. The search strategy will be designed and conducted in collaboration with an experienced librarian from the University of Alberta (UofA) (ED), and reviewed by another librarian from UofA using the Peer Review of Electronic Search Strategies (PRESS) checklist⁹. Table 2 shows the search strategy for the Ovid MEDLINE electronic database which used the economic evaluations filter from CADTH¹⁰.

Study records: data management, selection and data collection process

All references will be imported into Covidence Systematic Review Software which will support the screening process.

Table 2. Search strategy for the Ovid MEDLINE electronic database

Line	Keywords
1	Varicose Ulcer/
2	((Leg or legs or ankle* or calf or lower-limb* or lower-extremity* or venous or varicose or stasis) adj3 (ulcer* or non-healing wound* or slow-healing wound*)).mp.
3	1 or 2
4	compression bandages/ or stockings, compression/
5	(compression or bandage* or wrapping*).mp.
6	4 or 5
7	3 and 6
8	Economics/ or exp "Costs and Cost Analysis"/ or Economics, Nursing/ or Economics, Medical/ or Economics, Pharmaceutical/ or exp Economics, Hospital/ or Economics, Dental/ or exp "Fees and Charges"/ or exp Budgets/ or budget*. ti,ab,kf. or (economic* or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. or (economic* or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 or (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. or (value adj2 (money or monetary)).ti,ab,kf. or exp models, economic/ or economic model*.ab,kf. or markov chains/ or markov.ti,ab,kf. or monte carlo method/ or monte carlo.ti,ab,kf. or exp Decision Theory/ or (decision* adj2 (tree* or analy* or model*)).ti,ab,kf.
9	7 and 8

All duplicate titles will be removed, and two reviewers (ACF and FPC) will independently screen titles and abstracts, according to the inclusion criteria. Included studies will then be assessed based on full text reading by the same reviewers independently. Any disagreement will be resolved by discussion, and if necessary, by a third reviewer.

A PRISMA flow chart (Figure 1) will be constructed according to the search process and included/excluded studies.

Data items

We will extract the following information from the included studies:

- Study details: title, author, year, journal, country.
- Study methods: aims, design, setting, sample size, participants, length of follow-up, details about intervention and comparator, analysis performed.
- Outcome measurements.
- Costs (direct, indirect).
- Cost-effectiveness ratio.
- Sensitivity analyses (if done).
- Author conclusion.
- Conflicts of interest.

Risk of bias / quality assessment

The methodological quality of the included studies will be assessed by the two reviewers independently using tools regarding the type of studies. Any disagreement will be resolved by discussion, and if necessary, by a third reviewer. The Cochrane Risk of Bias (ROB-2) tool will be used to assess RCTs and the Risk Of Bias In Non-randomized Studies – of Interventions (ROBINS-I) tool will be used to assess cohort and case control studies. The ROB-2 evaluates the study as “low risk of bias, some concerns, and high risk of bias”, based on five domains; and the ROBINS-I indicates the study as “low risk of bias, moderate risk of bias, serious risk of bias, critical risk of bias, and no information on which to base a judgment about the risk of bias for this domain” by three domains^{11,12}. Regarding the quality of economic evaluation studies, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) tool will be used by the reviewers¹³.

Data synthesis

The study characteristics and findings will be summarised using descriptive statistics where appropriate. Additionally, if possible, risk ratio (RR) and odd ratios (OR) for categorical outcome data or mean difference for continuous data, and 95% confidence interval (CI) will be calculated. For economic evaluation, incremental cost-effectiveness or cost/QALY ratios and ranges based on sensitivity analyses will be summarised.

Discussion

Our systematic review seeks to identify and describe economic evaluation studies relating to compression therapies for the

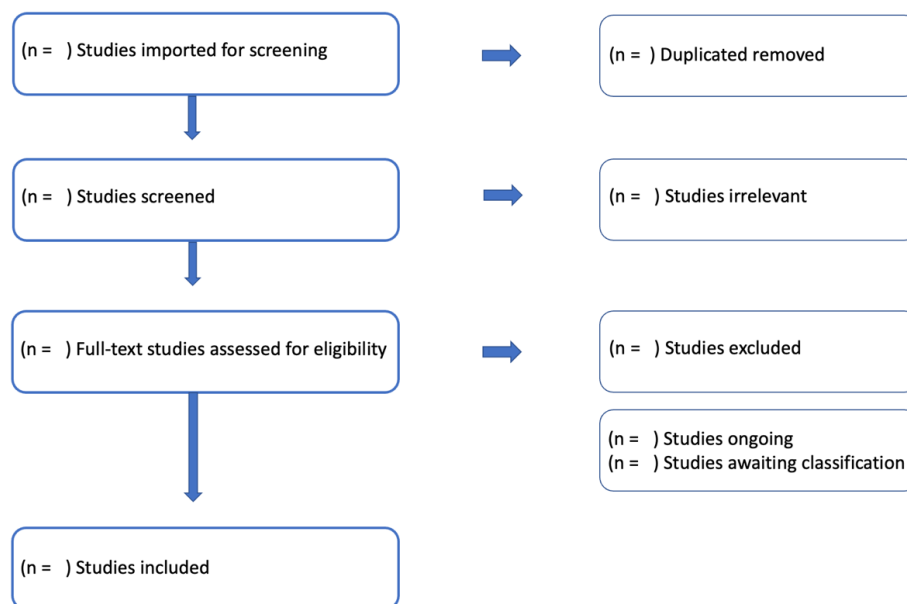


Figure 1. Flow chart for the systematic review process from the Covidence Systematic Review Software

treatment of VLU and to evaluate the quality of these studies. As demonstrated in the introduction, treatments for VLU are expensive and this pathology generates an important impact on individuals' wellbeing. Thus, it is important to identify and synthesise the available evidence about the cost-effectiveness of different compression systems, in different contexts, to expand knowledge, to support clinical decisions of health professionals, and importantly, to inform the allocation of resources for the most effective therapies. Ultimately, the aim is to improve the outcomes and quality of life of individuals with VLU.

From a systematic review it is possible to facilitate the construction of knowledge in a transparent and rigorous process. In addition, assessing the methodological quality of the studies is essential to understand the factors that can influence the findings.

On the other hand, due to differences in health system organisation, budgets and availability of products to treat VLU across countries, beyond the culture that can influence on the perception of quality of life, it may not be possible to conclude if one compression system is universally more cost-effective than others. However, the systematic review will contribute to identifying gaps in available evidence regarding types of compression systems, outcomes as to effectiveness, follow-up, sample size or context of studies. Such information can then help to inform more local decision making, taking into account those important broader considerations.

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Author contribution

All authors participated in the conception of this article, critically reviewing it and approving the final version to be published, agreeing to be responsible for all aspects of the work and ensuring that questions related to the accuracy and integrity of any part of this work are duly investigated and resolved.

Conflict of interest

The authors declare no conflicts of interest.

Ethics statement

This systematic review protocol does not require ethics approval as information will be obtained from publicly available databases.

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