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Compression bandages or stockings versus no compression for treating venous leg ulcers (Review)

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[Intervention Review]

Compression bandages or stockings versus no compression for treating venous leg ulcers

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ABSTRACT

Background

Leg ulcers are open skin wounds on the lower leg that can last weeks, months or even years. Most leg ulcers are the result of venous diseases. First-line treatment options often include the use of compression bandages or stockings.

Objectives

To assess the effects of using compression bandages or stockings, compared with no compression, on the healing of venous leg ulcers in any setting and population.

Search methods

In June 2020 we searched the Cochrane Wounds Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL), Ovid MEDLINE (including In-Process & Other Non-Indexed Citations), Ovid Embase and EBSCO CINAHL Plus. We also searched clinical trials registries for ongoing and unpublished studies, and scanned reference lists of relevant included studies as well as reviews, meta-analyses and health technology reports to identify additional studies. There were no restrictions by language, date of publication or study setting.

Selection criteria

We included randomised controlled trials that compared any types of compression bandages or stockings with no compression in participants with venous leg ulcers in any setting.

Data collection and analysis

At least two review authors independently assessed studies using predetermined inclusion criteria. We carried out data extraction, and risk-of-bias assessment using the Cochrane risk-of-bias tool. We assessed the certainty of the evidence according to GRADE methodology.

Main results

We included 14 studies (1391 participants) in the review. Most studies were small (median study sample size: 51 participants). Participants were recruited from acute-care settings, outpatient settings and community settings, and a large proportion (65.9%; 917/1391) of participants had a confirmed history or clinical evidence of chronic venous disease, a confirmed cause of chronic venous insufficiency,

or an ankle pressure/brachial pressure ratio of greater than 0.8 or 0.9. The average age of participants ranged from 58.0 to 76.5 years (median: 70.1 years). The average duration of their leg ulcers ranged from 9.0 weeks to 31.6 months (median: 22.0 months), and a large proportion of participants (64.8%; 901/1391) had ulcers with an area between 5 and 20 cm^2. Studies had a median follow-up of 12 weeks. Compression bandages or stockings applied included short-stretch bandage, four-layer compression bandage, and Unna's boot (a type of inelastic gauze bandage impregnated with zinc oxide), and comparator groups used included 'usual care', pharmacological treatment, a variety of dressings, and a variety of treatments where some participants received compression (but it was not the norm). Of the 14 included studies, 10 (71.4%) presented findings which we consider to be at high overall risk of bias.

Primary outcomes

There is moderate-certainty evidence (downgraded once for risk of bias) (1) that there is probably a shorter time to complete healing of venous leg ulcers in people wearing compression bandages or stockings compared with those not wearing compression (pooled hazard ratio for time-to-complete healing 2.17, 95% confidence interval (CI) 1.52 to 3.10; I^2 = 59%; 5 studies, 733 participants); and (2) that people treated using compression bandages or stockings are more likely to experience complete ulcer healing within 12 months compared with people with no compression (10 studies, 1215 participants): risk ratio for complete healing 1.77, 95% CI 1.41 to 2.21; I^2 = 65% (8 studies with analysable data, 1120 participants); synthesis without meta-analysis suggests more completely-healed ulcers in compression bandages or stockings than in no compression (2 studies without analysable data, 95 participants).

It is uncertain whether there is any difference in rates of adverse events between using compression bandages or stockings and no compression (very low-certainty evidence; 3 studies, 585 participants).

Secondary outcomes

Moderate-certainty evidence suggests that people using compression bandages or stockings probably have a lower mean pain score than those not using compression (four studies with 859 participants and another study with 69 ulcers): pooled mean difference −1.39, 95% CI −1.79 to −0.98; I^2 = 65% (two studies with 426 participants and another study with 69 ulcers having analysable data); synthesis without meta-analysis suggests a reduction in leg ulcer pain in compression bandages or stockings, compared with no compression (two studies without analysable data, 433 participants). Compression bandages or stockings versus no compression may improve disease-specific quality of life, but not all aspects of general health status during the follow-up of 12 weeks to 12 months (four studies with 859 participants; low-certainty evidence).

It is uncertain if the use of compression bandages or stockings is more cost-effective than not using them (three studies with 486 participants; very low-certainty evidence).

Authors' conclusions

If using compression bandages or stockings, people with venous leg ulcers probably experience complete wound healing more quickly, and more people have wounds completely healed. The use of compression bandages or stockings probably reduces pain and may improve disease-specific quality of life. There is uncertainty about adverse effects, and cost effectiveness.

Future research should focus on comparing alternative bandages and stockings with the primary endpoint of time to complete wound healing alongside adverse events including pain score, and health-related quality of life, and should incorporate cost-effectiveness analysis where possible. Future studies should adhere to international standards of trial conduct and reporting.

PLAIN LANGUAGE SUMMARY

Compression bandages or stockings versus no compression for treating venous leg ulcers

Key messages

Compared with not using compression, compression therapy that uses bandages or stockings to treat venous leg ulcers:

- probably heals venous leg ulcers more quickly;

- probably increases the number of people whose ulcer has completely healed after 12 months;

- probably reduces pain; and

- may improve some aspects of people’s quality of life.

However, there is still uncertainty about whether or not compression therapy causes unwanted side effects, and if the health benefits of using compression outweigh its cost.

What are leg ulcers?

Leg ulcers are open skin wounds on the lower leg that can last weeks, months or even years. Most leg ulcers are caused by venous diseases that affect the circulation of blood in leg veins. Venous leg ulcers can cause distress and pain to patients, and can be very costly to the health service.

What did we want to find out?

Standard treatment options for venous leg ulcers often include compression therapy. This involves applying external pressure around the lower leg to help the return of blood from the legs to the heart. Compression therapy uses bandages, stockings or other devices.

We wanted to find out if compression therapy delivered by bandages and stockings compared with no compression:

- heals venous leg ulcers;

- has any unwanted effects;

- improves people's quality of life;

- has health benefits that outweigh the costs (cost-effectiveness); and

- reduces pain.

What did we do?

We searched for randomised controlled trials (clinical studies where the treatment or care people receive is chosen at random). This type of study design provides the most reliable health evidence about the effects of a treatment. We searched for studies that evaluated the effects of any types of compression bandages or stockings compared with no compression in people affected with venous leg ulcers in any care setting. We compared and summarised their results, and rated our confidence in the evidence, based on factors such as study methods and sizes.

What did we find?

We found 14 studies (1391 people, average age: 70.1 years) that lasted on average for 12 weeks. People in eight of the 14 studies were treated in outpatient and community settings. People had venous leg ulcers that had lasted for 22 months on average, and most ulcers had an area between 5 and 20 cm^2.

The studies used three types of compression therapy: short-stretch bandage, four-layer compression bandage, and Unna's boot (a type of compression bandage containing zinc oxide). These therapies were compared with no compression in forms of 'usual care', pharmacological treatment, a variety of dressings, and a variety of treatments where only some participants received compression (but it was not the norm).

(1) Venous leg-ulcer healing and unwanted effects

Compared with no compression, the evidence suggests that:

- people wearing compression bandages or stockings probably experience complete ulcer healing more quickly; and

- more people treated using the compression bandages or stockings are likely to experience complete ulcer healing within 12 months.

However, we did not find clear evidence to tell if using compression bandages or stockings causes any unwanted effects.

(2) Other effects

The evidence suggests that, compared with not using compression, the use of compression bandages or stockings:

- probably reduces pain more than not using compression; and

- may improve some aspects of people's quality of life in 12 weeks to 12 months.

However, we are uncertain if the use of compression bandages or stockings results in health benefits that outweigh their costs.

What limited our confidence in the evidence?

Most studies were small (51 people on average) and 10 of the 14 included studies used methods that could introduce errors in their results.

How up-to-date is this review?

The evidence in this Cochrane Review is current to June 2020.

SUMMARY OF FINDINGS

Summary of findings 1. Compression bandages or stockings compared with no compression for treating venous leg ulcers

Compression bandages or stockings compared with no compression for treating venous leg ulcers

Patient or population: people with venous leg ulcers

Setting: community and acute-care settings

Intervention: compression bandages or stockings

Comparison: no compression

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Time-to-complete wound healing follow-up: range 1 day to 12 months	5 studies (733 participants) with time-to-event data: HR 2.17 (95% CI 1.52 to 3.10)[a]	733 (5 RCTs)	⊕⊕⊕⊖ Moderate[b]	There is probably a shorter time to complete healing of venous leg ulcers in people wearing compression bandages or stockings compared with those not wearing compression
Proportion of wounds completely healed during follow-up follow up: range 1 day to 12 months	8 studies (1120 participants) with analysable data: RR 1.77 (95% CI 1.41 to 2.21) Two studies (95 participants) without analysable data: 1 study reported 71% of leg ulcers completely healed in short-stretch bandages and 25% in usual care. 1 study reported 82% of 21 participants with ulcers healed when using compression plus local povidone-iodine (Betadine) and 62% of 21 participants with ulcers healed when using local povidone-iodine (Betadine)	1215 (10 RCTs)	⊕⊕⊕⊖ Moderate[c]	People treated with compression bandages or stockings probably have more completely healed venous leg ulcers during follow-up to 12 months than people not in compression
Adverse events follow-up: range 8 weeks to 12 months	3 studies (585 participants) with adverse event data that were systematically collected: RR 0.98 (95% CI 0.25 to 3.80) [a]	585 (3 RCTs)	⊕⊖⊖⊖ Very low [d,e,f]	It is uncertain whether there is any difference in the risk of adverse events associated with using compression and not using compression
Participant health-related quality of life/ health status follow-up: 12 weeks to 12 months	Two studies (426 participants): pooled MD in the total score of the Charing Cross Venous Ulcer Questionnaire (lower scores = better quality of life) −6.87 (95% CI −13.10 to −0.64) between using compression bandages or stockings and no compression, but data analysis showed no difference in the physical component, mental component, and functional status of the SF-12.	859 (4 RCTs)	⊕⊕⊖⊖ Low[g]	Compression bandages or stockings may improve participant health-related quality of life for some (but not all) aspects during the follow-up of 12 weeks to 12 months

	Two studies without analysable data (433 participants): 1 study (233 participants) stated that, for most dimensions of the SF-36 and EuroQol, health status deteriorated over time but was not different between 4-layer bandages and usual care. 1 study (200 participants) reported a statistical difference in some dimensions of the SF-36 (including physical function, role-physical, mental health) and the disease-specific quality of life instrument for chronic lower limb venous insufficiency (CIVIQ) (physical, social, and global dimensions) but not in others			in comparison with no compression
Cost effectiveness follow-up: 12 weeks and 12 months	Two studies without incremental mean cost per incremental gain in benefit: 1 study (53 participants) reported that the short-stretch bandage was more cost-effective than usual care as it could be washed and reused repeatedly. 1 study (200 participants) showed that the median cost per leg healed was significantly less for 4-layer bandages than dressings (P = 0.04). 1 study (233 participants) with incremental mean cost per incremental gain in benefit: incremental cost-effectiveness ratio = GBP 2.46 (95% CI −31.94 to 99.12) per ulcer-free week between 4-layer bandage in leg ulcer clinics and no compression	486 (3 RCTs)	⊕⊖⊖⊖ Very low [h,i,j]	It is uncertain whether compression bandages or stockings are cost effective compared with no compression in wound healing
Mean pain score median follow-up period 12 weeks (minimum 12 weeks maximum 12 months)	Two studies with 426 participants and another study with 69 ulcers reported analysable data, with pain measured by either a 10-point visual analogue scale or a scale with grades from 1 to 10: pooled MD −1.39 (95% CI −1.79 to −0.98). Two studies without analysable data (433 participants), neither reported the range of scales used: 1 study (233 participants) stated that people treated with 4-layer bandages were more likely to experience a reduction in leg ulcer pain per month than those using usual care; and another study (200 participants) reported a lower median of pain scores among those using 4-layer bandages than those using dressings (median 18.8, IQR 6.3 to 37.5; and 31.3, 18.8 to 43.8, respectively; P = 0.14).	859 participants and 69 ulcers in other participants (5 RCTs)	⊕⊕⊕⊖ Moderate[k]	The use of compression probably reduces mean pain score compared with no compression.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: Confidence interval; **HR:** Hazard Ratio; **IQR:** interquartile range; **MD:** mean difference; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a]One included study (84 participants with 87 ulcers) in these analyses reported clustered data whilst the other studies reported data by participant; the absolute effect could not be estimated directly.
[b]Downgraded once for risk of bias (one study with clustered data and another small study were at high overall risk of bias in domains other than performance bias, and the other three studies with most of the data in this synthesis were at unclear overall risk of bias).
[c]Downgraded once for risk of bias (six studies having 569/1215 (46.8%) participants were at high risk of bias in the domains other than performance bias and the other four were at unclear risk of bias in some but not all domains).
[d]Downgraded once for risk of bias (two studies with the larger numbers of participants were at high risk of bias in some domains and one study contributing 30.6% weight was at unclear risk of bias).
[e]Downgraded twice for substantial inconsistency as the clustered data were inconsistent with the data reported by participant.
[f]Downgraded once for imprecision because the CIs appeared to include the possibility of both benefit and harm as well as no effect.
[g]Downgraded twice for substantial inconsistency due to the variation of the reported results, particularly in terms of health status.
[h]Downgraded once for risk of bias (one small study was at high overall risk of bias in domains other than performance bias and the other two studies were at unclear risk of bias in some domains).
[i]Downgraded once for indirectness (results from two studies did not appear to be expressed as incremental mean cost per incremental gain in benefit).
[j]Downgraded once for inconsistency in terms of cost-effectiveness results between studies.
[k]Downgraded once for risk of bias as two (of all six included) studies with 345 participants (a small proportion) were at high overall risk of bias.

BACKGROUND

Description of the condition

Leg ulcers are open skin wounds on the lower leg (typically below the knee and mainly above the ankle) that can last weeks, months or even years. They occur as a consequence of arterial or venous insufficiency, or both. Less frequently, chronic leg ulceration may occur due to some other disease, such as rheumatoid disease or rarer conditions (Bafaraj 2014). Most leg ulcers are the result of venous disease (Jockenhöfer 2014), where blood flow in the veins is impaired by vein damage, obstruction and calf muscle pump failure (Eberhardt 2014). These problems mean that blood no longer returns efficiently from the legs to the heart and the pressure within the veins rises (Ghauri 2010). The precise chain of events that links high venous pressures with skin breakdown and subsequent chronic wounds is not fully understood.

Leg ulcers of mixed aetiology (those that have more than one cause) usually involve a combination of venous and arterial disease. Open skin ulceration that is due solely to limb ischaemia (a lack of oxygen reaching the leg tissues, i.e. arterial disease) is less common.

Current, accurate estimates of the proportion of leg ulcers due to specific aetiologies can be hard to identify because most studies do not differentiate between venous, arterial or mixed aetiologies of leg ulceration, or do so for each limb but not for each person (Moffatt 2004; Srinivasaiah 2007; Vowden 2009a). Two point-prevalence surveys undertaken in the north of England estimated that venous ulceration has a prevalence of approximately 0.30 cases per 1000 population in the UK (Cullum 2016; Gray 2018), whilst mixed arterial/venous leg ulceration has a prevalence of 0.11 per 1000 (Cullum 2016). A review of studies of the prevalence of complex wounds suggests that there are limited high-quality data for estimating the burden of venous leg ulceration in lower- and middle-income countries (Cullum 2016).

A differential diagnosis of the underlying aetiology of a specific leg ulcer is made by taking a clinical history, physical examination, laboratory tests and other assessments (SIGN 2010). Typically, the latter includes an assessment of the arterial blood supply to the leg using the ankle-brachial pressure index (ABPI), measured using a hand-held Doppler ultrasound scanner.

Leg ulcers are associated with considerable cost to patients and to healthcare providers. Two systematic reviews summarised the literature on health-related quality of life in people with leg ulcers (Herber 2007; Persoon 2004). Both included qualitative and quantitative evaluations and reported that the presence of leg ulceration was associated with pain, restriction of work and leisure activities, impaired mobility, sleep disturbance, reduced psychological well-being and social isolation. Recent research suggests that people with complex wounds, including those with venous leg ulcers, commonly see complete wound healing as their most desirable outcome (Cullum 2016). Leg ulceration is typically a long-term condition, with periods of healing followed by recurrence stretching over years.

The financial cost of treating a person with an open venous leg ulcer in the UK was estimated at approximately GBP 1700 per year at 2012 prices (Ashby 2014). Nursing time comprises a large part of ulcer treatment costs. A study in Bradford, UK (population approximately 500,000) estimated that for the financial year 2006 to 2007, GBP 1.69 million was spent on dressings and compression bandages, and GBP 3.08 million was spent on nursing time (estimates derived from resource-use data for all wound types, not just venous leg ulcers) (Vowden 2009b). In the USA the estimated healthcare cost for people with venous leg ulcers was USD 14.9 billion (2012 prices, all payers including Medicare, private, self-insured) (Rice 2014). In four community wound-care clinics in Queensland, Australia, the mean weekly cost for each patient with a venous leg ulcer was estimated as AUD 294.72 at 2016/2017 prices for those receiving guideline-based care (i.e. with at least one ABPI and compression therapy) (Barnsbee 2019).

Description of the intervention

The first-line treatment for venous leg ulcers is compression therapy in the form of bandages, stockings or other devices (Partsch 2015). This application of external pressure around the lower leg assists venous return (blood flow back to the heart) and reduces venous reflux. This review focuses on the effects of compression delivered by bandages and stockings compared with no compression.

Compression bandages

Bandages are categorised as retention, support or compression, depending on their performance in standardised laboratory tests. Compression bandages are further divided according to the amount of force required to extend them and therefore the level of compression that they can apply to a limb. Furthermore, the laboratory performance of a bandage may not reflect its performance in clinical use, as this depends upon operator training and application technique (specifically, whether the bandage is applied as a spiral or figure-of-eight, how many layers are applied and the amount of extension used). Compression systems commonly used for venous leg ulcers are listed below (Thomas 1995).

- Class 3a: light-compression bandages; apply 14 mmHg to 17 mmHg pressure at the ankle when applied in a simple spiral, e.g. Elset (Mölnlycke).
- Class 3b: moderate-compression bandages; apply 18 mmHg to 24 mmHg pressure at the ankle when applied as a simple spiral, e.g. Velkomp (Datt Mediproducts Pvt. Limited).
- Class 3c: high-compression bandages; apply 25 mmHg to 35 mmHg pressure at the ankle when applied as a simple spiral, e.g. Setopress (Mölnlycke), and Elodur forte (BSN Medical).
- Class 3d: extra-high-compression bandages; apply up to 60 mmHg pressure at the ankle when applied as a simple spiral.

Classification of compression systems

In 2008 a new compression bandage classification system was proposed, based on components rather than the number of 'layers' of bandage (Partsch 2008). The Partsch group recommended that the components of compression, such as orthopaedic wool, crepe bandage or cohesive elastic bandage, should be described. Other recommended classification criteria included sub-bandage pressure (measured in the medial gaiter area with the patient supine) and the elastic property of the overall compression system. The following are examples of multi-component bandage systems (listed for illustrative purposes only; not intended as practice recommendations).

- Short stretch/inelastic systems: orthopaedic padding plus one or two rolls of short stretch bandage (SSB).
- Inelastic paste systems: paste bandage plus support bandage, e.g. Setocrepe (Mölnlycke).
- Two-component bandage systems: orthopaedic padding plus elastic bandage, e.g. 3M™ Coban™ 2 Compression System.
- Four-component bandage systems: orthopaedic padding plus support bandage (crepe) plus class 3a bandage, e.g. PROFORE™ compression system (Smith & Nephew).

The earliest Cochrane Review of compression for venous leg ulcers (Cullum 2001) defined different compression systems by the number of layers whereas, in line with the recommendations of the consensus group outlined above, subsequent versions refer to components. Nonetheless, where a trial treatment is the original Charing Cross four-layer bandage, or a close variant of it, we have continued to use the term 'four-layer bandage' (4LB), as this is an internationally-recognised bandage system.

It is more difficult to classify different compression systems in relation to sub-bandage pressures since, in general, this information is not available from clinical trial reports. In order to gain further insights into the optimal way to classify different compression systems, we consulted with experts in wound management and invited them to complete a survey (informing the previous update of this review) (O'Meara 2012). The survey listed different types of compression against various classifications, and respondents were asked to provide the best choice of classification in their opinion. In addition, free-text comments were invited. We used the information gleaned from this exercise to classify different types of compression therapy for the previous update of this review (O'Meara 2012).

Compression stockings

Compression stockings (or hosiery) can be used to treat open ulcers and to reduce the risk of recurrence post-healing. Stockings are classified according to the level of compression they apply to the limb. Importantly, the pressure applied by stockings is subject to less operator variability than bandages.

- Class 1: light-support stockings; provide 14 mmHg to 17 mmHg pressure at the ankle. Used to treat varicose veins.
- Class 2: medium-support stockings; provide 18 mmHg to 24 mmHg pressure at the ankle. Used to treat more severe varicosities, and to prevent venous leg ulcers.
- Class 3: strong-support stockings; provide 25 mmHg to 35 mmHg pressure at the ankle. Used to treat severe chronic hypertension and severe varicose veins, and to prevent venous leg ulcers.

Alongside compression, wound dressings are almost always applied to open ulcers. Dressings protect the surface of the ulcer, absorb exudate and can be antimicrobial. A series of reviews has addressed the comparative effectiveness of dressings for venous ulcers (Norman 2018; O'Meara 2013; O'Meara 2015). Other treatments for venous leg ulcers include venous surgery (removal of incompetent superficial veins (Gohel 2018)) and drugs such as pentoxifylline (Jull 2012).

How the intervention might work

Generally, compression therapy is thought to work by applying an external pressure to the leg which assists venous return (blood flow back to the heart) and reduces venous reflux (Woo 2013). Partsch has suggested that compression:

- reduces oedema by reducing capillary filtration, moving fluid from compressed tissues to non-compressed tissues and improving lymphatic drainage (Partsch 2011); and
- reduces the pressure in the veins by increasing venous blood flow and reducing venous pooling (Partsch 2011).

The use of compression to treat venous leg ulcers is not without risk. Whilst Mosti 2012 has suggested that compression may increase arterial inflow, if the applied pressure exceeds the local arterial perfusion pressure then arterial inflow will be reduced, which risks ischaemia.

National clinical guidelines in the UK and USA recommend that all people presenting with a leg ulcer be screened for arterial disease using Doppler-aided measurement of the ABPI (Bolton 2014; SIGN 2010). Clinically significant arterial disease is often defined as an ABPI of below 0.8. People with venous leg ulceration who have an ABPI of between 0.5 and 0.8 may be eligible to receive modified (reduced) compression (Moffatt 2007).

Why it is important to do this review

Venous leg ulcers have a large impact on people's lives and incur high costs to health services; compression therapy is currently the first-line treatment. Since the publication of the original Cochrane Review of compression bandages and stockings for venous leg ulcers (Cullum 2001), the number of relevant randomised controlled trials (RCTs) has more than doubled, the range of compression modalities has increased, and the classification of compression modalities has been refined. We update the evidence from the review (O'Meara 2012) in order to offer up-to-date evidence for decision-makers, and have decided to break down the previous version into separate reviews by compression modality. We will then review all compression modalities together in an overview, which will incorporate a network meta-analysis (Salanti 2012), in order to rank the different treatments on their individual probabilities of being the most effective compression modalities for healing venous leg ulcers. This particular review provides evidence about the comparison of compression bandages or stockings versus no compression.

OBJECTIVES

To assess the effects of using compression bandages or stockings, compared with no compression, on the healing of venous leg ulcers in any setting and any population.

METHODS

Criteria for considering studies for this review

Types of studies

We included published and unpublished RCTs, including cluster-RCTs and cross-over trials, irrespective of language of report. We excluded studies which used quasi-randomised methods to allocate treatment (e.g. alternation or odd/even case numbers). We included trials if the application of compression was the only systematic difference between study arms.

Types of participants

We included randomised controlled trials which recruited people of any age with venous leg ulceration (which may also be described as 'stasis' or 'varicose' ulceration) in any care setting. As the method of diagnosis of venous ulceration could vary between studies, we applied no standardised definition, but each study had to refer to the use of compression for venous ulcers.

We included studies that recruited participants with a variety of wound types, including venous leg ulcers, if: a) the allocation of participants was stratified by wound type and included 'venous leg ulcer' as a group and results were presented (or available from the study authors) separately for this group; or b) studies included participants with non-venous leg ulcers, but these made up a maximum of 25% of the total study population and we assumed that any treatment effect applied to people with venous ulcers. We excluded RCTs which only recruited people with non-venous leg ulcers (e.g. arterial, or mixed) from the review.

Types of interventions

We included trials which compared the use of any compression bandage or stocking or any combination of compression with no compression (e.g. standard care, simple retention bandages, dressings alone) in participants with venous leg ulcers. We excluded trials where intermittent pneumatic compression was the mode of compression being evaluated, as this is the focus of another Cochrane Review (Nelson 2014).

Types of outcome measures

Assessment of outcomes at different follow-up periods

We grouped outcome data using the following time categories; we used our judgement to decide whether statistical pooling within these categories was appropriate.

- Short term: up to eight weeks.
- Medium term: between eight and 24 weeks.
- Long term: more than 24 weeks.

Where relevant, we reported outcomes at the latest time point available (assumed to be length of follow-up, if not specified) and the time point specified in the methods as being of primary interest (if this was different from the latest time point available).

Primary outcomes

The primary effectiveness outcome for this review was ulcer healing. Trialists used a range of different methods for measuring and reporting this outcome. RCTs that reported one or more of the following were considered as providing the most relevant and rigorous measures of wound healing.

- Time to complete wound healing (correctly analysed using survival, time-to-event approaches or median (or mean) time to healing, if it was clear that all wounds were healed at follow-up).
- Proportion of wounds completely healed during follow-up (frequency of complete healing).

We used the study authors' definitions of complete wound healing, and reported these where possible. Where both the complete wound-healing outcomes above were reported for a study, we presented both and gave precedence to time-to-healing in our interpretation where possible.

The primary safety outcome for the review was all reported adverse events. Where reported, and a clear methodology for the collection of adverse event data had been provided, we extracted data for all serious adverse events and all non-serious adverse events. We preferred to focus on the numbers of participants with adverse events in each study arm; the methodology should make it clear whether events were reported at the participant level or, if multiple events/people were reported, that an appropriate adjustment was made for data clustering.

Secondary outcomes

- Participant health-related quality of life/health status: measured using a standardised generic questionnaire such as EQ-5D (Herdman 2011), SF-36 (Ware 1992), SF-12 (Ware 1996) or SF-6 (Craig 2013), or wound-specific questionnaires such as the Cardiff Wound Impact Schedule (Price 2004). We did not include ad hoc measures of quality of life that were not likely to be validated and would not be common to multiple trials.
- Cost effectiveness: within-trial cost-effectiveness analysis comparing mean differences in effects with mean cost differences between the two arms. Data extracted could be incremental mean cost per incremental gain in benefit (incremental cost-effectiveness ratio (ICER)). We also extracted other relative cost-effectiveness measures (e.g. net monetary benefit) and cost analysis findings.
- Mean pain score (including pain at dressing change): measured as a continuous outcome using a validated scale such as a visual analogue scale (VAS) or other recognised measurement instrument.

For changes to this section please see Differences between protocol and review.

Search methods for identification of studies

Electronic searches

We searched the following electronic databases to identify reports of relevant clinical trials:

- the Cochrane Wounds Specialised Register (searched 30 June 2020);
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2020, Issue 5) in the Cochrane Library (searched 30 June 2020);
- Ovid MEDLINE including In-Process & Other Non-Indexed Citations (1946 to 30 June 2020);
- Ovid Embase (1974 to 30 June 2020);
- EBSCO CINAHL Plus (Cumulative Index to Nursing and Allied Health Literature; 1937 to 30 June 2020).

The search strategies for the Cochrane Wounds Specialised Register, CENTRAL, Ovid MEDLINE, Ovid Embase and EBSCO CINAHL Plus can be found in Appendix 1. We combined the Ovid MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximising version (2008 revision) (Lefebvre 2021). We combined the Embase search with the Ovid Embase filter developed by the UK Cochrane Centre (Lefebvre 2021). We combined the CINAHL Plus search with the trial filter developed

by Glanville 2019 (Differences between protocol and review). There were no restrictions by language, date of publication or study setting.

We also searched the following trials registries:

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov) (searched 30 June 2020);
- World Health Organization (WHO) International Clinical Trials Registry Platform (apps.who.int/trialsearch/) (searched 28 August 2019). We could not search this database 30 June 2020 as it was unavailable due to heavy traffic generated by the COVID-19 situation.

Search strategies for clinical trial registries can be found in Appendix 1.

Searching other resources

We identified other potentially eligible trials or ancillary publications by carrying out a search of the reference lists of retrieved included trials, as well as relevant systematic reviews, meta-analyses and clinical practice guidelines for leg ulcers (Australian Wound Management Association 2011; Bolton 2014; Franks 2016; Marston 2016; O'Donnell 2014; SIGN 2010; Wittens 2015).

When necessary, we contacted authors of key papers and abstracts to request further information about their trials.

We did not perform a separate search for adverse effects of interventions used, but considered adverse effects described in included studies only.

Data collection and analysis

We carried out data collection and analysis according to the methods stated in the published protocol (Shi 2019), which were based on the *Cochrane Handbook for Systematic Reviews of Interventions* (McKenzie 2021). Changes from the protocol or previous published versions of the review are documented in Differences between protocol and review.

Selection of studies

Two review authors independently assessed the titles and abstracts of the citations retrieved by the searches for relevance. After this initial assessment, we obtained full-text copies of all studies considered to be potentially relevant. Two review authors independently checked the full papers for eligibility, with disagreements resolved by discussion and, where required, the input of a third review author. Where the eligibility of a study was unclear we contacted study authors. We recorded all reasons for exclusion of studies for which we obtained full-text copies. We completed a PRISMA flowchart to summarise this process (Liberati 2009).

Where studies were reported in multiple publications or reports, we obtained all publications. Whilst the study was included only once in the review, obtaining all publications maximised the amount of data we extracted. We also examined any relevant retraction statements and errata for information.

Data extraction and management

We extracted and summarised details of the eligible studies using a data extraction sheet. One review author extracted data and another review author independently checked all data (Differences between protocol and review). We resolved any disagreements through discussion, consulting a third review author where required. Where data were missing from reports, we contacted the study authors to obtain this information.

Where possible we extracted the following data:

- country of origin;
- trial design (e.g. parallel, cluster);
- study start date and end date;
- study population, including key related medical histories, diagnosis methods, the aetiology of leg ulcers (e.g. post-thrombotic syndrome, varicose veins, chronic venous reflux), the onset or recurrence of leg ulcers, and the location of leg ulcers;
- care setting;
- eligibility criteria and key baseline participant data (total number of participants, age, sex, duration of leg ulcers, baseline leg ulcer area);
- details of the interventions, including compression devices used, and duration of interventions applied;
- descriptions of any co-interventions or standard care;
- follow-up period;
- unit of randomisation (e.g. leg ulcer, limb, or participant);
- numbers of participants randomised to each intervention;
- unit of analyses;
- number of ulcers per person;
- primary and secondary outcomes measured;
- data about time to complete wound healing: hazard ratio (HR) and its 95% confidence interval (CI), or any data that will allow its calculation (Parmar 1998; Tierney 2007);
- data on the proportion of wounds completely healed during follow-up: odds ratio (OR) and its 95% CI, or numbers of participants who have leg ulcers completely healed in each arm, both at the latest time point and (if different) at another time specified as of primary interest in the Methods section;
- whether a Kaplan Meier plot was displayed;
- missing data rates per arm, and reasons for 'missingness', including the number of people who died;
- publication status of study; and
- source of funding for trial.

Assessment of risk of bias in included studies

Two review authors independently assessed each included study using the Cochrane tool for assessing risk of bias (Higgins 2017). This tool addresses seven specific domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete data, selective outcome reporting, and other issues (Differences between protocol and review). In this review we included unit-of-analysis issues under the domain of 'other issues', for example where a cluster-randomised trial had been undertaken but analysed at the individual level in the study report. We assessed blinding of participants and personnel, blinding of outcome assessment,

and incomplete outcome data for each of the review outcomes separately. We note that blinding of participants and personnel as to whether or not participants had been allocated to compression is impossible and therefore performance bias is a risk. Performance bias may be introduced when awareness of treatment allocation results in deviations from intended interventions and/or differential co-interventions use or care between groups not specified in study protocol which may influence outcomes. We scrutinised study reports and protocols (where available) to understand if, and how, studies attempted to minimise and document protocol deviations and differential care/co-interventions compensated for this: for example, the study protocol might have been used to highlight the need to balance co-interventions as well as potentially measuring and reporting this.

We assessed risk of bias for each domain as either low risk, high risk or unclear risk. Since wound healing is a subjective outcome, unblinded outcome assessment represents a high risk of bias (Hróbjartsson 2012). We therefore recorded only open intervention studies with blinded outcome assessment as being at low risk of detection bias.

We resolved all disagreements in risk-of-bias assessment by discussion and, where required, we sought the input of a third review author. Where possible, useful and feasible, when a lack of reported information resulted in a judgement of unclear risk of bias, we contacted study authors for clarification. We present our assessment of risk of bias using two risk-of-bias summary figures; one is a summary of bias for each item across all studies, and the second shows a cross-tabulation of each trial by all of the risk-of-bias items. We classified studies with an assessment of high risk of bias for one or more of the seven domains as being at high risk of bias overall for the specified outcome (Differences between protocol and review).

For trials using cluster randomisation, we planned to consider the risk of bias in relation to: recruitment bias, baseline imbalance, loss of clusters, incorrect analysis and comparability with individually-randomised trials (Higgins 2017; Eldridge 2016) (Appendix 2). However, we did not include any studies with a cluster design.

Measures of treatment effect

For dichotomous outcomes (e.g. proportion of participants who have wounds completely healed during follow-up), we present the risk ratio (RR) with 95% confidence intervals (CIs). For continuous outcomes we present the mean difference (MD) with 95% CIs, for trials that used the same assessment scale. If trials that reported continuous data used different assessment scales, we present the standardised mean difference (SMD) with 95% CIs.

Time-to-event data (e.g. time to complete wound healing) are reported as hazard ratios (HRs) where possible, in accordance with the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2021). If studies reporting time-to-event data (e.g. time to healing) did not report a HR, then, when feasible, we estimated this using other reported outcomes (such as numbers of events) through the application of available statistical methods (Parmar 1998; Tierney 2007). We only considered median time to healing without survival analysis as a valid outcome if reports specified that all leg ulcers had healed (i.e. if the trial authors treated time-to-healing as a continuous measure, as there was no censoring).

Unit of analysis issues

We noted whether trials presented outcomes at the level of the leg ulcer, the limb or the participant, and whether there may have been multiple ulcers reported for the same participant. One included study (Kikta 1988) randomised at the participant level and outcomes were measured at the wound level, e.g. leg ulcer healing; we treated the participant as the unit of analysis when the number of leg ulcers assessed appeared to be equal to the number of participants (e.g. one leg ulcer per person).

A particular unit-of-analysis issue may occur in trials if randomisation was carried out at the participant level, with the allocated treatment used on multiple leg ulcers per participant, but data are presented and analysed per leg ulcer (clustered data). We noted whether data for multiple ulcers on a participant were (incorrectly) treated as independent within a study, or were analysed using within-participant analysis methods. If clustered data were incorrectly analysed, we recorded this as part of the risk-of-bias assessment. For an individually-randomised trial, such data on multiple leg ulcers were collected and analysed where applicable:

- only in a proportion of participants; in this case, we only extracted and presented relevant data but did not treat the trial as a cluster trial to seek for an analysis because the trial incorrectly included a mixture of individual and clustered data; or
- in all participants; in this case, we planned to treat the trial as a cluster trial and incorporate relevant data in meta-analyses if the trial was analysed correctly. Where a cluster trial was incorrectly analysed, we planned to record this in the risk-of-bias assessment. Where possible we planned to approximate the correct analyses based on guidance in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2021).

Useful information for approximating the correct analyses include:

- the number of clusters randomised to each arm or the average size of each cluster;
- the outcome data ignoring the cluster design; and
- an estimate of the intracluster correlation coefficient (ICC).

However, we did not include any cluster trials. As noted above, we analysed data that were available in one of three included studies that randomised individual participants but reported data by ulcers (i.e. clustered data).

For cross-over trials, we planned to only consider outcome data at the first intervention phase (i.e. prior to cross-over) as eligible. However, we were not able to obtain such data from the authors of the only cross-over trial included.

Dealing with missing data

It is common for there to be data missing from trial reports. Excluding participants from the analysis post-randomisation or ignoring participants who are lost to follow-up compromises the randomisation and potentially introduces bias into the trial. If we thought that study authors might be able to provide some missing data, we attempted to contact them, but it is likely that data will often be missing because of loss to follow-up.

In individual studies, when data for the proportion of leg ulcers healed were presented, we assumed that randomly-assigned participants not included in an analysis had an unhealed leg ulcer at the end of the follow-up period (i.e. they were considered in the denominator but not in the numerator). We examined the impact of this assumption through doing a sensitivity analysis (see Sensitivity analysis) in which we assumed participants with missing data had a healed leg ulcer (i.e. they were included in both the numerator and the denominator). When a trial did not specify participant group numbers before dropout, we presented only complete-case data. For the time-to-healing analysis using survival analysis methods, dropouts should be accounted for as censored data. Hence all participants contribute to the analysis. We acknowledged that such analysis assumes that dropouts were missing at random and that there was no pattern of 'missingness'.

We presented data for all categorical secondary outcomes as a complete-case analysis. For continuous secondary outcome variables (i.e. quality of life, pain score), we presented available data from the study reports/study authors and did not impute missing data. We planned to calculate measures of variance when these were missing (Deeks 2021) or we planned to contact study authors, where possible. Where these measures of variation remained unavailable, we planned to exclude the study from any relevant meta-analyses. However, we did not carry out these because all relevant included studies either fully reported the measures of variance or only reported narrative findings.

Assessment of heterogeneity

Assessment of heterogeneity can be a complex, multi-faceted process. Firstly, we considered clinical and methodological heterogeneity, that is the degree to which the included studies varied in terms of participants' characteristics (e.g. mean age, proportion of participants by sex, methods of diagnosing leg ulcers), interventions (e.g. delivery approaches of compression systems), outcome definitions and other characteristics such as duration of follow-up. This assessment of clinical and methodological heterogeneity was supplemented by information about statistical heterogeneity. We assessed statistical heterogeneity using the Chi^2 test (a significance level of P value less than 0.10 was considered to indicate statistically significant heterogeneity) in conjunction with the I^2 measure (Higgins 2003). I^2 examines the percentage of total variation across RCTs that is due to heterogeneity rather than chance (Higgins 2003). Very broadly, we considered that I^2 values of 25% or less did not indicate important heterogeneity, and values of more than 75% indicated considerable heterogeneity (Deeks 2021; Higgins 2003).

These statistical tests are recognised to be underpowered and should only be used as an indicator of heterogeneity. Clinical, methodological and statistical heterogeneity should therefore be considered together for the overall assessment of heterogeneity. Where there was no clinical or statistical heterogeneity, we used a fixed-effect model. In the absence of clinical heterogeneity and in the presence of some statistical heterogeneity (I^2 over 50%), we used a random-effects model; however, we did not anticipate pooling data across studies where heterogeneity was considerable (I^2 over 75%). Where there was evidence of considerable heterogeneity we explored this further if required: see Data synthesis.

Assessment of reporting biases

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. Publication bias is one of a number of possible causes of small-study effects, that is, a tendency for estimates of the intervention effect to be more beneficial in smaller RCTs. Funnel plots allow a visual assessment of whether small-study effects may be present in a meta-analysis. A funnel plot is a simple scatter plot of the intervention effect estimates from individual RCTs against some measure of each trial's size or precision (Page 2021). Funnel plots are only informative when there are a substantial number of studies included in an analysis; we planned to present funnel plots for meta-analyses that included at least 10 RCTs, using Review Manager 5 (RevMan 2020). However, we did not produce any funnel plots because all the meta-analyses we conducted contained fewer than 10 studies.

Data synthesis

We summarised details of included studies in a narrative review according to the comparison between intervention and comparator, the participants, and the outcome measurement including the follow-up duration. We considered clinical and methodological heterogeneity and undertook pooling if studies appeared appropriately similar in terms of participants, intervention comparison, and outcome assessment including follow-up duration. Where studies were not similar enough for pooling, we present the results of included studies narratively.

Once we had decided to pool the results of individual studies, we used a random-effects approach for meta-analysis. Conducting meta-analysis with a fixed-effect model in the presence of even minor heterogeneity may provide overly-narrow confidence intervals. We planned to only use a fixed-effect approach when clinical and methodological heterogeneity was assessed to be minimal, with the assumption that a single underlying treatment effect was being estimated. We used Chi^2 and I^2 to quantify heterogeneity but not to guide the choice of model for meta-analysis. We exercised caution when meta-analysed data were at risk of small-study effects, because a random-effects model may be unsuitable. In this case, or where there were other reasons to question the selection of a fixed-effect or random-effects model, we assessed the impact of the approach using sensitivity analyses to compare results from alternate models (Thompson 1999). We reported any evidence that suggested that the use of a particular model might not be robust.

We produced pooled estimates of the treatment effect using Review Manager 5 (RevMan 2020) and presented data using forest plots where possible. For time-to-event data, we plotted (and, if appropriate, pooled) estimates of HRs and 95% CIs as presented in the study reports, using the generic inverse variance method in Review Manager 5 (RevMan 2020). Where time-to-healing was analysed as a continuous measure, but it was not clear if all wounds healed, we documented use of the outcome in the study, but did not summarise or use the data in any meta-analysis.

We included only the relevant arms where a trial involves multiple arms. If two or more arms in comparison with control were eligible for the same meta-analysis, we pooled data on the two or more arms and compared them with control.

Subgroup analysis and investigation of heterogeneity

When there appeared to be considerable between-study heterogeneity we planned to explore the causes using the steps proposed by Cipriani 2013:

- check the data extraction and data entry for errors and possible outlying studies;
- if outliers existed, perform sensitivity analysis by removing them; and
- if heterogeneity was still present, we planned to perform subgroup analyses/meta-regression for study-level characteristics (see below) in order to explain heterogeneity as much as possible (Thompson 1999).

For subgroup analysis/meta-regression, we considered four study-level characteristics: funding sources (binary: not-for-profit versus other/unclear); overall risk of bias (binary: low and unclear risk of bias versus high risk of bias); study designs (binary: parallel versus other designs); and follow-up duration (continuous). However, none of our meta-analyses or syntheses included more than 10 studies for a feasible subgroup analysis, so we did not undertake subgroup analysis by any of these factors.

Sensitivity analysis

For pooled analyses, where possible, we undertook sensitivity analyses to explore the impact of the following:

- assuming participants with missing data had a healed leg ulcer (i.e. they were included in both the numerator and the denominator) followed by the analysis with the assumption that participants with missing data had unhealed leg ulcers;
- removing unpublished data (i.e. abstracts and dissertations) from the analysis;
- changing effects model (i.e. using random-effects model for the main analysis, followed by a repeated analysis with a fixed-effect model); and
- removing clustered data from the analysis.

Summary of findings and assessment of the certainty of the evidence

We presented the main results of the review in summary-of-findings tables. These tables present key information about the certainty of the evidence, the magnitude of the effects of the interventions examined and the sum of available data for the main outcomes (Schünemann 2021).

We present the following outcomes in the summary-of-findings tables:

- time to complete wound healing when analysed using appropriate survival analysis methods;
- proportion of wounds completely healed during the trial period;
- all reported adverse events;
- participant health-related quality of life/health status;
- cost effectiveness;
- mean pain score (Differences between protocol and review).

We used the principle of the GRADE approach to assess the certainty of the body of evidence associated with all outcomes (see Quality of the evidence). The GRADE approach defines the certainty of a body of evidence for the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The assessment of the certainty of a body of evidence using the GRADE approach involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schünemann 2021). The certainty of evidence can be assessed as being high, moderate, low or very low; RCT evidence has the potential to be high certainty.

When making decisions about methodological quality, we downgraded our assessment of the certainty of the evidence only when studies were classed as being at an overall high risk of bias. We did not downgrade for assessments of unclear overall risk of bias unless an outcome finding had unclear risk of bias in all domains, where we considered it as being at high overall risk of bias.

In assessing the precision of effect estimates we followed GRADE guidance using the combination of optimal information size (OIS), and the 95% CIs of effect estimates:

- if the OIS criterion was not met, downgraded for imprecision, unless the sample size was very large (at least 2000, and perhaps 4000, participants);
- if the OIS criterion was met and the 95% CI excluded no effect (i.e. the CI around the RR excludes 1.0), did not downgrade for imprecision; and
- if the OIS criterion was met, and the 95% CI overlapped no effect (i.e. CI includes RR of 1.0) downgraded for imprecision if the CI failed to exclude important benefit or important harm (i.e. the 95% CIs included a relative risk reduction or increase of 25% or more).

For binary outcomes, we calculated the OIS on the basis of a relative risk reduction or increase of between 20% and 30%, as outlined in the GRADE Handbook and summarised below.

- Time to wound healing: OIS = 524 participants for a reduction in hazard of time to healing of 25% (with 100 days' recruitment and 100 days' follow-up: 80% power; alpha 5% and median time to healing in control group of 90 days).
- Proportion of wounds healed: OIS = 308 participants for an increased relative risk of wound healing of 25% (80% power; alpha 5%; proportion healed in control group = 45.08%).
- All reported adverse events: OIS = 295 participants for a decreased relative risk of adverse events of 25% (80% power; alpha 5%; proportion reported adverse events in control group = 45%).

For continuous outcomes, we used the rule-of-thumb threshold (OIS = 400) suggested by Schünemann 2013.

We considered downgrading twice for imprecision when, in addition to the rules above, the number of outcome events was considered to be low.

When assessing the remaining domains, we followed GRADE guidance (Schünemann 2013). Where data were not pooled we presented GRADE assessments for the above outcomes narratively in a summary-of-findings table (Murad 2017).

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies; and Characteristics of studies awaiting classification.

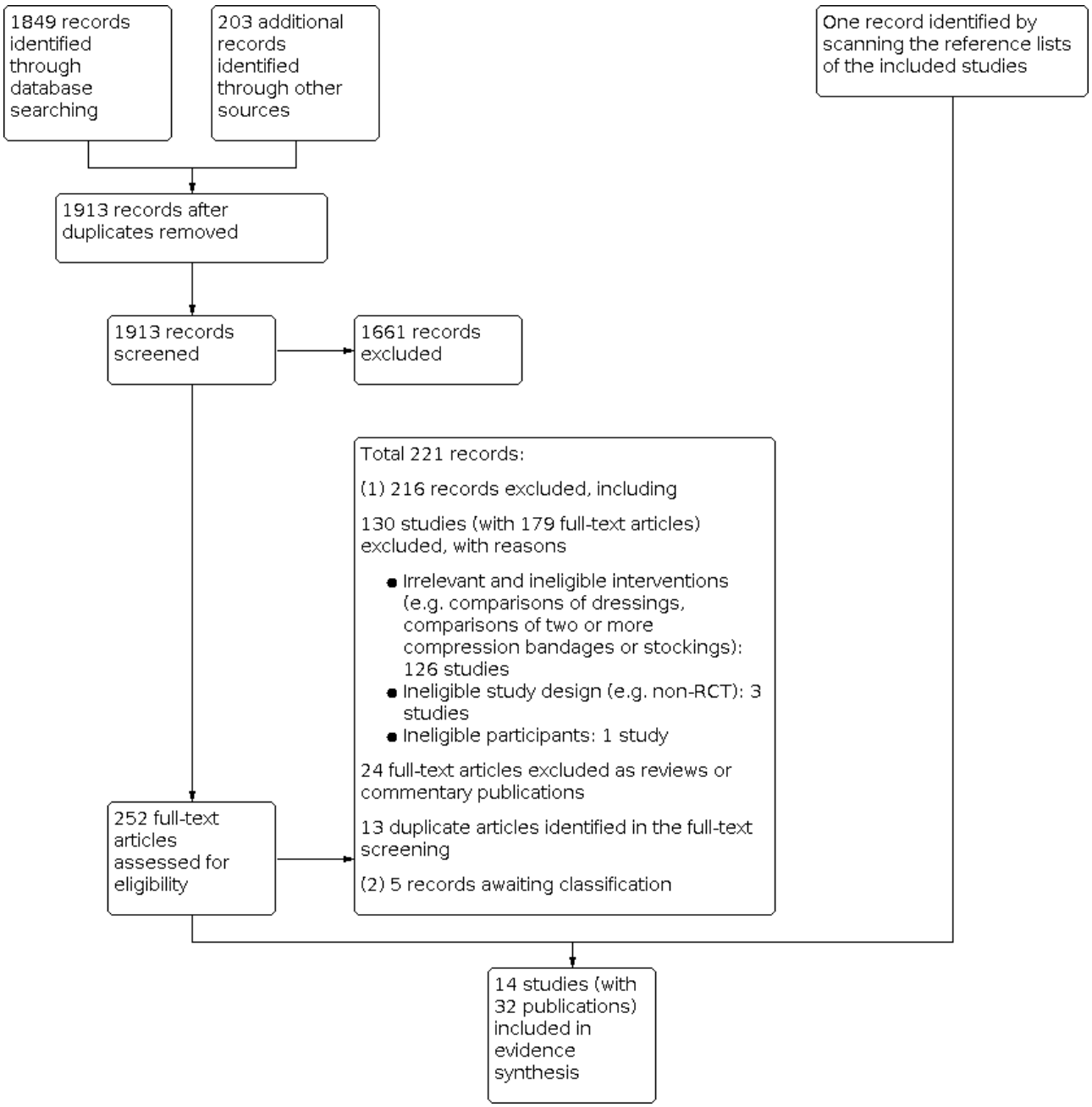
Results of the search

The electronic searches identified 2052 records, including 1849 from electronic databases and 203 from trial registries. We excluded 139 duplicate records and screened 1913 records, of which we identified 252 as potentially eligible and obtained them in full-text. Following full-text screening we considered 31 records of 13 studies to be eligible for inclusion in this review (Cardoso 2019; Charles 1991; Daróczy 2006; Eriksson 1984a; Kikta 1988; Morrell 1998; O'Brien 2003; Rubin 1990; Taradaj 2007; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012).

From other resources, we identified Groenewald 1984 by scanning the reference list of Kikta 1988.

In total we include 14 studies (with 32 publications) in this review, of which Wong 2008a and Wong 2008b were from the same doctoral thesis: Wong 2008a was a feasibility study and Wong 2008b was the associated full trial. See Figure 1.

Figure 1. Study flow diagram.



Included studies

Types of studies

Of the 14 included studies (all RCTs) 13 had a parallel-group design (Charles 1991; Daróczy 2006; Eriksson 1984a; Groenewald 1984; Kikta 1988; Morrell 1998; O'Brien 2003; Rubin 1990; Taradaj 2007; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012), and Cardoso 2019 applied a cross-over design.

Ten of the 14 studies used individual participants as the unit of randomisation and analysis (Daróczy 2006; Eriksson 1984a; Groenewald 1984; Morrell 1998; O'Brien 2003; Rubin 1990; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012); one appeared to use legs as the unit of randomisation (i.e. randomising legs affected by venous ulcers into different study arms) and analysed outcome data by ulcers (Cardoso 2019); and three appeared to have individuals as the unit of randomisation but ulcers as the unit of analysis (Charles 1991; Kikta 1988; Taradaj 2007).

Of the 14 studies, eight had two arms and six had three arms (Daróczy 2006; Eriksson 1984a; Taradaj 2007; Wong 2008a; Wong 2008b; Wong 2012), while two of these (Daróczy 2006; Taradaj 2007) had a third arm that was not relevant to this review.

Five of the 14 included studies (with 854 participants) were conducted at more than one research site (Kikta 1988; Morrell 1998; Rubin 1990; Wong 2008b; Wong 2012). The included studies were conducted in: Brazil (Cardoso 2019), Hong Kong (Wong 2008a; Wong 2008b; Wong 2012), Hungary (Daróczy 2006), Ireland (O'Brien 2003), Poland (Taradaj 2007), Sweden (Eriksson 1984a), South Africa (Groenewald 1984), the UK (Charles 1991; Morrell 1998; Taylor 1998), and USA (Kikta 1988; Rubin 1990), most of which are high-income and upper-middle-income economies.

In the 14 studies the median follow-up duration was 12 weeks (range: one day to 12 months).

Types of participants

Age and sex at baseline

The 14 studies enrolled a total of 1391 participants with venous leg ulcers (median study sample size: 51 participants; range: 11 to 321). Across the eight studies that specified participant sex (Cardoso 2019; Morrell 1998; O'Brien 2003; Taradaj 2007; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012), 526 (50.1%) of participants were male and 524 (49.9%) were female. The average participant age was specified in 11 studies, with a median of 70.1 years (range: 58.0 to 76.5 years) (Cardoso 2019; Charles 1991; Daróczy 2006; Eriksson 1984a; Morrell 1998; O'Brien 2003; Taradaj 2007; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012).

The aetiology of leg ulcers

Of the 14 studies, 12 (917 participants) described their participants as those with leg ulcers and with some markers of a venous aetiology, in terms of either a history or clinical evidence of chronic venous disease or a confirmed chronic venous insufficiency, or both (Cardoso 2019; Daróczy 2006; Kikta 1988; O'Brien 2003; Taradaj 2007; Wong 2008a; Wong 2008b; Wong 2012); having an ankle pressure/brachial pressure ratio (APBI) greater than 0.8 (Charles 1991; Morrell 1998; O'Brien 2003; Rubin 1990; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012) or 0.9 (Taradaj 2007). The two remaining studies described their participants as people with venous leg ulcers but did not specify the aetiology of leg ulcers or APBI value (Eriksson 1984a; Groenewald 1984).

Duration of leg ulcers and ulcer size at baseline

Of the 14 studies, nine reported the average duration of leg ulcers at baseline; the median was 22.0 months (range: 9.0 weeks to 31.6 months) (Charles 1991; Groenewald 1984; Kikta 1988; Morrell 1998; O'Brien 2003; Taradaj 2007; Wong 2008a; Wong 2008b; Wong 2012). Additionally, 11 of the 14 studies reported the average area size of leg ulcers at baseline: three studies (278 participants) having ulcers on average smaller than 5 cm^2 (Daróczy 2006; O'Brien 2003; Taylor 1998); four studies (615 participants) having ulcers between 5 and 10 cm^2 (Kikta 1988; Wong 2008a; Wong 2008b; Wong 2012); two studies (286 participants) having ulcers between 10 and 20 cm^2 (Charles 1991; Morrell 1998); and two studies (85 participants) with ulcers larger than 20 cm^2 (Rubin 1990; Taradaj 2007).

Care settings

Care settings were specified for 10 studies: two recruited participants from hospitals (Cardoso 2019; Taradaj 2007); one from an outpatient setting (Groenewald 1984); and seven from community settings (Charles 1991; Morrell 1998; O'Brien 2003; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012).

Types of interventions

Compression bandages or stockings (including the duration of applying compression and the frequency of changes) and comparators evaluated in the 14 studies are listed in Table 1.

A variety of compression bandages or stockings was evaluated in the 14 included studies, including elastic short-stretch bandages (five studies; Charles 1991; Taradaj 2007; Wong 2008a; Wong 2008b; Wong 2012); four-layer bandages including the Charing Cross bandaging technique (six studies; Morrell 1998; Taylor 1998; O'Brien 2003; Wong 2008a; Wong 2008b; Wong 2012); and Unna's boot (five studies; Cardoso 2019; Eriksson 1984a; Groenewald 1984; Kikta 1988; Rubin 1990). One study (Daróczy 2006) did not specify the type of compression therapies used. The sub-bandage resting pressure applied was specified in seven studies (854 participants; Cardoso 2019; Charles 1991; O'Brien 2003; Taradaj 2007; Wong 2008a; Wong 2008b; Wong 2012) with a minimum of 18 mmHg and a maximum of 50 mmHg, whilst other studies (537 participants) did not specify the pressure level.

A wide range of treatments was described as comparators, including medicines (two studies; Daróczy 2006; Taradaj 2007), usual care received from district nurses (three studies; Charles 1991; Morrell 1998; Taylor 1998); and dressings (nine studies; Cardoso 2019; Eriksson 1984a; Groenewald 1984; Kikta 1988; O'Brien 2003; Rubin 1990; Wong 2008a; Wong 2008b; Wong 2012). Of the 14 studies, 10 (878 participants) did not specify the use of compression bandages or stockings for participants in comparators arms; three studies stated that their comparators did not preclude compression bandages or stockings (469 participants; Morrell 1998; O'Brien 2003; Taylor 1998) and one (44 participants; Eriksson 1984a) replaced one control arm with double-layer bandage during the study period as the treatments used as the comparator were unavailable.

Seven studies specified co-interventions they applied (e.g. specific dressings) (Charles 1991; Groenewald 1984; Kikta 1988; Rubin 1990;

Taradaj 2007; Taylor 1998; Wong 2012), all stated or indicated that the same co-interventions were applied in all study groups.

Source of funding

Of the 14 included studies, six specified the sources of funding, including: Morrell 1998 funded by a public health authority; O'Brien 2003 and Taylor 1998 financially supported by the producers of compression devices; Wong 2008a and Wong 2008b funded by a university; and Wong 2012 funded by both a public authority and device companies.

Excluded studies

We excluded 130 studies (with 179 records). The main reasons for exclusions were: irrelevant and ineligible interventions (e.g. comparisons of dressings, comparisons of two or more compression bandages or stockings; 126 studies); ineligible study design (e.g. non-RCT; 3 studies); and ineligible participants (one study). We also identified 13 duplicates in screening full texts (see Figure 1).

Ongoing studies

We did not identify any ongoing studies.

Studies awaiting classification

We identified five studies (five records) that we could not classify as being eligible or not, as we were unable to obtain the full-text versions despite extensive efforts, in part due to more limited access to intra-library loans during the COVID-19 period (Cherry 1990; Jünger 2008; Kuznetsov 2009; Robinson 1988; Stacey 2000).

Risk of bias in included studies

We summarise risk-of-bias assessments for the primary outcome of this review in Figure 2 and Figure 3.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

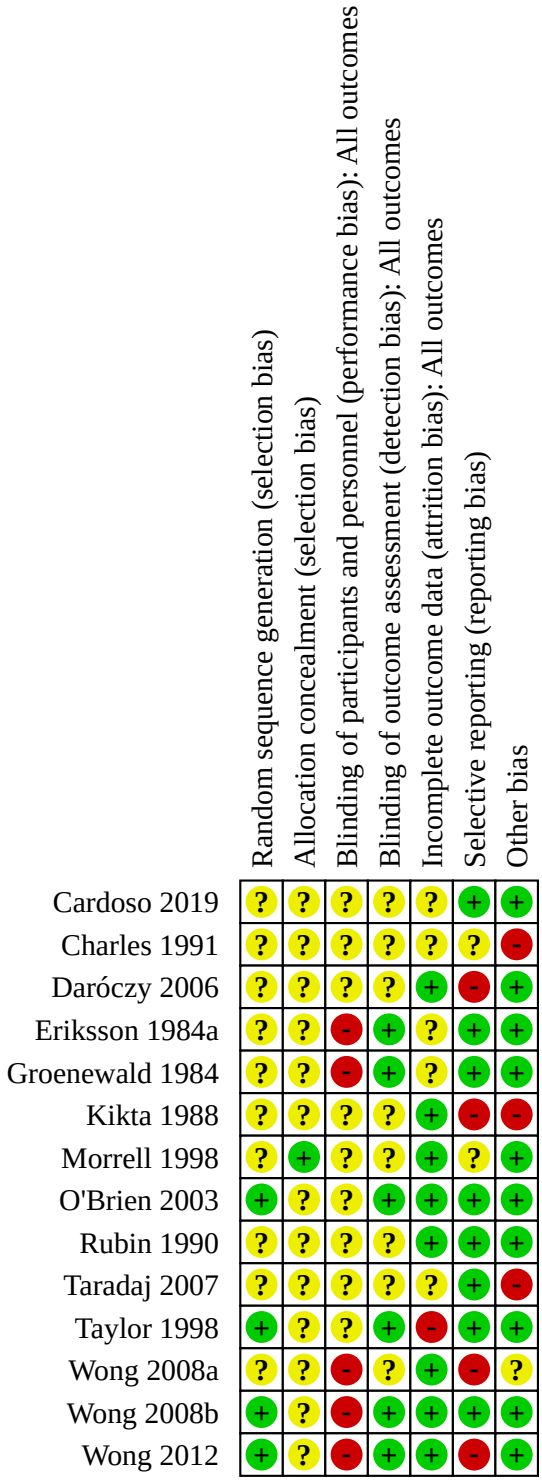
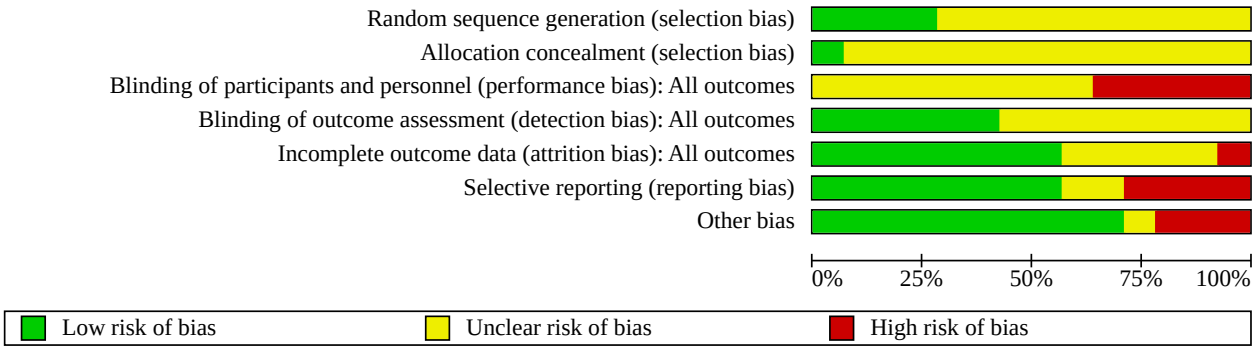


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



We judged four of the 14 studies to have an unclear overall risk of bias for the primary outcome (Cardoso 2019; Morrell 1998; O'Brien 2003; Rubin 1990). We judged the remaining 10 studies as having findings at high overall risk of bias.

Allocation

Of the 14 studies, four used appropriate methods to generate the random sequence and were judged to have low risk of selection bias (O'Brien 2003; Taylor 1998; Wong 2008b; Wong 2012). The remaining 10 studies did not adequately describe the randomisation methods.

Of the 14 studies, only Morrell 1998 was judged to have low risk of selection bias due to allocation concealment, because serially-numbered, sealed, opaque allocation envelopes were used to adequately conceal allocation. The remaining 13 studies had an unclear risk of bias judgement due to the lack of relevant information.

Blinding

Five of the 14 studies were judged as being at high risk of performance bias for the leg-ulcer healing outcome because they clearly stated that the blinding of participants and personnel was difficult to implement or was not implemented (Eriksson 1984a; Groenewald 1984; Wong 2008a; Wong 2008b; Wong 2012); and it was unclear if attempts were made to mitigate the risk. The remaining nine studies did not give sufficient information for judging if their risk of performance bias was high or low.

We judged six of the 14 studies to have low risk of detection bias for leg-ulcer healing outcome (Eriksson 1984a; Groenewald 1984; O'Brien 2003; Taylor 1998; Wong 2008b; Wong 2012): all six studies applied devices to measure leg ulcer areas reliably, or involved independent outcome assessors for outcome measurement, or both. The remaining eight studies did not give sufficient information for judging if their risk of detection bias was high or low.

Incomplete outcome data

Of the 14 studies, Taylor 1998 was judged to have high risk of attrition bias for the leg-ulcer healing outcome because there was a high proportion of dropouts and intention-to-treat (ITT) analysis was not performed. We rated eight studies at low risk of attrition bias (Daróczy 2006; Kikta 1988; Morrell 1998; O'Brien 2003; Rubin 1990; Wong 2008a; Wong 2008b; Wong 2012): all had low attrition rates (or no attrition), or ITT analysis was performed, or both. The remaining five studies had an unclear risk of bias judgement.

Selective reporting

We judged four of the 14 studies to be at high risk of reporting bias (Daróczy 2006; Kikta 1988; Wong 2008a; Wong 2012). The feasibility study by Wong 2008a measured multiple outcomes but only reported week-12 ulcer-healing outcome data. There were two publications for the Wong 2012 study, with one retracted by the corresponding journal; but the retracted publication appeared to contain a specific outcome that was not included in the unretracted publication. Charles 1991 and Morrell 1998 were judged as being at unclear risk of reporting bias and the remaining eight studies appeared to be free of this bias.

Other potential sources of bias

Of the 14 studies, we rated three at high risk of other bias because they used individuals as the unit of randomisation but leg ulcers as the unit of analysis (Charles 1991; Kikta 1988; Taradaj 2007). We judged Wong 2008a to be at unclear risk of other bias. We judged all the remaining studies to be free of other bias.

Effects of interventions

See: **Summary of findings 1** Compression bandages or stockings compared with no compression for treating venous leg ulcers

See Summary of findings 1.

Unless otherwise stated we used a random-effects analysis throughout; each pooled result presented is an average effect, rather than a common effect, and should be interpreted as such.

Comparison 1: Compression bandages or stockings compared with no compression (14 studies, 1391 participants)

All 14 studies assessed this comparison, of which Cardoso 2019 did not report analysable data for any outcomes.

Primary outcomes

Time-to-complete wound healing (follow-up period one day to 12 months)

Seven studies (1096 participants) reported this outcome. See Appendix 3 for the outcome data. We were unable to collect

analysable data from Daróczy 2006 and Taylor 1998. We pooled time-to-event data from five studies (733 participants: Kikta 1988; Morrell 1998; O'Brien 2003; Taylor 1998; Wong 2008b). Note that Wong 2008b reported a multivariable analysis adjusted for covariates (age, initial ulcer size, and ulcer duration). Kikta 1988 contained clustered data (participants randomised but outcome data reported on multiple ulcers for some participants); as the number of ulcers (87 ulcers) was close to the number of participants (n = 84) ulcer-level data were included here. The pooled hazard ratio (HR) for healing is 2.17 (95% confidence interval (CI) 1.52 to 3.10; I^2 = 59%; Analysis 1.1).

Moderate-certainty evidence suggests there is probably a shorter time to complete healing of venous leg ulcers in people wearing compression bandages or stockings compared with those not wearing compression. We downgraded the evidence across the five studies once for risk of bias (one study with clustered data and another small study were at high overall risk of bias in domains other than performance bias, and the other three studies with most of the data in this synthesis were at unclear overall risk of bias).

Subgroup analysis

As noted above, these studies are heterogeneous in terms of unit of analysis, care setting, follow-up durations, risk of bias, and compression therapies applied. However, we did not perform any prespecified subgroup analysis because there are fewer than 10 studies.

Sensitivity analyses

- ***Sensitivity analysis of removing unpublished data (i.e. abstracts and dissertations)*** . When the doctoral thesis Wong 2008b was removed from the data analysis, the evidence remained consistent with the main analysis (Appendix 4).
- ***Sensitivity analysis with fixed-effect rather than random-effects model*** . The use of a fixed-effect model resulted in no change in effect estimates. The evidence remained consistent with the main analysis (Appendix 4).
- ***Post hoc sensitivity analysis of removing clustered data***. When Kikta 1988 was removed, the result remained consistent with the main analysis (Appendix 4).

Proportion of wounds completely healed (follow-up of one day to 12 months)

Ten studies (1215 participants) reported this outcome (Charles 1991; Daróczy 2006; Kikta 1988; Morrell 1998; O'Brien 2003; Rubin 1990; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012). See Appendix 3 for the outcome data.

Eight of the 10 studies reported analysable data: seven studies (1036 participants) (Morrell 1998; O'Brien 2003; Rubin 1990; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012) reported data by participant whilst Kikta 1988 reported clustered data (84 participants with 87 ulcers) but ulcer-level data were included here, as the number of participants approximately equals the number of ulcers. The pooled risk ratio (RR) is 1.77 (95% CI 1.41 to 2.21; I^2 = 65%; Analysis 1.2).

Of the remaining two studies (95 participants) without analysable data, Charles 1991 reported that 71% of leg ulcers completely healed in short-stretch bandages and 25% in usual care. Daróczy 2006 reported that 82% of 21 participants with ulcers healed when using compression plus local povidone-iodine (Betadine) and 62% of 21 participants with ulcers healed when using local povidone-iodine (Betadine).

Across the 10 studies, there is moderate-certainty evidence that people treated with compression bandages or stockings probably have more completely-healed venous leg ulcers during follow-up to 12 months than people not using compression. We downgraded the certainty of the evidence once for risk of bias (of the 10 studies, six with 569/1215 (46.8%) participants were at high risk of bias in the domains other than performance bias and the other four were at unclear risk of bias in some but not all domains).

Subgroup analysis

The studies are heterogeneous in terms of unit of analysis, care setting, follow-up duration, risk of bias, and compression therapies applied and there was some statistical heterogeneity (Chi^2 test P value = 0.006; Tau^2 = 0.06; I^2 = 65%). As noted in Subgroup analysis and investigation of heterogeneity, we removed an extreme value (Morrell 1998) and found that once it was removed, I^2 went from 65% to 0% (Chi^2 test P value = 0.51; Tau^2 = 0.00; I^2 = 0%) but the pooled RR of 1.94 (95% CI 1.67 to 2.26) remained consistent with Analysis 1.2 and still favoured the use of compression bandages or stockings. Morrell 1998 is notably different from the other studies, in that 53% of 3433 participant visits in the control arm involved provision of compression whilst the control arms of other studies either did not deliver compression or only delivered for a small proportion of participants. We did not perform any prespecified subgroup analysis because there are fewer than 10 included studies in Analysis 1.2.

Sensitivity analyses

- ***Sensitivity analysis of considering participants with missing data as having unhealed leg ulcers*** . Four of the eight studies in Analysis 1.2 had missing data (Kikta 1988; Taylor 1998; Wong 2008a; Wong 2008b). The main analysis was not sensitive to considering participants with missing data as having unhealed ulcers (Appendix 4).
- ***Sensitivity analysis of removing unpublished data (i.e. abstracts and dissertations)*** . The main analysis was not sensitive to the removal of the doctoral theses Wong 2008a; Wong 2008b from Analysis 1.2 (Appendix 4).
- ***Sensitivity analysis with a fixed-effect rather than random-effects model*** . The main analysis was not sensitive to application of a fixed-effect model (Appendix 4).
- ***Post hoc sensitivity analysis of removing clustered data***. When Kikta 1988 was removed, the result remained consistent with the main analysis (Appendix 4).

Adverse events (follow-up period 8 weeks to 12 months)

Ten studies reported adverse events (Eriksson 1984a; Groenewald 1984; Kikta 1988; Morrell 1998; O'Brien 2003; Rubin 1990; Taylor 1998; Wong 2008a; Wong 2008b; Wong 2012). See Table 2. However, only three studies appeared to collect adverse event data following a prespecified method: two studies (501 participants) reported data by participant (Wong 2008b; Wong 2012) whilst Kikta 1988 reported clustered data (84 participants with 87 ulcers) and ulcer-level data were included here, as the number of participants approximately equals the number of ulcers. The pooled RR is 0.98 (95% CI 0.25 to 3.80; I^2 = 74%; Analysis 1.3). A post hoc sensitivity analysis of

removing Kikta 1988 that reported clustered data resulted in a pooled RR of 1.60 (95% CI 0.74 to 3.43; I^2 = 40%).

It is uncertain whether there is any difference in the risk of adverse events associated with using compression and not using compression. Evidence is of very low certainty, downgraded once for risk of bias (two studies with the larger numbers of participants were at high risk of bias in some domains and one study contributing 30.6% of the weight was at unclear risk of bias), twice for substantial inconsistency, as the clustered data were inconsistent with the data reported by participant, and once for imprecision because the CIs appeared to include the possibility of both benefit and harm as well as no effect.

Secondary outcomes

Participant health-related quality of life/health status (follow-up period 12 weeks to 12 months)

Five studies (964 participants) reported this outcome and the outcome measurements varied between studies (Morrell 1998; O'Brien 2003; Wong 2008a; Wong 2008b; Wong 2012). We synthesised evidence from all these studies, except for Wong 2008a which did not present the endpoint outcome data.

All data reported in these studies are summarised in Table 3. We pooled data from two studies (426 participants with available data; Wong 2008b; Wong 2012; Analysis 1.4). The MD in the total score of the Charing Cross Venous Ulcer Questionnaire (lower scores = better quality of life) is −6.87 (95% CI −13.10 to −0.64) between using compression bandages or stockings and no compression, which favours the use of compression bandages or stockings. However, Analysis 1.4 showed no difference in the physical component, mental component, and functional status of the SF-12 (higher scores = better quality of life).

Of the two studies that had no analysable data, Morrell 1998 (233 participants) stated that, for most dimensions of the SF-36 and EuroQol, health status deteriorated over time but was not different between four-layer bandages and usual care. O'Brien 2003 (200 participants) reported a statistical difference, favouring the use of compression bandages or stockings, in some dimensions of the SF-36 (including physical function, role-physical, mental health) and the disease-specific quality of life instrument for chronic lower limb venous insufficiency (CIVIQ) (physical, social, and global dimensions), but not in others.

Overall, low-certainty evidence suggests that compression bandages or stockings may improve participant health-related quality of life in some (but not all) aspects during the follow-up of 12 weeks to 12 months in comparison with no compression. We downgraded the certainty of the evidence twice for substantial inconsistency due to the variation in the reported results, particularly for health status.

Cost effectiveness (follow-up period 12 weeks and 12 months)

Three studies (486 participants) reported this outcome (Charles 1991; Morrell 1998; O'Brien 2003), but we were unable to pool their data.

Without reporting any data, Charles 1991 (53 participants) noted that the short-stretch bandage was more cost-effective than usual care, as it could be washed and reused repeatedly. Morrell 1998 (233 participants) reported an incremental cost-effectiveness ratio of GBP 2.46 (95% CI −31.94 to 99.12) per ulcer-free week (1995 prices) associated with using the four-layer bandage in leg-ulcer clinics compared with no compression delivered outside the clinic setting. Using a cost analysis, O'Brien 2003 (200 participants) reported that the median cost per leg healed was significantly less for four-layer bandages than for dressings (P = 0.04).

It is uncertain whether compression bandages or stockings are cost-effective compared with no compression in wound healing. Evidence is of very low certainty, downgraded once for risk of bias (one small study was at high overall risk of bias in domains other than performance bias, and the other two studies were at unclear risk of bias in some domains), once for indirectness (the outcomes in Charles 1991 and O'Brien 2003 did not appear to be expressed as incremental mean cost per incremental gain in benefit), and once for inconsistency in cost-effectiveness results between studies.

Mean pain score (median follow-up period 12 weeks minimum 12 weeks maximum 12 months)

Six studies (1048 participants) reported this outcome, and varied in the way they measured pain (Kikta 1988; Morrell 1998; O'Brien 2003; Wong 2008a; Wong 2008b; Wong 2012). All data reported in the included studies are summarised in Table 4.

Of the six studies, Wong 2008a did not report endpoint outcome data. We pooled data from three studies with analysable data: two (426 participants having available data) reported data by participant (Wong 2008b; Wong 2012), whilst Kikta 1988 reported ulcer-level (clustered) data (69 ulcers with available data) and the ulcer-level data were included here. The analysis showed people using compression bandages or stockings had a lower mean pain score than those using no compression (i.e. dressings) (MD −1.39, 95% CI −1.79 to −0.98; Analysis 1.5). A post hoc sensitivity analysis removing Kikta 1988 that reported clustered data resulted in a pooled MD of −1.48 (95% CI −2.05 to −0.91; I^2 = 29%).

Of the other two studies that did not report analysable data, Morrell 1998 (233 participants) stated that people treated with four-layer bandages were more likely to experience a reduction in leg ulcer pain per month than those using usual care; and O'Brien 2003 (200 participants) reported a lower median of pain scores among those using four-layer bandages than those using dressings (median 18.8, IQR 6.3 to 37.5; and 31.3, 18.8 to 43.8, respectively; P = 0.14).

Moderate-certainty evidence suggests the use of compression probably reduces mean pain score compared with no compression. Across the five studies with data or results synthesised, we downgraded the evidence certainty once for risk of bias, as two studies with 345 participants were at high overall risk of bias.

DISCUSSION

Summary of main results

We report a review of 14 RCTs on the effects of compression compared with no compression on the healing of venous leg ulcers. Compression bandages and stockings used in the included studies varied and some study reports did not adequately define the compression. The most frequently used systems were short-stretch bandages, four-layer compression and Unna's boot. The no-compression comparators also varied across the included studies and included 'usual care' where no details were specified, pharmacological treatment, a variety of dressings, and

a wide variety of treatments where some participants received compression (but it was not the norm).

Primary outcomes

There is moderate-certainty evidence that there is probably a shorter time to complete healing of venous leg ulcers in people wearing compression bandages or stockings compared with those not wearing compression over a 12-month follow-up (five studies with 733 participants); and that people treated with compression bandages or stockings probably have more completely healed venous leg ulcers during follow-up to 12 months than people not using compression (10 studies with 1215 participants). It is uncertain whether there is any difference in adverse effect rates between using compression bandages or stockings and no compression (three studies with 585 participants; very low-certainty evidence).

Secondary outcomes

Moderate-certainty evidence suggests that the use of compression bandages or stockings probably reduces pain compared with no compression (five studies with 859 participants and 69 ulcers in other participants).

There is low-certainty evidence that compression bandages or stockings versus no compression may improve disease-specific quality of life but not all aspects of general health status during the follow-up of 12 weeks to 12 months (four studies with 859 participants).

There is uncertainty as to whether use of compression bandages or stockings is more cost-effective than not using them (three studies with 486 participants).

Overall completeness and applicability of evidence

As a result of the extensive literature searches, we consider that this review covers all potential RCT evidence on compression bandages or stockings versus no compression for healing venous leg ulcers. However, there are limitations in the completeness and applicability of the evidence identified.

Whilst compression bandages and stockings are widely used, data on the effects of compression bandages or stockings on ulcer healing are sparse for the numbers of studies and participants, and the duration of follow-up: 14 studies included in this review enrolled a total of 1391 participants, with a median study sample size of 51 participants (range: 11 to 321). Only four studies enrolled more than 100 participants and they together accounted for 67% (934/1391) of the participants; they were all from community settings that were most represented in the review. Three of these four studies were conducted in more than one research site. The duration of follow-up was relatively short, with a median follow-up duration of 12 weeks.

Participants included in the studies had average ages ranging from 58.0 to 76.5 years. The included studies all described their participants as having venous leg ulcers, but only 66% (917/1391) of participants had leg ulcers with a clearly-specified aetiology (a history or clinical evidence of chronic venous disease, the confirmed cause of chronic venous insufficiency, or both), or had an APBI of greater than 0.8 or 0.9. The duration of leg ulcers amongst study participants had a median of 22.0 months (range: 9.0 weeks to 31.6 months). The average baseline area of leg ulcers amongst study participants also varied: three studies had participants with an average ulcer size of less than 5 cm^2; four had ulcers between 5 and 10 cm^2; two had ulcers between 10 and 20 cm^2; and two had ulcers larger than 20 cm^2.

Participants were recruited from community or outpatient settings and most were from high-income and upper-middle-income economies.

Studies included in this review used a range of compression bandages or stockings, including elastic short-stretch bandages (five studies); four-layer bandage including the Charing Cross bandaging technique (six studies); and Unna's boot (five studies). There were no studies of systems such as inelastic paste systems, e.g. Setocrepe, or two-component bandage systems e.g. 3M Coban 2 Compression System.

The magnitude of sub-bandage resting pressure applied varied between studies: only seven included studies specified the pressure applied for 854 participants (minimum 18 mmHg, maximum 50 mmHg; i.e. moderate or high compression according to Thomas 1995).

Another limitation in the included studies was the variation in comparators applied, including medications (two studies), usual care from community nurses (three studies); and dressings (nine studies). Importantly, in three studies, participants in the no-compression groups could receive compression (Morrell 1998; O'Brien 2003; Taylor 1998), and one small study (Eriksson 1984a) replaced the dressings comparator with compression bandages during the study period.

Whilst this review included a total of 14 studies, there is a very limited evidence base on adverse effects, participant health-related quality of life, and cost effectiveness.

We note that we did not synthesise evidence on the outcome of participant adherence to compression treatment, as we initially planned, because this outcome was only relevant to the compression arm of these studies. Also, studies aiming to evaluate ulcer healing can only provide observational data for the ulcer recurrence outcome. We therefore did not consider evidence on ulcer recurrence as an outcome in this review, as we had initially planned.

Quality of the evidence

We assessed the certainty of evidence for all six outcomes using GRADE. We report our assessment results in Summary of findings 1, where we present the number of studies and the number of participants contributing to evidence synthesis. Evidence from two of the six syntheses was of very low certainty, one was of low certainty and three were of moderate certainty. Our downgrading was largely due to high overall risk of bias, and inconsistency across the studies.

Limitations in study design

We downgraded once for five of the six evidence syntheses for overall risk of bias. When judging overall risk of bias, we considered all domains. However, in assessing evidence certainty, we acknowledge that the blinding of participants and personnel is impractical for the comparison of compression bandages or stockings versus no compression and did not downgrade for this

blinding. We judged that 10 of the 14 studies were at high overall risk of bias and seven of the 10 studies were at high risk of bias in domains other than blinding of participants and personnel.

Indirectness of evidence

We considered all the evidence to be direct (and so did not downgrade), except that two of the three studies included in cost-effectiveness evidence synthesis appeared to report cost analyses rather than full cost-effectiveness evaluations, which express cost effectiveness as incremental mean cost per incremental gain in benefit, or vice versa.

Inconsistency of results and unexplained heterogeneity

We downgraded for inconsistency for three evidence syntheses, largely because we found statistical heterogeneity in these syntheses or inconsistency of reported results between studies. The three outcomes this relates to are adverse events, health-related quality of life, and cost effectiveness.

Note that none of these meta-analyses or syntheses included more than 10 studies for a feasible subgroup analysis; so, despite the fact that we found heterogeneity by unit of analysis, overall risk of bias, care settings, follow-up durations, or compression therapies applied between the included studies, we only considered the unit-of-analysis factor in our evidence syntheses, but did not consider other factors for subgroup analysis.

Imprecision of results

We only downgraded for imprecision for the adverse event synthesis, as the numbers of participants included in other meta-analyses or syntheses were more than our estimated optimal information size (OIS). The downgrading for adverse events was due to the wide confidence intervals in the data analysis.

Publication bias

We did not downgrade for publication bias because firstly we have confidence in the comprehensiveness of our literature searches, and secondly we did not find any clear evidence of non-reporting bias of study results. Although we planned to produce funnel plots for meta-analysis to visually inspect for publication bias, there was no analysis including more than 10 studies.

Potential biases in the review process

We followed prespecified methods to review evidence in order to prevent potential bias in the review process. We ran comprehensive electronic searches, searched trial registries, and checked references of included studies and systematic reviews identified in electronic searches. We also contacted study authors of four studies (Cardoso 2019; Wong 2008a; Wong 2008b; Wong 2012) to clarify details. We included a study that had one retracted publication (Wong 2012).

This review also has limitations. Firstly, we did not consider the differences between specific compression bandages or stockings: four-layer compression, Unna's boot and short-stretch bandages were covered by the generic term of compression bandages or stockings. Similarly, the difference between specific comparators was not considered in this review. Because of these, heterogeneity between studies in this review was inevitable. However, because of the limited number of included studies, we did not undertake subgroup analysis by the types of specific compression bandages or stockings or specific comparators. Secondly, for all of the six outcomes in this review, the included studies measured outcomes differently, or reported outcome data in ways that could not be meta-analysed. For example, of the seven studies which included data for the 'Time to complete wound healing' outcome, we were only able to pool data for five studies (Analysis 1.1). We therefore did not undertake or rely on any single meta-analysis in summarising the findings and assessing the certainty of evidence. We reviewed all studies included for any outcome and assessed the certainty of evidence using the approach described in Murad 2017. Thirdly, in terms of the data on time to complete wound healing, we estimated the HRs and CIs for two studies included in Analysis 1.1 (Kikta 1988; Taylor 1998) using the methods described in Tierney 2007, whilst recognising that those calculated data (and the associated meta-analysis) might be inaccurate. We noted that the time-to-event data analysis using the HRs and CIs we calculated appeared to agree with associated binary data analyses, as we expected.

Agreements and disagreements with other studies or reviews

Our electronic searches identified three systematic reviews or meta-analyses (De Carvalho 2018; Mauck 2014; Weller 2012b) that were published following O'Meara 2012 (the review for which this is a major update).

Of these four reviews, only two had evidence for compression bandages or stockings versus no compression: O'Meara 2012 focused on the clinical effectiveness of using compression bandages or stockings versus no compression on venous leg-ulcer healing, whilst Weller 2012b reviewed RCT-based economic evaluations on this topic.

This review includes all relevant RCTs identified by O'Meara 2012 and Weller 2012b and added a further six studies. This review applied new Cochrane methodological requirements (e.g. the use of GRADE assessments) that were not used in O'Meara 2012 or Weller 2012b. As a result of the inclusion of more studies and applications of new methods, this review provides updated evidence, finding moderate-certainty evidence that use of compression bandages or stockings results in a shorter complete wound-healing time and a higher proportion of people having complete wound healing. This is consistent with O'Meara 2012, concluding that 'there is some evidence that venous ulcers heal more rapidly with compression than without.'

Pain is a common complication experienced by people affected by venous leg ulcers. Although application of compression may cause pain temporarily, ulcer-related pain can be chronic. This review has identified new evidence that the use of compression bandages and stockings probably reduces pain compared with no compression.

Our review also found evidence, albeit uncertain, on the cost effectiveness of using compression bandages and stockings.

AUTHORS' CONCLUSIONS

Implications for practice

People with venous leg ulcers who wear compression bandages or stockings probably experience wound healing more quickly, and more people are likely to experience complete ulcer healing than people who do not wear compression. This is moderate-certainty

evidence, meaning that the true effect is likely to be close to the reported estimate of the effect in this review. Risk of bias of some of the included studies resulted in downgrading of the certainty of evidence. The use of compression bandages or stockings probably reduces pain and may improve disease-specific quality of life. However, uncertainty remains about the relative risks of adverse effects, and the cost effectiveness of compression bandages or stockings versus no compression.

Implications for research

In many countries, compression bandages and stockings have become essential components of care for people with venous leg ulcers. Future research should focus on identifying the most effective and acceptable ways of delivering compression. Future studies should collect and analyse data on adverse events and cost effectiveness, and should explore whether certain modes of compression are associated with more patient adherence and greater acceptability.

Limitations in the existing evidence are due to studies with small sample sizes and suboptimal RCT designs. Given that the baseline prevalence of venous leg ulcers is not high and most people with this condition stay in community settings, future research can be conducted in multiple research sites and should carefully consider sample size calculations. Over-estimation of event rates that fail to occur can lead to imprecision and less robust effect estimates.

Future studies should also consider carefully the choice of outcomes they report; time-to-event data for complete wound healing should be used in trials. Careful and consistent assessment and reporting of adverse events including pain score need to be undertaken. Further studies should aim to collect and report health-related quality of life using validated measures and should include cost-effectiveness analysis where possible. Participant adherence to compression bandages or stockings may be key to successful wound healing and should be considered in any future research.

Any future trials must be undertaken to the highest standard possible. Whilst it is challenging to avoid the risk of performance bias in trials of compression devices, where applicable, strictly implementing a standardised intervention plan can help to minimise risk. It is also important to ensure that protocols mandate balanced use of co-interventions (e.g. dressings) across trial arms. Follow-up periods should be for as long as possible, and clinically relevant in different settings.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Cardoso 2019

Study characteristics	
Methods	**Study objective**: to evaluate the oedema evolution of the venous ulcer–affected lower limb by means of electric bioimpedance with the use of the Unna's boot and the non-compressive dressing **Trial design (e.g. parallel group) including research sites:** cross-over, single site **Follow-up period**: 1 day **Number of arms**: 2 **Study start date and end date**: September 2014 to December 2016 **Care setting**: not described
Participants	**Study population**: adults with venous leg ulcers **Eligibility criteria**: people aged 18 years or older with leg ulcers and a history and physical examination compatible with chronic venous disease included. Exclusion criteria: a history suggestive of chronic arterial disease, active infections, and joint immobility excluded. **Sex (M:F)**: 0:11 **Age (years)**: 50 to 76 years (mean age: 63 years; SD = 7.5 years). **Duration of leg ulcers**: not described **Baseline leg ulcer area**: not described **Group difference**: not described **Total number of participants**: 15 legs of 11 individuals **Unit of analysis (including number of ulcers per person)**: ulcers/legs **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: legs
Interventions	**Intervention characteristics**

Cardoso 2019 *(Continued)*

	Unna's boot • **Details of interventions (including compression devices used, and duration of interventions applied)**: made of 10% zinc oxide, acacia gum, glycerol, castor oil, and deionized water; expected to cause compression of 18 – 24 mmHg • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: not described • **Number of participants analysed**: not described Conventional dressing • **Details of interventions (including compression devices used, and duration of interventions applied)**: not described • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: not described • **Number of participants analysed**: not described
Outcomes	*Time-to-complete wound healing* • Not reported *Proportion of wounds completely healed during follow-up* • Not reported *Adverse events* • Not reported *Participant health-related quality of life/health status* • Not reported *Cost effectiveness* • Not reported *Mean pain score* • Not reported **Outcomes that are not considered in this review but reported in trials**: • Volume of the oedema
Identification	**Publication type/ status (e.g. conference abstract):** full paper **Trial protocol**: not described **Source of funding**: not described **Country of origin**: Brazil **Comments**: this paper formed part of the thesis ''Unna boot therapy in reducing edema in patients with venous injuries'', Medicine School of Sao Jose do Rio Preto, 2018. The author was contacted to request outcome data but no data on relevant outcomes were provided, although the authors replied that ulcer healing outcome was observed **Contact information**: Luciana Ventura Cardoso, Av. Constituicao, 1306, Boa Vista, Sao Jose do Rio Preto, SP CEP 15025-120, Brazil. Tel.: +55 17 991233647. (E-mail: lu_famerp@hotmail.com).
Notes	

Cardoso 2019 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The order of events considering the use of Unna's boot and traditional dressing was randomly assigned by chance and drawing a number from an envelope determined the type of dressing to be used until the next evaluation." Comment: unclear risk of bias because the method of generating random numbers is not clear
Allocation concealment (selection bias)	Unclear risk	Quote: "The order of events considering the use of Unna's boot and traditional dressing was randomly assigned by chance and drawing a number from an envelope determined the type of dressing to be used until the next evaluation." Comment: unclear risk of bias because it is unclear how concealment is implemented
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no information provided
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Charles 1991

Study characteristics	
Methods	**Study objective**: to compare the results of the short-stretch bandage application with the present treatment being used for venous leg ulcers in the locality **Trial design (e.g. parallel group) including research sites**: parallel, community locality of Paddington and North Kensington, UK **Follow-up period**: 3 months **Number of arms**: 2 **Study start date and end date**: not described **Care setting**: community
Participants	**Study population**: community patients with an APBI of greater than 0.8, measured by vascular flow detector.

Charles 1991 *(Continued)*

Eligibility criteria: venous leg ulcer patients in the community locality of Paddington and North Kensington with an APBI of greater than 0.8, measured by vascular flow detector

Sex (M:F): not described

Age (years): mean 78 (range 55 to 99) in short-stretch bandage and 75 (range 37 to 91) in control

Duration of leg ulcers: on average 32 months (range 4 months to 28 years) in short-stretch bandage and 25 (range 4 months to 10 years) in control

Baseline leg ulcer area: mean 12 cm^2 (range 1.5 to 52) in short-stretch bandage and 15 (range 1 to 88) in control

Group difference: not described

Total number of participants: 53 patients (no. of ulcers unspecified)

Unit of analysis (including number of ulcers per person): probably ulcer

Unit of randomisation (e.g. leg ulcer, limb, or participant): patients

Interventions

Intervention characteristics

Short-stretch bandage

- **Details of interventions (including compression devices used, and duration of interventions applied)**: using a Rosidal k short-stretch washable compression bandage. Treated exclusively by the project nurse. Applied spirally starting from the toes and ending below the knee with a 50% overlap and no more than 90% stretch; bandage changed... 1 to 3 times a week. Mean pressure under bandages 33 mmHg
- **Descriptions of any co-interventions or standard care**: no change of primary wound application
- **Number of participants randomised**: n = 27 participants
- **Number of participants analysed**: 27

Control

- **Details of interventions (including compression devices used, and duration of interventions applied)**: continuing to receive care from experienced district nurses as treated previously. None treated with the short-stretch bandages
- **Descriptions of any co-interventions or standard care**: no change of primary wound application
- **Number of participants randomised**: n = 26 participants
- **Number of participants analysed**: 26

Outcomes

Time-to-complete wound healing

- Not reported

Proportion of wounds completely healed during follow-up

- **Outcome type**: binary
- **Time points**: 3 months
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: ulcer area measured weekly by tracing the perimeter of the ulcer onto an acetate sheet
- **Definition**: not described
- **Missing data and reasons (including the number of people who died)**: not described
- **Notes**: unit of analysis is probably ulcers.

Adverse events

- Not reported

Charles 1991 *(Continued)*

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- Not reported
- **Notes**: these outcome data were not available. However, the short-stretch bandage is claimed to be "cost effective, as it retains its elasticity despite being washed and reused repeatedly."

Mean pain score

- Not reported

Outcomes that are not considered in this review but reported in trials:

- Pressure measurements
- Proportions of leg ulcers with a reduction in size of more than half
- Leg circumference

Identification	**Publication type/ status (e.g. conference abstract):** full paper (Charles 1991); short report (Charles 1992 (see Charles 1991))
	Trial protocol: not provided
	Source of funding: not described; Lohmann UK, Stone, Aylesbury supplying the bandages, padding and the use of an Oxford monitor for this project
	Country of origin: UK
	Comments: the authors stated this paper was part of a research project submitted to the Parkside Health Authority (the project report was not obtained)
	Contact information: Hildegard Charles, BSc NDN PWT, Paddington and North Kensington locality
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients with an ankle pressure index < 0.8 were randomly divided into a control and an experimental group" Comment: unclear risk of bias because of the lack of information on random number generation
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided
Incomplete outcome data (attrition bias)	Unclear risk	Comment: no information provided

Charles 1991 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	Comment: no information provided
Other bias	High risk	Comment: high risk of bias because the unit of randomisation was participants but the unit of analysis was probably leg ulcers

Daróczy 2006

Study characteristics	
Methods	**Study objective**: to assess the effectiveness of (1) topical povidone-iodine with and (2) without compression bandages, (3) to compare the efficacy of systemic antibiotics and topical antimicrobial agents to prevent the progression of superficial skin ulcers **Trial design (e.g. parallel group) including research sites:** prospective, randomised controlled study **Follow-up period**: 12 weeks **Number of arms**: 3 (only 2 included in this review as 3rd group assessed antibiotic use) **Study start date and end date:** November 2003 to November 2004 **Care setting:** not reported
Participants	**Study population**: ulcerated stasis dermatitis due to chronic venous insufficiency. Their clinical stage was determined by clinical, aetiological, anatomical and pathological classification **Eligibility criteria**: ulcerated stasis dermatitis due to chronic venous insufficiency **Sex (M:F)**: not reported **Age (years)**: 58 ± 8 years **Duration of leg ulcers**: not reported **Baseline leg ulcer area**: sizes of the superficial ulcers < 5 cm **Group difference**: not reported **Total number of participants**: 42 in relevant arms (a further 21 participants were included in an antibiotic arm) **Unit of analysis (including number of ulcers per person)**: participants **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: participants
Interventions	**Intervention characteristics** Local povidone-iodine (Betadine) with compression • **Details of interventions (including compression devices used, and duration of interventions applied)**: local povidone-iodine (Betadine) with compression. Compression device and duration of intervention not reported • **Descriptions of any co-interventions or standard care**: none reported • **Number of participants randomised**: 21 • **Number of participants analysed**: 21 Local povidone-iodine (Betadine) without compression

Daróczy 2006 *(Continued)*

- **Details of interventions (including compression devices used, and duration of interventions applied)**: local povidone-iodine (Betadine) without compression
- **Descriptions of any co-interventions or standard care**: not reported
- **Number of participants randomised**: 21
- **Number of participants analysed**: 21

Outcomes

Time-to-complete wound healing

- Not reported
- **Notes**: the authors claimed to evaluate time to ulcer healing but did not present such data

Proportion of wounds completely healed during follow-up

- **Outcome type**: binary
- **Time points**: not reported
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: not reported
- **Definition**: the healing rate of the superficial, infected ulcers
- **Missing data and reasons (including the number of people who died)**: none

Adverse events

- Not reported

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- Not reported

Mean pain score

- Not reported

Outcomes that are not considered in this review but reported in trials:

- Relapse of superficial bacterial infections in Betadine vs systemic antibiotics. Not relevant to this review

Identification

Publication type/ status (e.g. conference abstract): full paper

Trial protocol: not reported

Source of funding: not described

Country of origin: Hungary

Contact information: Prof. Dr. Judit Daroczy, Department of Dermatology and Lymphology, St. Stephan Hospital, Jahn Ferenc u. 62-66. HR-1195, Budapest. +36 1280 13 68

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "… patients were enrolled in this prospective randomised controlled study ..."

Daróczy 2006 *(Continued)*

		Comment: unclear risk of bias because random sequence generation not specified
Allocation concealment (selection bias)	Unclear risk	Quote: "… patients were enrolled in this prospective randomised controlled study ..." Comment: unclear risk of bias because allocation concealment not reported/specified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome group: healing rate of superficial, infected ulcers Comment: all participants were included in the analysis
Selective reporting (reporting bias)	High risk	Comment: the authors claimed to evaluate time to ulcer healing but did not present relevant data
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Eriksson 1984a

Study characteristics	
Methods	**Study objective**: to evaluate different methods of topical treatment of venous leg ulcers **Trial design (e.g. parallel group) including research sites:** parallel group **Follow-up period**: 8 weeks **Number of arms**: 3 **Study start date and end date**: not given **Care setting:** not reported
Participants	**Study population**: people with venous leg ulcers. **Eligibility criteria**: exclusion criteria are overt diabetes mellitus, manifest arterial insufficiency, clinical picture of erysipelas or cellulitis **Sex (M:F)**: overall 13:40 (among all 53 participants who were enrolled in an unrelated trial prior to the compression trial) **Age (years)**: mean 70.1 (among all 53 participants who were enrolled in an unrelated trial prior to the compression trial) **Duration of leg ulcers**: not reported **Baseline leg ulcer area**: not reported **Group difference**: comparable in terms of all variables except for high blood glucose levels, and history of previous thrombosis (among participants of the trial 1)

Eriksson 1984a *(Continued)*

Total number of participants: 44 participants in the compression trial

Unit of analysis (including number of ulcers per person): participants

Unit of randomisation (e.g. leg ulcer, limb, or participant): participants

Interventions	**Intervention characteristics** Porcine skin dressing • **Details of interventions (including compression devices used, and duration of interventions applied)**: Skin-tec(R) (Astra-Syntex, Sweden) applied to the ulcer after cleaning with saline. Treatment stopped during the study as the dressing was no longer available. Double-layer bandage then introduced • **Descriptions of any co-interventions or standard care**: none reported • **Number of participants randomised**: n = 11 participants • **Number of participants analysed**: not given Metallina aluminium foil dressing • **Details of interventions (including compression devices used, and duration of interventions applied)**: Metalline® dressing has an aluminium surface and changed in the same manner as the porcine skin. Applied throughout the study • **Descriptions of any co-interventions or standard care**: none reported • **Number of participants randomised**: n = 20 participants • **Number of participants analysed**: not given Double-layer bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: consisted of an inner stocking impregnated with a zinc oxide paste (ACO, Sweden) and an outer elastic bandage (Tensoplast, Smith & Nephew Ltd., GB). Applied in place for 1 - 2 weeks at a time • **Descriptions of any co-interventions or standard care**: not reported • **Number of participants randomised**: n = 13 participants • **Number of participants analysed**: not given
Outcomes	*Time-to-complete wound healing* • Not reported *Proportion of wounds completely healed during follow-up* • Not reported *Adverse events* • **Notes**: 6 participants treated by aluminium foil stopped before the end of the study because of poor effect (ulcer size increase or infections, or both). No case abandoned in double-layer bandage and compression did not give any symptoms of peripheral arterial circulatory insufficiency *Participant health-related quality of life/health status* • Not reported *Cost effectiveness* • **Notes**: Porcine skin expensive but double-layer bandage comparatively cheap *Mean pain score* • Not reported **Outcomes that are not considered in this review but reported in trials**:

Eriksson 1984a *(Continued)*

- The area size and volume of the ulcers at 4 weeks

Identification	**Publication type/ status (e.g. conference abstract):** full paper **Trial protocol**: not reported **Source of funding**: not described **Country of origin**: Sweden **Contact information**: G. Eriksson, Departments of Dermatology, Dandeyd Hospital, Stockholm, Sweden
Notes	Eriksson 1984a presented results of 2 trials: the 2-week trial 1 compared 0.9% sodium chloride in sterile water with dextranomer beads through randomising 53 participants with venous leg ulcers and 9 patients excluded because of ulcer healing or reasons unrelated to the trial 2 prior to the conduct of trial 2. With the remaining 44 participants, trial 2 was undertaken to compare 2 dressing methods with a compression bandage method. Only data from trial 2 were extracted for this review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "... the patients were randomised for three different treatments." Comment: unclear risk of bias because the randomisation method is not described
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Outcome group: ulcer healing Quote: "The investigation was designed as a randomised open trial" Comment: high risk of bias because this trial is claimed to be "open" label.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: ulcer healing Quote: "Stereophotogrammetry was used as an objective method of measurement of the healing process" Comment: low risk of bias because ulcer outcomes are measured using the objective stereophotogrammetry as the authors claim
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no information provided.
Selective reporting (reporting bias)	Low risk	Comment: the authors claimed to evaluate time to ulcer healing but did not present relevant data. The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias.

Groenewald 1984

Study characteristics	
Methods	**Study objective**: to compare hydrocolloid dressings with conventional treatment (compression bandage) for the treatment of venous leg ulcers **Trial design (e.g. parallel group) including research sites:** parallel group **Follow-up period**: 8 weeks **Number of arms**: 2 **Study start date and end date**: not given **Care setting**: outpatient setting
Participants	**Study population**: people with venous stasis ulcers **Eligibility criteria**: not given **Sex (M:F)**: overall ratio 1:3 among overall clinic population (not for eligible participants) **Age (years)**: not described **Duration of leg ulcers**: some with recent onset; most with more than 6 months and some for many years **Baseline leg ulcer area**: not given **Group difference**: not given **Total number of participants**: 72 participants **Unit of analysis (including number of ulcers per person)**: participants **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: participants
Interventions	**Intervention characteristics** Hydrocolloid dressings • **Details of interventions (including compression devices used, and duration of interventions applied)**: skin cleansing performed in the same way as control group plus hydrocolloid dressing applied according to the prescribed procedure • **Descriptions of any co-interventions or standard care**: see conventional treatment • **Number of participants randomised**: n = 36 participants • **Number of participants analysed**: not given Conventional treatment (compression bandage) • **Details of interventions (including compression devices used, and duration of interventions applied)**: skin cleansing (washing ulcers and surrounding area with povidone-iodine solution and povidone-iodine ointment swabbed) plus compression bandage consisted of a 2.5 cm-thick foam rubber pad placed directly over the ulcerated and immediately surrounding area, while the foot and lower leg were bound with a zinc oxide-impregnated gauze band covered by an elastic bandage • **Descriptions of any co-interventions or standard care**: as above • **Number of participants randomised**: n = 36 participants • **Number of participants analysed**: not given
Outcomes	*Time-to-complete wound healing* • Not reported *Proportion of wounds completely healed during follow-up*

Groenewald 1984 *(Continued)*

- Not reported

Adverse events

- **Notes**: "Few unfavourable effects were recorded during the trial in the patients treated with hydrocolloid dressings." "An increased tendency toward fungus infections was noted in some cases treated with hydrocolloid dressings." 7 of 36 withdrew in hydrocolloid dressing due to non-compliance (n = 2) and treatment stopped (n = 5 including 2 having pain and irritation and 3 with overwhelming sepsis); 6 of 36 withdrew in compression bandage due to treatment changes required (overwhelming sepsis and ulcer size increase)

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- Not reported

Mean pain score

- Not reported

Outcomes that are not considered in this review but reported in trials:

- Reduction in ulcer size presented as the outcome measure. Mean reduction in ulcer size of 67.64% in hydrocolloid dressing and 22.62% in compression bandage (P < 0.0001; SE = 3.51)
- Participant adherence to compression treatment. This outcome is not measured using a prespecified method. 7 of 36 withdrew in hydrocolloid dressing due to non-compliance (n = 2) and treatment stopped (n = 5 including 2 having pain and irritation and 3 with overwhelming sepsis); 6 of 36 withdrew in compression bandage due to treatment changes required (overwhelming sepsis and ulcer size increase)

Identification	**Publication type/ status (e.g. conference abstract):** full paper **Trial protocol**: not reported **Source of funding**: not described **Country of origin**: South Africa **Contact information**: J.H. Groenewald, Departments of Vascular Surgery, University of Stellenbosch, South Africa
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were selected randomly for treatment either with hydrocolloid dressing or by conventional methods" Comment: unclear risk of bias because the randomisation method is not described
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Outcome group: ulcer healing Quote: "The nature of the dressing made a double-blind study impractical"

Groenewald 1984 *(Continued)*

		Comment: high risk of bias because the authors claimed it is challenging to blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: ulcer healing Quote: "... reduction in ulcer size as the main criterion for the evaluation of results. This could be measured fairly accurately by a technician who was not otherwise involved in the trial" Comment: low risk of bias because study authors took measures to reduce the risk of detection bias in measuring ulcer sizes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no information provided
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Kikta 1988

Study characteristics	
Methods	**Study objective**: not given **Trial design (e.g. parallel group) including research sites:** parallel, randomised controlled trial, multi-site (University of Illinois Hospital, Westside Veterans Administration Hospital, and Cook County Hospital Vascular Surgery Clinics, USA) **Follow-up period**: 6 months **Number of arms**: 2 **Study start date and end date:** not described (randomisation between February 1986 and January 1987) **Care setting:** hospital (clinics)
Participants	**Study population**: leg ulcers caused by chronic venous insufficiency **Eligibility criteria**: included people with leg ulcers caused by chronic venous insufficiency. Excluded those with the presence of arterial insufficiency as measured by Doppler-derived ABPI of less than 0.7, uncontrolled diabetes mellitus, the use of cancer chemotherapeutic agents or systemic steroids, recent venous surgery, infected ulcers, and inability to comply with treatment or follow-up **Sex (M:F)**: not described **Age (years)**: not described **Duration of leg ulcers**: mean 45 (SEM 12) weeks in hydroactive dressing (number of ulcers unspecified (n = 39 ulcers)); 51 (17) in Unna's boot (number of ulcers unspecified (n = 30 ulcers)), Student's t test P-value = 0.77 **Baseline leg ulcer area**: mean 8.6 (SEM 2.1) cm^2 in hydroactive dressing (number of ulcers unspecified (n = 39 ulcers)); 9.0 (2.2) in Unna's boot (number of ulcers unspecified (n = 30 ulcers)), Student's t test P-value = 0.88

Kikta 1988 *(Continued)*

Group difference: no statistically significant differences between groups in many variables (e.g. age; sex; race; type of previous ulcer treatment; pre-randomisation use of antibiotics; origin of chronic venous insufficiency; the incidence of previous venous, arterial, or orthopaedic operations; prior use of elastic stockings; the incidence of ischaemic heart disease, congestive heart failure, diabetes mellitus, hypertension, pulmonary, renal, and hepatic diseases; the use of oral contraceptives or tobacco; the presence of obesity or alcoholism; elevated levels of serum haemoglobin, glucose, albumin, and creatinine; whether the ulcer was new or recurrent; ABIs; and PPG-VRT)

Total number of participants: 84 participants with 87 ulcers

Unit of analysis (including number of ulcers per person): ulcers, approximately 1 ulcer per person

Unit of randomisation (e.g. leg ulcer, limb, or participant): participants

Interventions	**Intervention characteristics** Unna's boot • **Details of interventions (including compression devices used, and duration of interventions applied)**: this compression therapy is a moist paste bandage impregnated with zinc oxide, calamine lotion, and glycerine, wrapped snugly about the entire leg in direct contact with the ulcer, worn continuously, and changed weekly. Duration of Unna's boot applied unspecified • **Descriptions of any co-interventions or standard care**: all participants received instruction on leg elevation, restriction of standing activities, care for associated medical problems, and the importance of compliance and follow-up. At each clinic visit, ulcers were washed with dilute chlorhexidine solution followed by 3% hydrogen peroxide, rinsed with normal saline solution, and allowed to air-dry • **Number of participants randomised**: number of participants unknown, 42 ulcers • **Number of participants analysed**: 30 ulcers Hydroactive dressing • **Details of interventions (including compression devices used, and duration of interventions applied)**: DuoDERM (Convatec-Squibb, Princeton, N. J.) hydroactive dressing (HD) is an occlusive, virtually oxygen-impermeable, wafer-like sheet of hydrophilic particles encased in an inert hydrophobic polymer matrix placed on an adhesive plastic backing. Compression was not applied in HD. HD is replaced at least once a week. Duration of HD applied unspecified • **Descriptions of any co-interventions or standard care**: all participants received instruction on leg elevation, restriction of standing activities, care for associated medical problems, and the importance of compliance and follow-up. At each clinic visit, ulcers were washed with dilute chlorhexidine solution followed by 3% hydrogen peroxide, rinsed with normal saline solution, and allowed to air-dry • **Number of participants randomised**: number of participants unknown, 45 ulcers • **Number of participants analysed**: 39 ulcers
Outcomes	*Time-to-complete wound healing* • **Outcome type**: time-to-event • **Time points**: not relevant • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: not described • **Definition**: mean time to ulcer healing • **Missing data and reasons (including the number of people who died)**: 6 of 45 dropouts in hydroactive dressing and 12 of 42 in Unna's boot. No reason given *Proportion of wounds completely healed during follow-up* • **Outcome type**: binary • **Time points**: not described • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: not described • **Definition**: ulcer healing within 6 months

Kikta 1988 *(Continued)*

- **Missing data and reasons (including the number of people who died)**: 6 of 45 dropouts in hydroactive dressing and 12 of 42 in Unna's boot

Adverse events

- **Outcome type**: binary
- **Time points**: not described
- **Measurement method (e.g. scale, self-reporting)**: not described
- **Definition**: total numbers of ulcers with complications requiring cessation of therapy within 6 months

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- Not reported
- **Notes**: weekly costs of therapy per participant mean USD 14.24 (SEM 1.63) in hydroactive dressings; USD 11.76 (0.56) in Unna's boot; Student's t test P-value 0.16

Mean pain score

- **Outcome type**: continuous
- **Time points**: not reported
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: participants self-rated using a linear scale with grades from 1 to 10; 1 = least painful
- **Definition (including ulcer stage)**: evaluating dressing in terms of pain
- **Missing data and reasons (including the number of people who died)**: not reported

Outcomes that are not considered in this review but reported in trials:

- Proportion of wounds completely healed or improved during follow-up
- Participants self-reported convenience of using either intervention (rated using a linear scale with grades from 1 to 10; 1 = most convenient)
- Participants self-reported ease of change (rated using a linear scale with grades from 1 to 10; 1 = easiest to change)

Identification	**Publication type/ status (e.g. conference abstract):** full paper **Trial protocol**: not described **Source of funding**: not described **Country of origin**: USA **Comments**: this study was presented at the combined breakfast program of the Society for Vascular Surgery and the International Society for Cardlovascular Surgery, North American Chapter, Toronto, Ontario, Canada, 09 June 1987. However, the abstract is not available **Contact information**: D. Preston Flanigan, M.D., Chief, Division of Vascular Surgery (m/c 957), University of Illinois at Chicago, 1740 West Taylor St., Suite 2200, Chicago, IL 60612
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "... patients with leg ulcers caused by chronic venous insufficiency were randomised to receive local wound care with either UB or HD ..."

Kikta 1988 *(Continued)*

		Comment: unclear risk of bias because the method of random sequence generation is not specified
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided Outcomes: pain Comment: high risk of bias because this outcome is self-rated by participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Eighteen patients withdrew from study participation within 2 weeks of randomization, leaving 69 ulcers in 66 patients available for analysis" Quote: "There was no statistically significant difference (p = 0.11, FET) between the number withdrawing from the HD group (6 of 45) and the UB group (12 of 42) ... Despite the greater withdrawal rate from the UB group, there was still a statistically significant difference in healing rates (p = 0.01, log rank test) between ..." Outcome: proportion of wounds completely healed Comment: low risk of bias because despite a high proportion of dropouts, results are consistent between life-table analysis that incorporates dropouts, and Chi^2 test that excludes dropouts Outcome: pain Comment: high risk of bias because dropout rate is higher in Unna's boot group than hydroactive dressing group and pain could be one of likely reasons why dropouts occur Outcome: other outcomes Comment: unclear risk of bias.
Selective reporting (reporting bias)	High risk	Comment: high risk of bias because participant compliance seems prespecified but its results are not presented
Other bias	High risk	Comment: high risk of bias because the unit of randomisation was participants but the unit of analysis was probably leg ulcers

Morrell 1998

Study characteristics	
Methods	**Study objective**: to establish the relative cost effectiveness of community leg-ulcer clinics that use 4-layer compression bandaging versus usual care provided by district nurses **Trial design (e.g. parallel group) including research sites:** parallel, multi-site (8 clinics of 4 community trusts in Trent) **Follow-up period**: 12 months

Morrell 1998 *(Continued)*

	Number of arms: 2 **Study start date and end date**: recruitment from September 1994 to May 1995 **Care setting**: 8 community-based research clinics in 4 trusts in Trent, UK
Participants	**Study population**: people with venous leg ulcers **Eligibility criteria**: enrolled those with 1 or more venous ulcers on 1 or both lower limbs above the foot; their ulcers with at least 3 months duration, and assessed by the Doppler technique. Patients with an ABPI of 0.8 or less, indicating peripheral arterial disease, were excluded **Sex (M:F)**: 43:77 in 4-layer bandaging and 35:78 in usual care **Age (years)**: mean 73.2 (SD 11.6) in usual care; 73.8 (10.9) in 4-layer bandaging **Duration of leg ulcers**: mean 29.7 (SD 82.3) months in usual care; 27.5 (53.8) in 4-layer bandaging **Baseline leg ulcer area**: mean 16.9 (SD 40.8) cm^2 in usual care; 16.2 (28.9) in 4-layer bandaging **Group difference**: no difference **Total number of participants**: 233 **Unit of analysis (including number of ulcers per person)**: participants **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: participants
Interventions	**Intervention characteristics** 4-layer bandaging in a leg-ulcer clinic (Charing Cross) • **Details of interventions (including compression devices used, and duration of interventions applied)**: 4-layer bandaging in the community-based leg-ulcer clinic, with a weekly treatment, following the Charing Cross bandaging technique • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: n = 120 participants • **Number of participants analysed**: 120 participants for ITT analysis Usual care at home by the district nursing service • **Details of interventions (including compression devices used, and duration of interventions applied)**: usual care provided at home by the district nursing service and chosen by individual district nurses attending the participant; did not preclude the use of compression treatment (Collins 1997; Collins 1998); 53% of 3433 visits at home used some form of compression treatment, but none received the same package of care as 4-layer bandaging. Compression used in usual-care group not able to sustain a clinically effective pressure over 1 week (Brereton 1997) • **Descriptions of any co-interventions or standard care**: usual care as the arm • **Number of participants randomised**: n = 113 participants • **Number of participants analysed**: 113 for ITT analysis
Outcomes	*Time-to-complete wound healing* • **Outcome type**: time-to-event • **Time points**: 12 months • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: not reported • **Definition**: time to complete healing of all ulcers within 12 months (defined as re-epithelialisation of ***all ulcers***) • **Missing data and reasons (including the number of people who died)**: 103 in 4-layer bandaging and 90 in usual care completed the study; 9 died, 2 moved away, 3 hospitalised, 3 dropped out in 4-layer

Morrell 1998 *(Continued)*

bandaging; 7 died, 2 referred elsewhere, 6 moved away, 3 hospitalised, 3 admitted to nursing home, 1 dropped out in usual care. ITT analysis performed

- **Notes**: The definition of this outcome was changed (time to complete healing of all ulcers in methods, but time to initial leg ulcer healing in results).

Proportion of wounds completely healed during follow-up

- **Outcome type**: binary
- **Time points**: 12 weeks
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: not reported
- **Definition**: healing rates of participants' ulcers (defined as re-epithelialisation of ***all ulcers***)
- **Missing data and reasons (including the number of people who died)**: see above

Adverse events

- **Outcome type**: binary
- **Notes**: this outcome was not observed; but death data were available in patients' flow chart.

Participant health-related quality of life/health status

- **Outcome type**: binary
- **Time points**: 12 weeks, 12 months
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: self-reported; measured using the SF 36, EuroQol, and the Frenchay activities index
- **Definition**: not described
- **Missing data and reasons (including the number of people who died)**: not described

Cost effectiveness

- **Time points (time horizon)**: 12 months
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: incremental cost effectiveness ratio (additional cost for gaining the benefit of ulcer-free weeks). In estimating this, mean total NHS costs per participant was used for the cost measure (including the cost of treatment for leg ulcers and cost of use of other health services), valued at 1995 prices. Unit costs taken from local service providers or national data sources. Weeks free from ulcers were used as benefit's measure
- **Definition**: additional cost for gaining the benefit of ulcer-free weeks.
- **Missing data and reasons (including the number of people who died)**: complete data on resource use available for 66% (214/323) of clinic visits and 62% (2110/3429) of home visits
- **Notes**: "The additional cost for the clinic group treatment (£14.51) for achieving the benefit of 5.9 ulcer free weeks gave an incremental cost effectiveness ratio of £2.46 (− £31.94 to £99.12) per ulcer free week." One way sensitivity analysis performed for different assumptions. Mean total NHS costs per patient was inconsistent between Abstract and Results.

Mean pain score

- **Outcome type**: continuous
- **Time points**: 12 weeks and 12 months
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting):** self-reported; measured using McGill short form pain questionnaire (SF MPQ)
- **Definition**: not described
- **Missing data and reasons (including the number of people who died)**: not given.

Outcomes that are not considered in this review but reported in trials:

- Patient satisfaction (Collins 1997)

Morrell 1998 *(Continued)*

- Variations in usual care (Collins 1998)
- Ulcer recurrence
- Patients' tolerance of leg ulcer treatments

Identification	**Publication type/ status (e.g. conference abstract):** full papers (Brereton 1997; Collins 1997; Collins 1998; Morrell 1996; Morrell 1998) **Trial protocol**: not provided **Source of funding**: funded by the former Trent Regional Health Authority (now NHS Executive Trent) **Country of origin**: UK **Comments**: this study has 5 publications and all sources have consistent results **Contact information**: Dr Morrell j.morrell1@sheffield.ac.uk
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "A random assignment schedule and serially numbered, sealed, opaque allocation envelopes were prepared in advance for each of the eight clinic sites" Comment: unclear risk of bias because the random-number generation method is not described
Allocation concealment (selection bias)	Low risk	Quote: "A random assignment schedule and serially numbered, sealed, opaque allocation envelopes were prepared in advance for each of the eight clinic sites" Comment: low risk of bias because allocation is likely concealed properly
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Outcome group: all outcomes Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome group: all outcomes Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome group: all outcomes Quote: "All the data analysis was by intention to treat" Comment: low risk of bias because ITT analysis was performed
Selective reporting (reporting bias)	Unclear risk	Comment: unclear risk of bias because of the inconsistency in terms of primary outcome measurement between methods and results (the measure of "time to complete healing of all ulcers" claimed in methods, but "time to initial leg ulcer healing" presented in results)
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

O'Brien 2003

Study characteristics	
Methods	**Study objective**: to compare the cost effectiveness of 4-layer bandaging with that of alternative dressings available for venous leg ulcers in a pragmatic randomised clinical trial **Trial design (e.g. parallel group) including research sites:** parallel **Follow-up period**: 12 weeks **Number of arms**: 2 **Study start date and end date:** recruitment from April 1999 to August 2000 **Care setting:** community
Participants	**Study population**: people with a venous leg ulcer **Eligibility criteria**: those with a venous leg ulcer who were not being treated with 4-layer bandaging; venous ulcers defined with clinical evidence of venous disease, the resting ABPI = 0.9 or greater, and no other cause identified **Sex (M:F)**: 35:65 in 4LB; 33:67 in control **Age (years)**: mean 71.7 (SD 9.8) in 4LB; 71.4 (11.5) in control **Duration of leg ulcers**: median 9 (IQR 4 to 27) weeks in 4LB; 11 (5 to 28) in control **Baseline leg ulcer area**: median 3.5 (IQR 1.3 to 8.1) cm^2 in 4LB; 2.7 (1.6 to 6.2) in control **Group difference**: no difference **Total number of participants**: 200 **Unit of analysis (including number of ulcers per person)**: participant **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: participant
Interventions	**Intervention characteristics** Four-layer bandaging • **Details of interventions (including compression devices used, and duration of interventions applied)**: comprising a sterile wound contact layer, a natural padding bandage, a light conformable bandage, a light compression bandage and a flexible cohesive bandage. This combined system provided sustained external compression of 40 mmHg at the ankle • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: n = 100 participants • **Number of participants analysed**: n = 100 participants Usual care (alternative dressings) • **Details of interventions (including compression devices used, and duration of interventions applied)**: including an assortment of topical dressings, such as hydrocolloids, alginates, paraffin and iodine dressings. Absorbency dressings, low-pressure bandages and elasticated support also used (5 participants had compression applied at some stage during the 3-month study interval) • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: n = 100 participants • **Number of participants analysed**: n = 100
Outcomes	*Time-to-complete wound healing* • **Outcome type**: time-to-event

O'Brien 2003 *(Continued)*

- **Time points**: 12 weeks
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: photographs taken; not described who assessed the outcome (probably nurses)
- **Definition**: time to heal the leg ulcer; healing = full epithelialisation and no scab present; among those with bilateral leg ulcers, the leg with the larger surface area of ulceration considered
- **Missing data and reasons (including the number of people who died)**: 1 died and 2 lost to follow-up in 4LB and 0 died or lost in control; ITT analysis performed

Proportion of wounds completely healed during follow-up

- **Outcome type**: binary
- **Time points**: 12 weeks
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: see above
- **Definition**: see above
- **Missing data and reasons (including the number of people who died)**: see above
- **Notes**: adjusted healing rates (age, baseline ulcer area and duration, and history of DVT, rheumatoid arthritis and diabetes) reported but not extracted for this review.

Adverse events

- **Outcome type**: binary
- **Time points**: 12 weeks
- **Data and results (including summary results, or any data that will allow its calculation)**: 1 died in 4LB but information not reported in control group.
- **Notes**: this outcome is unlikely measured using a prespecified method.

Participant health-related quality of life/health status

- **Outcome type**: continuous
- **Time points**: 6 weeks
- **Reporting**: partially reported
- **Measurement method (e.g. scale self-reporting)**: participants interviewed and disease-specific quality-of-life instrument for chronic lower limb venous insufficiency (CIVIO) used, as well as the SF-36 generic questionnaire. CIVIO is a 20-item, and 4-domain (psychosocial, physical functioning, social functioning and pain) questionnaire designed for chronic venous disease (lower score = better quality of life). SF-36 with a score from 0 to 100 (higher score = better health)
- **Definition**: health-related quality of life
- **Missing data and reasons (including the number of people who died)**: questionnaires completed for 92.9% (79/85) and 95.8% (91/95) patients who remained unhealed at 6 weeks in 4LB and control groups (the rest of participants did not complete questionnaires because of their healing)

Cost effectiveness

- **Time points**: 12 weeks
- **Definition:** median cost per leg healed (for cost-effectiveness analysis); and cost per patient (for cost analysis). Cost valued in Euros; and considered these resources: dressing products, nurses' time, mileage expenses, and GP and hospital services
- **Missing data and reasons (including the number of people who died):** 2 missed in 4LB but reasons not specified
- **Note:** ***cost analysis:*** median (IQR) EUR 209.7 (137.5 – 269.4) in 98 participants; EUR 234.6 (168.2 – 345.1) in 100 participants; ***cost-effectiveness analysis*** : median cost per leg healed significantly less for 4-layer bandage treatment (P = 0·040)

Mean pain score

- **Outcome type**: continuous
- **Time points**: 6 weeks

O'Brien 2003 *(Continued)*

- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: participants interviewed and disease-specific quality-of-life instrument for chronic lower limb venous insufficiency (CIVIO) used. CIVIO has the domain of pain (lower overall score = better quality of life)
- **Definition**: pain measured in CIVIO
- **Missing data and reasons (including the number of people who died)**: questionnaires completed for 92.9% (79/85) and 95.8% (91/95) participants who remained unhealed at 6 weeks in 4LB and control groups (missing data for the rest of participants because of their unhealing)
- **Notes**: 12-week data not collected.

Outcomes that are not considered in this review but reported in trials:

- Mean reduction in ulcer size.
- Participant compliance to compression

Identification	**Publication type/ status (e.g. conference abstract):** full papers (see O'Brien 2003) **Trial protocol**: not available **Source of funding**: Smith & Nephew Ltd provided an educational grant to fund this study **Country of origin**: Ireland **Comments**: the authors presented the cost per leg ulcer healed for economic analysis in which the benefit was measured as leg ulcer healed **Contact information**: Mr P. E. Burke, Department of Vascular Surgery, St John's Hospital, Limerick, Ireland (e-mail: vsherlock@mwhb.ie).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "… a random 'intervention' or 'control' list was generated for 200 patients by computer …" Comment: low risk of bias because of the use of a proper randomisation method
Allocation concealment (selection bias)	Unclear risk	Quote: "Before the study began, a random 'intervention' or 'control' list was generated for 200 patients by computer, and the results were entered sequentially into sealed numbered envelopes. These envelopes were assigned to consecutive patients once consent had been obtained" Comment: unclear risk of bias because they do not describe if envelopes are opaque
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: ulcer healing Quote: "The ulcerated area was measured and photographed by the research officer" Quote: "a photograph of the site was taken to provide an objective review of outcome"

O'Brien 2003 *(Continued)*

		Comment: low risk of bias because attempts are made to reduce the risk of detection bias Outcome group: cost Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome group: ulcer healing and cost analysis Quote: "Intention-to-treat analysis was carried out" Quote: "Data missing for two patients" in Table 2 of O'Brien 2003 (for cost). Comment: low risk of bias because of ITT analysis performed and very low rate of missing data (2 of 100 in 4LB) for cost analysis Outcome group: quality of life Comment: unclear risk of bias because the rates of missing data are 15% in 4LB and 5% in control. The missing is due to ulcer healing among them and questionnaires only completed for those with unhealed ulcers at 6 weeks (92.9%, 79/85 in 4LB; and 95.8%, 91/95 in control)
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Rubin 1990

Study characteristics	
Methods	**Study objective**: not given **Trial design (e.g. parallel group) including research sites:** multi-site, randomised, prospective, blinded trial. Cleveland Ohio Veterans Administration Medical Centre, University Hospitals of Cleveland, and Cleveland Metropolitan General Hospital, USA **Follow-up period**: 12 months **Number of arms**: 2 **Study start date and end date:** not described **Care setting:** hospital
Participants	**Study population**: ambulatory patients with lower-extremity chronic venous stasis ulceration **Eligibility criteria**: patients with lower-extremity chronic venous stasis ulceration enrolled; those with history of non-compliance, presence of significant lower-extremity arterial insufficiency (as determined by Doppler ABPIs of less than 0.8), history of collagen vascular disease/uncontrolled diabetes/other ongoing dermatological disorders/chronic corticosteroid therapy excluded **Sex (M:F)**: not described **Age (years)**: not described **Duration of leg ulcers**: not described **Baseline leg ulcer area**: ranged from 6.0 cm - 270 cm^2 (mean 32.2cm^2) for Polyurethane Foam Dressing (PFD) group. Ranged from 0.02 – 600 cm^2 (mean 76.0 cm^2) for Unna Boot group. Students t test P = 0.03

Rubin 1990 *(Continued)*

Group difference: ulcers of Unna boot group larger than those of dressing group. Initial bacterial culture results were positive in 13 (76.4%) of 17 limbs from PFD group and 12 (63.1%) of 19 limbs from Unna boot group – not statistically significant

Total number of participants: 36 participants

Unit of analysis (including number of ulcers per person): participants, and wound healing rates

Unit of randomisation (e.g. leg ulcer, limb, or participant): participant

Interventions	**Intervention characteristics** Polyurethane Foam Dressing • **Details of interventions (including compression devices used, and duration of interventions applied)**: Polyurethane Foam Dressing (PFD; Synthaderm Armour Pharmaceutical Co Ltd, East Sussex, UK) is a "synthetic skin" preparation consisting of closed-cell polyoxyethylene glycol foam separating hydrophobic and hydrophilic surfaces. Applied and removed by the individual hospital-based nursing personnel. Duration of PFD application not described. Changed weekly or bi-weekly • **Descriptions of any co-interventions or standard care**: all wounds were cleansed routinely with skin wound-cleansing solution (Shur-Cleans 20% poloxamer). All participants had elastic bandages applied in an identical manner, from the toes to the knees • **Number of participants randomised**: n = 17 participants • **Number of participants analysed**: 17 and 8 participants (9 withdrew) Unna's boot • **Details of interventions (including compression devices used, and duration of interventions applied)**: a gauze bandage impregnated with glycerine, zinc oxide, and calamine lotion. Applied and removed by the individual hospital-based nursing personnel. Duration of Unna boot application not described. Changed weekly or bi-weekly • **Descriptions of any co-interventions or standard care**: all wounds were cleansed routinely with skin wound-cleansing solution (Shur-Cleans 20% poloxamer). All participants had elastic bandages applied in an identical manner, from the toes to the knees • **Number of participants randomised**: n = 19 participants • **Number of participants analysed**: 19 participants
Outcomes	*Time-to-complete wound healing* • Not reported *Proportion of wounds completely healed during follow-up* • **Outcome type**: binary • **Time points**: not described • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: not described • **Definition**: complete wound healing • **Missing data and reasons (including the number of people who died)**: ITT analysis performed for this outcome; 9 of the 17 in PFD group withdrew prior to 12 months due to wound odour *Adverse events* • **Outcome type**: binary • **Time points**: not described • **Measurement method (e.g. scale, self-reporting)**: not described • **Definition**: wound complications necessitating hospital admission or cessation of therapy • **Note**: no wound complications necessitating hospital admission of cessation of therapy in either group. 9 of 17 participants in PFD group withdrew due to wound odour

Rubin 1990 *(Continued)*

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- Not reported

Mean pain score

- Not reported

Outcomes that are not considered in this review but reported in trials:

- Overall wound healing rates (cm^2 per day). Withdrawn participants included in analysis. 0.07 cm^2/day for PDF group. 0.5 cm^2/day for Unna boot group. (P = 0.004, Students t test)
- Participant compliance with the Unna boot

Identification	**Publication type/ status (e.g. conference abstract):** full paper **Trial protocol**: not described **Source of funding**: not described **Country of origin**: USA **Contact information**: Dr Rubin, Department of Surgery, University Hospitals of Cleveland, 2074 Abington Road, Cleveland, OH 44106
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Each patient was randomised by the study coordinator to either a PFD or Unna boot dressing treatment protocol." Comment: unclear risk of bias because the method of random-sequence generation is not specified
Allocation concealment (selection bias)	Unclear risk	Quote: "The study coordinator did not see the randomization card and was therefore blinded as to the treatment cohort" Comment: unclear risk of bias because it is unclear if allocation is concealed so that investigators cannot foresee assignment of participants
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided on who/how outcomes were assessed
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome: complete wound healing Quote: "9 (52.9%) of 17 participants of group 1 withdrew from the study due to wound odor"

Rubin 1990 *(Continued)*

		Comment: low risk of bias because although 9/17 participants withdrew before study end from group 1 but no withdrawals from group 2, the authors performed ITT analysis for this outcome
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Taradaj 2007

Study characteristics	
Methods	**Study objective**: to evaluate the effect of sonotherapy and compression therapy compared with pharmacological treatment on the healing of venous ulcers after surgery **Trial design (e.g. parallel group) including research sites:** parallel group and single site **Follow-up period**: 8 weeks **Number of arms**: 2 (of 3 arms) eligible **Study start date and end date**: not given **Care setting**: general, vascular and transplantation surgery clinic of an independent public hospital in Katowice, Poland
Participants	**Study population**: people with venous ulcers who had had surgery using modified Babcock's method **Eligibility criteria**: Doppler blood-flow testing of lower limb arteries undergone. Patients with ABPI higher than 0.9 included and those with ulcers of a different aetiology than the venous one excluded. Those with diabetes, atherosclerosis, rheumatoid arthritis, taking glycolyl steroids, and with metal implants in the ultrasound site excluded **Sex (M:F)**: 9:16 compression; 13:11 control **Age (years)**: 61.6 (8.3) and range 43 to 78 compression; 62.3 (9.5) and range 40 to 79 control **Duration of leg ulcers**: 36 (39) and range 6 to 176 compression; 32 (35) and range 2 to 120 control **Baseline leg ulcer area**: 24.4 (12.9) compression; 22.0 (15.5) control **Group difference**: comparable for all variables assessed **Total number of participants**: 49 (of 73 patients eligible for inclusion in this review) **Unit of analysis (including number of ulcers per person)**: not given, probably ulcers **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: participants
Interventions	**Intervention characteristics** Elastic bandage compression and pharmacotherapy • **Details of interventions (including compression devices used, and duration of interventions applied)**: underwent compression therapies using elastic short-stretch Sigvaris bandages and pharmacotherapy. Ankle pressure of approximately 30 mmHg used for superficial vein insufficiency and about 40 mmHg for co-existing deep vein insufficiency. Graded pressure exerted and decreased in the proximal direction. Compression applied for 7 weeks • **Descriptions of any co-interventions or standard care**: modified Babcock surgery • **Number of participants randomised**: n = 25 patients

Taradaj 2007 *(Continued)*

- **Number of participants analysed**: not given

Control (pharmacological treatment)

- **Details of interventions (including compression devices used, and duration of interventions applied)**: only pharmacologically treated and no additional treatment
- **Descriptions of any co-interventions or standard care**: modified Babcock surgery
- **Number of participants randomised**: n = 24 patients
- **Number of participants analysed**: not given

Outcomes

Time-to-complete wound healing

- Not reported

Proportion of wounds completely healed during follow-up

- **Outcome type**: binary
- **Time points**: 7 weeks
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: the healing of venous ulcers assessed using a subjective method on the basis of a daily examination of healing phases (epidermis, the amount of granulation tissue, purulent discharge, etc.); cavities periodically photographed. Planimetry used as the objective method to assess ulcer changes (e.g. the total surface area and the volume of ulceration); measured once a week
- **Definition**: relative healing rates (weekly rate of change in total surface and ulceration rate)
- **Missing data and reasons (including the number of people who died)**: not described
- **Note**: no data on proportion of wounds completely healed

Adverse events

- Not reported

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- Not reported

Mean pain score

- Not reported

Outcomes that are not considered in this review but reported in trials:

- Change of ulcer length in relation to baseline
- Change of ulcer width in relation to baseline
- Change of ulcer field in relation to baseline
- Change of granulation surface area in relation to baseline

Identification

Publication type/ status (e.g. conference abstract): full paper (Polish)

Trial protocol: not reported

Source of funding: not described

Country of origin: Poland

Comments: ultrasound therapy plus pharmacological treatments were used as a third group in this trial. Data for this group were not extracted for this review, given it was not eligible

Taradaj 2007 *(Continued)*

	Contact information: Jakub Taradaj, Chair and Department of Medical Biophysics, Silesian Medical University in Katowice, Poland (email: jtaradaj@slam.katowice.pl)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: unclear risk of bias because randomisation method is not specified. From translator: "... random assignment ..."
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: no information provided
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	High risk	Comment: high risk of bias because the unit of randomisation was participants but the unit of analysis was probably leg ulcers

Taylor 1998

Study characteristics

Methods	**Study objective**: to compare healing rates and associated treatment costs of 4-layer high-compression bandaging and conventional management in the treatment of venous leg ulcers **Trial design (e.g. parallel group) including research sites:** parallel group **Follow-up period**: 12 weeks **Number of arms**: 2 **Study start date and end date**: not given **Care setting**: hospital-based leg ulcer service and community
Participants	**Study population**: people with venous stasis ulcers **Eligibility criteria**: consecutive patients presenting with venous ulcers and an ABPI > 0.8 **Sex (M:F)**: overall 11:19 among 30 complete cases; 7:9 in compression bandage and 4:10 in conventional management

Taylor 1998 *(Continued)*

Age (years): median 73 (range 28 to 85) in compression and 77 (60 to 84) in conventional

Duration of leg ulcers: 7 participants with ulcers < 6 months and 9 with > 6 months in compression; and 9 with < 6 months and 5 with > 6 months in conventional.

Baseline leg ulcer area: median 5.4 (range 0.4 to 74.8) cm^2 total area of all ulcers in compression; 4.2 (0.6 to 76.0) in conventional

Group difference: no difference in any variables assessed

Total number of participants: 36 patients (30 compliers analysed)

Unit of analysis (including number of ulcers per person): participants

Unit of randomisation (e.g. leg ulcer, limb, or participant): participants

Interventions	**Intervention characteristics** Four-layer compression bandage regimen • **Details of interventions (including compression devices used, and duration of interventions applied)**: 4-layer high-compression bandaging based on the Charing Cross regimen by nurses experienced in this technique; carried out weekly at home or community clinic • **Descriptions of any co-interventions or standard care**: applied hydrocolloids (Granuflex or Comfeel) for participants presenting with painful or very sloughy ulcers; otherwise used NA (Johnson & Johnson) • **Number of participants randomised**: n = 18 participants • **Number of participants analysed**: 16 participants treated and analysed Conventional management • **Details of interventions (including compression devices used, and duration of interventions applied)**: routine management by district nurses in the community as available on prescription form FP10; treated 2 or 3 times weekly in the home by their usual district nurse using a wide variety of application without restriction other than the application of high-compression bandaging • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: n = 18 participants • **Number of participants analysed**: 14 participants treated and analysed
Outcomes	*Time-to-complete wound healing* • **Outcome type**: time-to-event • **Time points**: 12 weeks • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: ulcer perimeter traced on to acetate weekly and area measured using a computerised planimeter; change in ulcer area indicating a quantitative measure of healing rate • **Definition**: median time to ulcer healing • **Missing data and reasons (including the number of people who died)**: 2 exclusions (1 patient died prior to treatment and 1 with treatment postponed due to scabies) in compression; 4 exclusions (1 died, 1 healed naturally before treatment, 1 treated with 4-layer high compression bandage, 1 developed cellulitis and required prolonged hospitalisation) in conventional. *Proportion of wounds completely healed during follow-up* • **Outcome type**: binary • **Time points**: 12 weeks • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: ulcer perimeter traced on to acetate weekly and area measured using a computerised planimeter; change in ulcer area indicating a quantitative measure of healing rate

Taylor 1998 *(Continued)*

- **Definition**: rate of ulcer healing and healing only judged to be complete when all the ulcers (per participant) had healed.
- **Missing data and reasons (including the number of people who died)**: see **Missing data and reasons** of the above outcome

Adverse events

- **Notes**: see **Missing data and reasons** of the above two outcomes

Participant health-related quality of life/health status

- Not reported

Cost effectiveness

- **Notes**: cost-effectiveness data not assessed. Median and ranges of weekly costs of treatments GBP 17.26 (13.45 to 20.16) in compression and GBP 21.07 (8.71 to 42.47) in conventional, P = 0.042 (mean difference GBP 6.45, 95% CI 1.22 to 11.68); treatments costs for trial GBP 116.87 (52.63 to 261.74) in compression and GBP 240.28 (74.65 to 588.05) in conventional, P = 0.016 (mean difference GBP 113.51, 95% CI 29.71 to 197.31)

Mean pain score

- Not reported

Outcomes that are not considered in this review but reported in trials:

- Number of visits.

Identification	**Publication type/ status (e.g. conference abstract):** full paper (Taylor 1998), 2 conference abstracts **Trial protocol**: not reported **Source of funding**: financial support from Medi (UK) Ltd; 3M Health Care providing Coban bandages **Country of origin**: UK **Contact information**: Mrs Adrienne Taylor, Clinical Nurse Specialist, Salford Community Trust, The Willows Centre for Health Care, Lords Avenue, Weaste, Salford M5 2JR, UK
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "... patients were randomly allocated to each treatment group using the method of minimization of prognostic factors" Comment: low risk of bias because of the use of a proper method equivalent to randomisation
Allocation concealment (selection bias)	Unclear risk	Comment: no information provided
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: no information provided
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: ulcer healing

Taylor 1998 *(Continued)*

		Quote: "Weekly, each patient had the perimeter of their ulcer traced on to acetate and the area measured using a computerized planimeter. The change in ulcer area gave a quantitative measure of healing rate" Comment: low risk of bias because attempts made to reduce the risk of detection bias in measuring ulcer healing Outcome group: cost outcome Quote: "the nurse completed a purpose-designed treatment inventory, detailing all the medications, consumables, distance travelled, travelling time, nursing grade and time to treat the patient" Comment: no information provided
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: high risk of bias because the overall proportion of dropouts reach 20% (2 of 18 in compression and 4 of 18 in conventional withdrew) and ITT analysis not performed (1 death in each group and 1 participant with ulcer healing before treatment could have been considered in analysis)
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Wong 2008a

Study characteristics	
Methods	**Study objective**: to examine the feasibility of the sampling method and to test the measuring instruments, data collection procedure, and study intervention **Trial design (e.g. parallel group) including research sites:** parallel, pilot, randomised trial, single site **Follow-up period**: 12 weeks **Number of arms**: 3 **Study start date and end date**: not given **Care setting**: community (1 general outpatient clinic)
Participants	**Study population**: older people with venous ulcer living in the community **Eligibility criteria**: inclusion of either men or women aged 55 years or older having confirmed venous leg ulcers (with partial or full-thickness skin loss) by clinical and vascular assessment (i.e. Doppler); without necrotic tissue; ability to understand and communicate in Cantonese; ABPI ≥ 0.8 indicating suitability for compression bandaging; have not previously received compression bandage. Exclusion of people with ulcers > 14 cm x 14 cm, with an ulcer duration of < 2 months; those with 2 or multiple leg ulcers, with known history of sensitivity to wound dressing or bandage used; with concurrent administration of drugs that may affect ulcer healing, such as corticosteroids or chemotherapeutics, ulcer accompanied with neoplasm skin or tissue infection, and trauma such as burn or surgical incision, diabetic patient receiving oral hypoglycaemic or insulin therapy because reduced pressure is required (from Wong 2008b) **Sex (M:F)**: 20:6 overall **Age (years)**: mean 68.9 (SD 9.4) overall **Duration of leg ulcers**: mean 22 (SD 31) months overall

Wong 2008a *(Continued)*

Baseline leg ulcer area: mean 8.24 (SD 8.7) cm^2 overall

Group difference: not given

Total number of participants: 30 participants (26 completed the pilot study)

Unit of analysis (including number of ulcers per person): participants, each with 1 ulcer

Unit of randomisation (e.g. leg ulcer, limb, or participant): participants

Interventions	**Intervention characteristics** Four-layer bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: 4-layer compression bandaging (Profore; Smith & Nephew PLC, Hull, UK), also described as elastic or long-stretch compression system, with 5 components: PROFORE WCL (primary dressing), PROFORE#1 (orthopaedic wool), PROFORE#2 (crepe bandage), PROFORE#3 (light compression bandage), PROFORE#4 (cohesive flexible bandage). Typically applied at weekly or bi-weekly intervals for 12 weeks. The sub-bandage resting pressure between 40 to 50 mmHg (from Wong 2008b) • **Descriptions of any co-interventions or standard care**: used along with the usual topical ulcer care, including a moist wound-healing dressing. • **Number of participants randomised**: 10 participants • **Number of participants analysed**: 9 completers Short-stretch bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: short-stretch compression system (Rosidal sys; Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany), also described as an inelastic compression system, consisting of 2 rolls of high-compression, textile-elastic short-stretch bandages named as the Rosidal K. It has 5 components: tg tubular bandage, Rosidal soft, Rosidal K, Profix, and Mollelast haft. Typically applied in weekly or bi-weekly intervals for 12 weeks. The sub-bandage ankle pressure of 25 - 40 mmHg (from Wong 2008b) • **Descriptions of any co-interventions or standard care**: used along with the usual topical ulcer care, including a moist wound-healing dressing • **Number of participants randomised**: 10 participants • **Number of participants analysed**: 9 completers Usual care • **Details of interventions (including compression devices used, and duration of interventions applied)**: usual care provided by the researcher and 3 clinic nurses, care provided by the researcher once a week and by clinic nurses for the rest of the week for 12 weeks, treatments including washing, cleansing, and wound dressings. Moist wound-healing dressing without compression. Applied alginates, films, foams or absorbent dressings, as well as a bio-cellulose dressing (Suprasorb A or A+Ag, Suprasorb F, Solvaline, Vliwazell, Suprasorb P, Suprasorb X or X+PHMB; Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany) (from Wong 2008b) • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: 10 participants • **Number of participants analysed**: 8 completers
Outcomes	*Time-to-complete wound healing* • Not reported *Proportion of wounds completely healed during follow-up* • **Outcome type**: binary • **Time points**: week 12 • **Reporting**: fully reported

Wong 2008a *(Continued)*

- **Measurement method (e.g. scale, self-reporting)**: used a digital planimetry tool (VeV VERGe Videometer) to assess reduction in ulcer area
- **Definition**: ulcer healing at week 12
- **Missing data and reasons (including the number of people who died)**: 2 recruited by mistake, 1 with wound infection at week 4, and 1 reported ankle movement restriction and refused to do follow-up

Adverse events

- **Time points**: week 12
- **Notes**: 1 with wound infection at week 4, and 1 reported ankle movement restriction

Participant health-related quality of life/health status

- Not reported
- **Notes**: outcome assessor unspecified; only data at baseline by groups presented

Cost effectiveness

- Not reported

Mean pain score

- Not reported
- **Notes**: outcome assessor unspecified; data at baseline by groups presented

Outcomes that are not considered in this review but reported in trials:

- Pain interference with various aspects of QOL

Identification	**Publication type/ status (e.g. conference abstract):** PhD thesis (Wong 2008b) **Trial protocol**: not described **Source of funding**: funded by the Special Grant for Conducting Research Aboard, the Chinese University of Hong Kong (2004) **Country of origin**: Hong Kong **Comments**: this was a pilot study of Wong 2008b; and both Wong 2008a and Wong 2008b were reported in a single doctoral thesis. Therefore, some data items of **Participants** and **Interventions** were extracted from Wong 2008b. Most domains of risk-of-bias table were judged based on Wong 2008b **Contact information**: Irene KY Wong
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: unclear risk of bias because information provided is insufficient for this domain's judgement
Allocation concealment (selection bias)	Unclear risk	Comment: unclear risk of bias because information provided is insufficient for this domain's judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Outcome group: all outcomes Quote: "participants and interviewers (data collectors) were not informed of the treatment allocation of the study participants for the duration of the study" (Wong 2008b).

Wong 2008a *(Continued)*

		Quote: "the interveners who performed wound dressing and/or bandaging were not blinded to the treatment groups. Blinding the interveners is not achievable ..." (Wong 2008b). Comment: high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: unclear risk of bias because information provided is insufficient for this domain's judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome group: all outcomes Quote: "The attrition rate was 7.1%" (Wong 2008a). Comment: low risk of bias because of a low attrition rate
Selective reporting (reporting bias)	High risk	Comment: high risk of bias because although this is a pilot study; the study protocol is not available; but it is clear that the study authors measured some outcomes and presented baseline data only rather than week 12 outcome data
Other bias	Unclear risk	Comment: unclear risk of bias because this is a pilot study report and no further information is available for other sources of bias judgement

Wong 2008b

Study characteristics	
Methods	**Study objective**: to compare the effects in venous leg-ulcer patients between short-stretch compression (SSB), 4-layer compression bandaging (4LB), and usual care with no compression (UC) **Trial design (e.g. parallel group) including research sites:** parallel, randomised controlled trial, multi-site **Follow-up period**: 6 and 12 weeks **Number of arms**: 3 **Study start date and end date**: recruited from August 2004 to March 2006 **Care setting**: community involving 6 general outpatient clinics located at the Kowloon East Cluster
Participants	**Study population**: older people with venous ulcer living in the community **Eligibility criteria**: inclusion of either men or women aged 55 years or older having confirmed venous leg ulcers (with partial or full-thickness skin loss) by clinical and vascular assessment (i.e. Doppler); without necrotic tissue; ability to understand and communicate in Cantonese; ABPI ≥ 0.8 indicating suitability for compression bandaging; have not previously received compression bandage. Exclusion of patients with ulcers > 14cm x 14cm, with an ulcer duration of < 2 months; those with 2 or multiple leg ulcers, with known history of sensitivity to wound dressing or bandage used; with concurrent administration of drugs that may affect ulcer healing, such as corticosteroids or chemotherapeutics, ulcer accompanied with neoplasm skin or tissue infection, and trauma such as burn or surgical incision, diabetic patient receiving oral hypoglycaemic or insulin therapy because reduced pressure is required **Sex (M:F)**: 121:59 overall **Age (years)**: mean 69.3 (SD 9.8) overall **Duration of leg ulcers**: mean 31.6 (SD 44.8) months overall

Wong 2008b *(Continued)*

Baseline leg ulcer area: mean 8.1 (SD 8.8) cm^2 overall

Group difference: no significant differences between groups in variables explored (e.g. age; sex; ulcer duration; ulcer size)

Total number of participants: 180 participants

Unit of analysis (including number of ulcers per person): participants, each with 1 ulcer

Unit of randomisation (e.g. leg ulcer, limb, or participant): participants

Interventions	**Intervention characteristics** Four-layer bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: 4-layer compression bandaging (Profore; Smith & Nephew PLC, Hull, UK), also described as elastic or long-stretch compression system, with 5 components: PROFORE WCL (primary dressing), PROFORE#1 (orthopaedic wool), PROFORE#2 (crepe bandage), PROFORE#3 (light compression bandage), PROFORE#4 (cohesive flexible bandage). Typically applied in weekly or bi-weekly intervals for 12 weeks. The sub-bandage resting pressure between 40 to 50 mmHg. • **Descriptions of any co-interventions or standard care**: used along with the usual topical ulcer care, including a moist wound-healing dressing • **Number of participants randomised**: 60 participants • **Number of participants analysed**: 46 completers Short-stretch bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: short-stretch compression system (Rosidal sys; Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany), also described as an inelastic compression system, consisting of 2 rolls of high compression, textile-elastic short-stretch bandages named as the Rosidal K. It has 5 components: tg tubular bandage, Rosidal soft, Rosidal K, Profix, and Mollelast haft. Typically applied at weekly or bi-weekly intervals for 12 weeks. The sub-bandage ankle pressure of 25 - 40 mmHg • **Descriptions of any co-interventions or standard care**: used along with the usual topical ulcer care, including a moist wound-healing dressing • **Number of participants randomised**: 60 participants • **Number of participants analysed**: 50 completers Usual care • **Details of interventions (including compression devices used, and duration of interventions applied)**: usual care provided by the researcher and 3 clinic nurses, cared provided by the researcher once a week and by clinic nurses for the rest of a week for 12 weeks, treatments including washing, cleansing, and wound dressings. Moist wound healing dressing without compression. Applied alginates, films, foams or absorbent dressings, as well as a bio-cellulose dressing (Suprasorb A or A+Ag, Suprasorb F, Solvaline, Vliwazell, Suprasorb P, Suprasorb X or X+PHMB; Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany) • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: 60 participants • **Number of participants analysed**: 54 completers
Outcomes	*Time-to-complete wound healing* • **Outcome type**: time-to-event • **Time points**: not relevant • **Reporting**: fully reported • **Measurement method (e.g. scale, self-reporting)**: complete ulcer healing defined according to the criteria of the Wound Healing Society as 100 percent re-epithelialisation of the wound surface with the absence of exudates

Wong 2008b *(Continued)*

- **Definition**: mean time to ulcer healing
- **Missing data and reasons (including the number of people who died)**: all included in analysis

Proportion of wounds completely healed during follow-up

- **Outcome type**: binary
- **Time points**: week 6 and 12
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: complete ulcer healing defined according to the criteria of the Wound Healing Society as 100 percent re-epithelialisation of the wound surface with the absence of exudates
- **Definition**: complete ulcer healing
- **Missing data and reasons (including the number of people who died)**: 30 dropouts including 10 for SSB, 14 for 4LB, and 6 for control

Adverse events

- **Outcome type**: binary
- **Time points**: not described
- **Measurement method (e.g. scale, self-reporting)**: probably not measured using a prespecified method
- **Definition**: total numbers of participants with adverse events
- **Notes**: the study authors reported hospitalisation due to medical conditions as a reason of withdrawals but did not consider it as adverse events (see Table 12 of Wong 2008b). The review authors did not extract relevant data here.

Participant health-related quality of life/health status

- **Outcome type**: continuous
- **Time points**: week 6 and 12
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: Chinese (Hong Kong) Short Form-12-item Health Survey (SF-12) as a generic QOL tool (a higher scoring = a better quality of life); Charing Cross Venous Ulcer Questionnaire (Chinese) as a disease-specific QOL measurement instrument (lower scores = better quality of life); all collected at weeks 12.
- **Definition (including ulcer stage)**: health-related quality of life
- **Missing data and reasons (including the number of people who died)**: 30 dropouts including 10 for SSB, 14 for 4LB, and 6 for control
- **Notes**: outcome assessor unspecified.

Cost effectiveness

- Not reported

Mean pain score

- **Outcome type**: continuous
- **Time points**: week 6 and 12
- **Reporting**: fully reported
- **Measurement method (e.g. scale, self-reporting)**: self-rated using Brief Pain Inventory instrument with a 10-point VAS scale with grades from 0 to 10; 0 = least painful. Collected at 12 weeks
- **Definition (including ulcer stage)**: ulcer-related pain severity
- **Missing data and reasons (including the number of people who died)**: 30 dropouts including 10 for SSB, 14 for 4LB, and 6 for control
- **Notes**: outcome assessor unspecified. Pain interference with various aspects of QOL measured but not extracted for this review.

Outcomes that are not considered in this review but reported in trials:

Wong 2008b *(Continued)*

- The average ulcer area
- Pain interference with various aspects of QOL
- Interface pressure
- Frenchay Activities Index for lifestyle activity

Identification	**Publication type/ status (e.g. conference abstract):** PhD thesis (Wong 2008b) **Trial protocol**: not described **Source of funding**: funded by the Special Grant for Conducting Research Aboard, the Chinese University of Hong Kong (2004) **Country of origin**: Hong Kong **Comments**: the trial has a pilot study Wong 2008a **Contact information**: Irene KY Wong
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “Eligible patients were randomly assigned to either one of the experimental groups or the control group by a random list ... A randomisation list with three treatment blocks was generated by a computer program before the study ...” Comment: low risk of bias because of the use of a proper method of generating random sequence.
Allocation concealment (selection bias)	Unclear risk	Quote: “The participants were allowed to open the envelope for grouping allocation only after the collection of baseline data. The patients were not informed whether they were assigned to an intervention or control group until the completion of the study. The strength of this allocation concealment in random trials ...” Comment: unclear risk of bias because information provided is insufficient for this domain’s judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Outcome group: all outcomes Quote: "participants and interviewers (data collectors) were not informed of the treatment allocation of the study participants for the duration of the study" Quote: "the interveners who performed wound dressing and/or bandaging were not blinded to the treatment groups. Blinding the interveners is not achievable ..." Comment: high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: ulcer healing and pain outcomes Quote: "This was a double-blind study, in which the interviewers who were responsible for the pre-test and post test data collections were not given any information regarding the group to which the participant was assigned" Quote: "The data collector then received the electronic file periodically and performed the perimeter tracing and area calculation using the Wound Mea-

Wong 2008b *(Continued)*

		surement System software. As a result, the data collector assessed the ulcer size without seeing the participant ..." Comment: low risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome group: time to healing Quote: "... only analyse the data of those participants who had received the treatment ... an intention to treat analysis was adopted during the process of survival analysis only" Comment: low risk of bias because of the use of ITT analysis. Outcome group: all other outcomes including healing incidence Comment: high risk of bias because despite a moderate rate of attrition (30/180, 16.7%) the excluded cases had larger ulcer sizes than those completed
Selective reporting (reporting bias)	Low risk	Comment: the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

Wong 2012

Study characteristics	
Methods	**Study objective**: to compare quality of life (QOL) aspects in venous leg ulcer patients over 55 years of age, of short-stretch compression (SSB), 4-layer compression bandaging (4LB) and usual care (UC) (moist wound-healing dressing, no compression) **Trial design (e.g. parallel group) including research sites:** parallel, randomised controlled trial, multi-site **Follow-up period**: 12 and 24 weeks **Number of arms**: 3 **Study start date and end date**: patients recruited from May 2007 to November 2008 **Care setting**: community (9 general outpatient clinics in the New Territories East Cluster, Kowloon East Cluster and the Kowloon Central Cluster)
Participants	**Study population**: leg ulcers caused by chronic venous insufficiency **Eligibility criteria**: inclusion of either men or women aged 55 years or older having confirmed venous leg ulcers (with partial or full-thickness skin loss) by clinical and vascular assessment (i.e. Doppler); without necrotic tissue; ability to understand and communicate in Cantonese; ABPI ≥ 0.8 indicating suitability for compression bandaging. Exclusion of people with ulcers of < 5 cm^2 or > 118 cm^2, with an ulcer duration of less than 4 weeks or longer than 1 year; those with 2 or multiple leg ulcers, either on 1 or both legs; those with an ABPI < 0.8 and those with concurrent administration of drugs that may affect ulcer healing, such as corticosteroids or chemotherapeutics **Sex (M:F)**: 206:115 overall **Age (years)**: mean 71.7 (SD 8.5) overall **Duration of leg ulcers**: mean 27.4 (SD 43.7) months overall **Baseline leg ulcer area**: mean 8.2 (SD 11.0) cm^2 overall

Wong 2012 *(Continued)*

	Group difference: no significant differences between groups in variables explored (e.g. age; sex; ulcer duration; ulcer size) **Total number of participants**: 321 patients, each with 1 ulcer **Unit of analysis (including number of ulcers per person)**: participants, each with 1 ulcer **Unit of randomisation (e.g. leg ulcer, limb, or participant)**: patients
Interventions	**Intervention characteristics** Four-layer bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: 4-layer compression bandaging (Profore; Smith & Nephew PLC, Hull, UK). Typically applied at weekly intervals for 24 weeks. The sub-bandage resting pressure between 40 to 50 mmHg • **Descriptions of any co-interventions or standard care**: used along with the usual topical ulcer care, including a moist wound-healing dressing • **Number of participants randomised**: 107 participants • **Number of participants analysed:** 87 participants for health-related quality of life and pain score outcome; 107 participants for ulcer-healing outcomes Short-stretch bandage • **Details of interventions (including compression devices used, and duration of interventions applied)**: short-stretch compression bandaging (Rosidal sys; Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany). Typically applied at weekly intervals for 24 weeks. The sub-bandage resting pressure between 40 to 50 mmHg • **Descriptions of any co-interventions or standard care**: used along with the usual topical ulcer care, including a moist wound-healing dressing. • **Number of participants randomised**: 107 participants • **Number of participants analysed**: 95 for health-related quality of life and pain score outcome; 107 for ulcer-healing outcomes Usual care • **Details of interventions (including compression devices used, and duration of interventions applied)**: moist wound-healing dressing without compression. Applied alginates, films, foams or absorbent dressings, as well as a bio-cellulose dressing (Suprasorb A or A+Ag, Suprasorb F, Solvaline, Vliwazell, Suprasorb P, Suprasorb X or X+PHMB; Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany) • **Descriptions of any co-interventions or standard care**: not described • **Number of participants randomised**: 107 participants • **Number of participants analysed**: 94 health-related quality of life and pain score outcome; 107 for ulcer-healing outcomes
Outcomes	*Time-to-complete wound healing* • **Outcome type**: time-to-event • **Time points**: not relevant • **Reporting**: partially reported • **Measurement method (e.g. scale, self-reporting)**: complete ulcer healing defined according to the criteria of the Wound Healing Society as 100 per cent re-epithelialisation of the wound surface with the absence of exudates (Wong 2008b). • **Definition**: mean time to ulcer healing • **Missing data and reasons (including the number of people who died)**: all included in analysis *Proportion of wounds completely healed during follow-up* • **Outcome type**: binary

Wong 2012 *(Continued)*

- **Time points**: week 12 and 24
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: used a digital planimetry tool (VeV VERGe Videometer) to assess reduction in ulcer area
- **Definition**: ulcer healing within 6 months
- **Missing data and reasons (including the number of people who died)**: all included in analysis.

Adverse events

- **Outcome type**: binary
- **Time points**: not described
- **Measurement method (e.g. scale, self-reporting)**: probably not measured using a prespecified method
- **Definition**: total numbers of participants with adverse events
- **Notes**: data on dropouts due to reasons other than adverse events were not extracted for this review. Data extracted for this review were based on Table 5 of Wong 2012 rather than its Figure 1 that had different numbers of dropouts due to adverse events.

Participant health-related quality of life/health status

- **Outcome type**: continuous
- **Time points**: week 12 and 24
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: Chinese (Hong Kong) Short Form-12-item Health Survey (SF-12) as a generic QOL tool (higher score = better status); Charing Cross Venous Ulcer Questionnaire (Chinese) as a disease-specific QOL measurement instrument (lower score = better status); both collected at weeks 0, 12 and 24
- **Definition (including ulcer stage)**: health-related quality of life.
- **Missing data and reasons (including the number of people who died)**: 20 of 107 in 4LB; 12 of 107 in SSB; and 13 of 107 in UC missed (all withdraws due to adverse events; specific adverse events given for 17 in 4LB; 12 in SSB and 16 in UC).
- **Notes**: outcome assessor unspecified. The study authors also measured Frenchay Activity Index (for functional status) but reported this and quality of life separately. The review authors did not extract the Frenchay Activity Index data for this review.

Cost effectiveness

- Not reported; cost data presented but not extracted for this review

Mean pain score

- **Outcome type**: continuous
- **Time points**: week 12 and 24
- **Reporting**: partially reported
- **Measurement method (e.g. scale, self-reporting)**: self-rated using Brief Pain Inventory instrument with a 10-point VAS scale with grades from 0 to 10; 0 = least painful. Collected at weeks 0, 12 and 24 (lower score = less pain)
- **Definition (including ulcer stage)**: ulcer-related pain severity
- **Missing data and reasons (including the number of people who died)**: not reported
- **Notes**: outcome assessor unspecified. Pain interference with various aspects of QOL measured but not extracted for this review.

Outcomes that are not considered in this review but reported in trials:

- The average ulcer area
- Pain interference with various aspects of QOL
- Interface pressure
- Frenchay Activitiy Index

Wong 2012 *(Continued)*

Identification	**Publication type/ status (e.g. conference abstract):** 2 full papers (Wong 2012; So 2014), retraction record, conference abstract **Trial protocol**: not described **Source of funding**: funded by the Health, Welfare and Food Bureau of Hong Kong (HHSRF #404060481) and a scientific grant of Lohmann & Rauscher GmbH & Co KG, Rengsdorf, Germany. **Country of origin**: Hong Kong **Comments**: Wong 2012 published in J Vass Surg 2012;55:1376-85 was retracted by the Journal's Editor-in-Chief because the study has been previously published in J Eur Acad Dermatol Venereol 2012;26:102-10. Data extracted for this review were based on the paper from J Eur Acad Dermatol Venereol 2012;26:102-10. Two authors (the leading and correspondence authors) participate in various scientific projects with medical device companies, such as Smith & Nephew and Lohmann & Rauscher. One author is an employee of Lohmann & Rauscher, the company that provided all the study products. **Contact information**: A. Andriessen. E-mail: anneke.a@tiscali.nl
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Eligible patients were randomly assigned to either one of the experimental groups (compression treatment) or the control group using a computer generated list after pre-test measurements were taken" Comment: low risk of bias because of the use of a proper method of generating random sequence
Allocation concealment (selection bias)	Unclear risk	Quote: "After confirming eligibility of a patient and obtaining informed consent, the clinical investigator digitally received the information on the allocation of the patient to one of the treatment groups" [based on retracted paper]. Comment: unclear risk of bias because information provided is insufficient for this domain's judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Outcome group: all outcomes Quote: "participants and interviewers (data collectors) were not informed of the treatment allocation of the study participants for the duration of the study" (Wong 2008b) Quote: "the interveners who performed wound dressing and/or bandaging were not blinded to the treatment groups. Blinding the interveners is not achievable ..." (Wong 2008b) Comment: high risk of bias because in our judgement it is clearly not possible to blind either participants or personnel and a related study (Wong 2008b) suggest that there is non-blinding of participants
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome group: all outcomes Quote: "This was a double-blind study, in which the interviewers who were responsible for the pre-test and post test data collections were not given any information regarding the group to which the participant was assigned" Comment: low risk of bias

Wong 2012 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome group: ulcer healing and time to healing Quote: "All 321 patients were included in the survival analysis on ulcer healing" Comment: low risk of bias because of the use of ITT analysis Outcome group: health of quality and pain Quote: "All withdrawn cases were regarded as unsuccessful in terms of treatment and all variables, including size and pain score" Quote: "Forty-five patients (14%) were withdrawn before the second data collection at week 24." Comment: unclear risk of bias because completed case data used for qualify of life and pain outcomes and the rate of dropouts is not high
Selective reporting (reporting bias)	High risk	Comment: high risk of bias because costs data presented in results - not mentioned in methods - of the retracted paper of Wong 2012 but not presented in the published paper. Additionally, patient's flow and outcome data presented in Wong (JEADV 2012, 26, 102–110) and the retracted paper (Wong JVS, 2012, 55,1376-1385) do not match
Other bias	Low risk	Comment: the study appears to be free of other sources of bias

4LB: four-layer bandage; ABPI: ankle:brachial pressure index; IQR: interquartile range; ITT: intention-to-treat; QOL: quality of life; SEM: standard error of the mean.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
ACTRN12608000599370	Ineligible intervention
ACTRN12613001213730	Ineligible intervention
Adderley 2014	Ineligible intervention
Akesson 2014	Ineligible study design
Allegra 2001	Ineligible intervention
Alvarez 2005	Ineligible intervention
Ashby 2014	Ineligible intervention
Balleste 2002	Ineligible intervention
Bertaux 2010	Ineligible intervention
Blair 1988	Ineligible intervention
Blecken 2005	Ineligible intervention
Bosanquet 1999	Ineligible intervention
Brennan 2010	Ineligible intervention

Study	Reason for exclusion
Brizzio 2010	Ineligible intervention
Callam 1992a	Ineligible intervention
Callam 1992b	Ineligible intervention
Cameron 1996	Ineligible intervention
Cherry 1998	Ineligible intervention
Colgan 1996	Ineligible intervention
Cordts 1992	Ineligible intervention
CTRI2010091000230	Ineligible intervention
Danielsen 1998	Ineligible intervention
De Abreu 2015	Ineligible intervention
DePalma 1999	Ineligible intervention
Dolibog 2013	Ineligible intervention
Dolibog 2014	Ineligible intervention
Duby 1993	Ineligible intervention
Eriksson 1984b	Ineligible intervention
Eriksson 1986	Ineligible intervention
EudraCT2007-004831-47	Ineligible intervention
Finlayson 2014	Ineligible intervention
Folguera-Álvarez 2016	Ineligible intervention
Folguera-Álvarez 2020	Ineligible intervention
Franek 2014	Ineligible intervention
Franks 1995	Ineligible intervention
Franks 1999	Ineligible intervention
Franks 2000	Ineligible intervention
Franks 2002	Ineligible intervention
Franks 2003	Ineligible intervention
Franks 2004a	Ineligible intervention
Franks 2004b	Ineligible intervention

Study	Reason for exclusion
Gardon-Mollard 2003	Ineligible intervention
Gillet 2019	Ineligible intervention
Gould 1993	Ineligible intervention
Gould 1998	Ineligible intervention
Harley 2000	Ineligible intervention
Harley 2004	Ineligible intervention
Harrison 2011	Ineligible intervention
Hendricks 1985	Ineligible intervention
Iglesias 2004	Ineligible intervention
ISRCTN47210331	Ineligible intervention
ISRCTN67751142	Ineligible intervention
Jawien 2008	Ineligible intervention
Jawien 2010	Ineligible intervention
Juenger 2005	Ineligible intervention
Jünger 2004a	Ineligible intervention
Jünger 2004b	Ineligible intervention
Jünger 2007	Ineligible intervention
Knight 1996	Ineligible intervention
Koksal 2003	Ineligible intervention
Kralj 1997	Ineligible intervention
Kucharzewski 2013	Ineligible intervention
Lazareth 2012	Ineligible intervention
Mancini 2009	Ineligible intervention
Mariani 2008	Ineligible intervention
McCollum 1997	Ineligible intervention
Meyer 2002	Ineligible intervention
Meyer 2003	Ineligible intervention
Milic 2007	Ineligible intervention

Study	Reason for exclusion
Milic 2010	Ineligible intervention
Moffatt 1999	Ineligible intervention
Moffatt 2001	Ineligible intervention
Moffatt 2003a	Ineligible intervention
Moffatt 2003b	Ineligible intervention
Moffatt 2003c	Ineligible intervention
Moffatt 2008	Ineligible intervention
Moffatt 2012	Ineligible intervention
Moody 1999	Ineligible intervention
Mosti 2011	Ineligible intervention
Mosti 2020	Ineligible intervention
NCT00534937	Ineligible intervention
NCT00558662	Ineligible intervention
NCT00821431	Ineligible intervention
NCT02015221	Ineligible intervention
NCT02284373	Ineligible intervention
NCT02364921	Ineligible intervention
NCT02561013	Ineligible intervention
NCT02680834	Ineligible intervention
NCT02728986	Ineligible intervention
NCT02729688	Ineligible intervention
NCT02782689	Ineligible intervention
NCT02790593	Ineligible intervention
NCT02798445	Ineligible intervention
NCT03396731	Ineligible intervention
NCT03404297	Ineligible population
NCT03544788	Ineligible intervention
NCT03736941	Ineligible study design

Study	Reason for exclusion
Nelson 1995	Ineligible intervention
Nelson 2004	Ineligible intervention
Nelson 2007	Ineligible intervention
Northeast 1990	Ineligible intervention
Olofsson 1996	Ineligible intervention
Partsch 1994	Ineligible intervention
Partsch 2001	Ineligible intervention
Polignano 2003	Ineligible intervention
Polignano 2004a	Ineligible intervention
Polignano 2004b	Ineligible intervention
Price 2008	Ineligible intervention
Robinson 1998	Ineligible intervention
Rocca 2012	Ineligible intervention
Russo 1999	Ineligible intervention
Sabolinski 1996	Ineligible intervention
Scriven 1998	Ineligible intervention
Scriven 2000	Ineligible study design
Smith Nephew 1991	Ineligible intervention
Szewcyzk 2010	Ineligible intervention
Taradaj 2009	Ineligible intervention
Tawfick 2013	Ineligible intervention
Torra i Bou 2003	Ineligible intervention
Travers 1992	Ineligible intervention
Tucker 2008	Ineligible intervention
Ukat 2003	Ineligible intervention
Van Laere 2010	Ineligible intervention
Vowden 2000	Ineligible intervention
Vowden 2001	Wrong study design

Study	Reason for exclusion
Walker 1996	Ineligible intervention
Weller 2012a	Ineligible intervention
Wilkinson 1997	Ineligible intervention
Wille 2002	Ineligible intervention
Zuccarelli 1997	Ineligible intervention

Characteristics of studies awaiting classification *[ordered by study ID]*

Cherry 1990

Methods	Not available
Participants	Not available
Interventions	Not available
Outcomes	Not available
Notes	Unable to obtain full text

Jünger 2008

Methods	Not available
Participants	Not available
Interventions	Not available
Outcomes	Not available
Notes	Unable to obtain full text

Kuznetsov 2009

Methods	Not available
Participants	Not available
Interventions	Not available
Outcomes	Not available
Notes	Unable to obtain full text

Robinson 1988

Methods	Not available
Participants	Not available
Interventions	Not available
Outcomes	Not available
Notes	Unable to obtain full text

Stacey 2000

Methods	Not available
Participants	Not available
Interventions	Not available
Outcomes	Not available
Notes	Unable to obtain full text

DATA AND ANALYSES

Comparison 1. Compression bandages or stockings compared with no compression

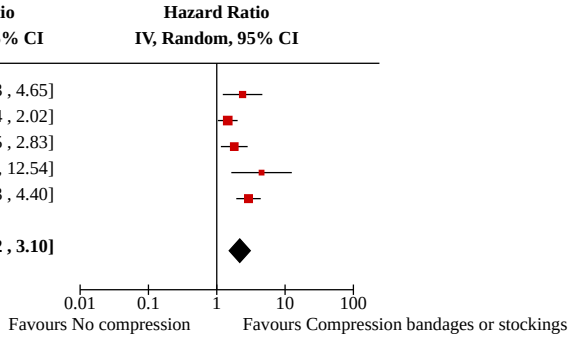
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Time-to-complete wound healing	5		Hazard Ratio (IV, Random, 95% CI)	2.17 [1.52, 3.10]
1.2 Proportion of wounds completely healed during follow-up	8	1123	Risk Ratio (M-H, Random, 95% CI)	1.77 [1.41, 2.21]
1.3 Adverse events	3	588	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.25, 3.80]
1.4 Participant health-related quality of life/health status	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.4.1 SF-12 (physical component)	2	426	Mean Difference (IV, Random, 95% CI)	2.46 [-1.62, 6.54]
1.4.2 SF-12 (mental component)	2	426	Mean Difference (IV, Random, 95% CI)	-0.74 [-2.57, 1.09]
1.4.3 SF-12 (functional status)	1	276	Mean Difference (IV, Random, 95% CI)	-0.60 [-2.55, 1.35]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4.4 Charing Cross Venous Ulcer Questionnaire (total score)	2	426	Mean Difference (IV, Random, 95% CI)	-6.87 [-13.10, -0.64]
1.5 Mean pain score	3	495	Mean Difference (IV, Random, 95% CI)	-1.39 [-1.79, -0.98]

Analysis 1.1. Comparison 1: Compression bandages or stockings compared with no compression, Outcome 1: Time-to-complete wound healing

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
Kikta 1988 (1)	0.87	0.34	15.9%	2.39 [1.23 , 4.65]
Morrell 1998	0.37	0.17	27.6%	1.45 [1.04 , 2.02]
O'Brien 2003	0.59	0.23	22.9%	1.80 [1.15 , 2.83]
Taylor 1998	1.51	0.52	9.1%	4.53 [1.63 , 12.54]
Wong 2008b (2)	1.07	0.21	24.4%	2.92 [1.93 , 4.40]
Total (95% CI)			**100.0%**	**2.17 [1.52 , 3.10]**

Heterogeneity: Tau² = 0.09; Chi² = 9.77, df = 4 (P = 0.04); I² = 59%
Test for overall effect: Z = 4.28 (P < 0.0001)
Test for subgroup differences: Not applicable



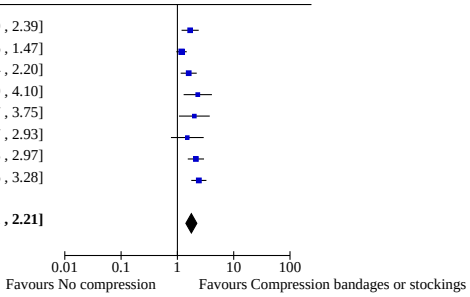
Footnotes

(1) The study reported ulcer-level data that were treated as participant-level data for this analysis (i.e. using participant as the unit of analysis) as the number of ulcers (n = 87)
(2) Adjusted HRs 3.14 (95% CI 1.74 to 5.67) for four-layer bandages and 2.72 (95% CI 1.53 to 4.86) for short-stretch bandages combined (both vs no compression)

Analysis 1.2. Comparison 1: Compression bandages or stockings compared with no compression, Outcome 2: Proportion of wounds completely healed during follow-up

Study or Subgroup	Compression bandages or stockings Events	Total	No compression Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Kikta 1988 (1)	33	42	21	45	14.0%	1.68 [1.19 , 2.39]
Morrell 1998	78	120	62	113	17.8%	1.18 [0.96 , 1.47]
O'Brien 2003	54	100	34	100	14.6%	1.59 [1.14 , 2.20]
Rubin 1990	18	19	7	17	8.8%	2.30 [1.29 , 4.10]
Taylor 1998	14	18	7	18	8.0%	2.00 [1.07 , 3.75]
Wong 2008a	15	20	5	10	7.4%	1.50 [0.77 , 2.93]
Wong 2008b (2)	98	120	23	60	14.5%	2.13 [1.53 , 2.97]
Wong 2012 (3)	149	214	31	107	15.1%	2.40 [1.76 , 3.28]
Total (95% CI)		**653**		**470**	**100.0%**	**1.77 [1.41 , 2.21]**
Total events:	459		190			

Heterogeneity: Tau² = 0.06; Chi² = 19.93, df = 7 (P = 0.006); I² = 65%
Test for overall effect: Z = 4.97 (P < 0.00001)
Test for subgroup differences: Not applicable



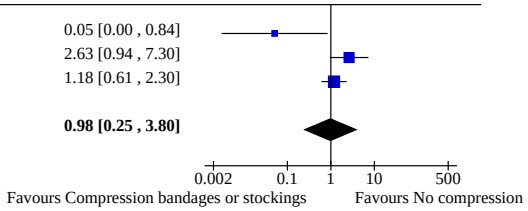
Footnotes

(1) The study reported ulcer-level data that were treated as participant-level data for this analysis (i.e. using participant as the unit of analysis) as the number of ulcers (n = 87) ≈ the number of participants (n = 84)
(2) Data on the two arms of compression bandages or stockings applied in Wong 2008b were combined into a single arm
(3) Data on the two types of compression bandages or stockings applied in Wong 2012 were combined into a single arm

Analysis 1.3. Comparison 1: Compression bandages or stockings compared with no compression, Outcome 3: Adverse events

Study or Subgroup	Compression bandages or stockings Events	Total	No compression Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Kikta 1988 (1)	0	42	10	45	16.0%	0.05 [0.00 , 0.84]
Wong 2008b	21	120	4	60	39.1%	2.63 [0.94 , 7.30]
Wong 2012 (2)	26	214	11	107	44.9%	1.18 [0.61 , 2.30]
Total (95% CI)		**376**		**212**	**100.0%**	**0.98 [0.25 , 3.80]**
Total events:	47		25			

Heterogeneity: Tau² = 0.95; Chi² = 7.63, df = 2 (P = 0.02); I² = 74%
Test for overall effect: Z = 0.03 (P = 0.97)
Test for subgroup differences: Not applicable

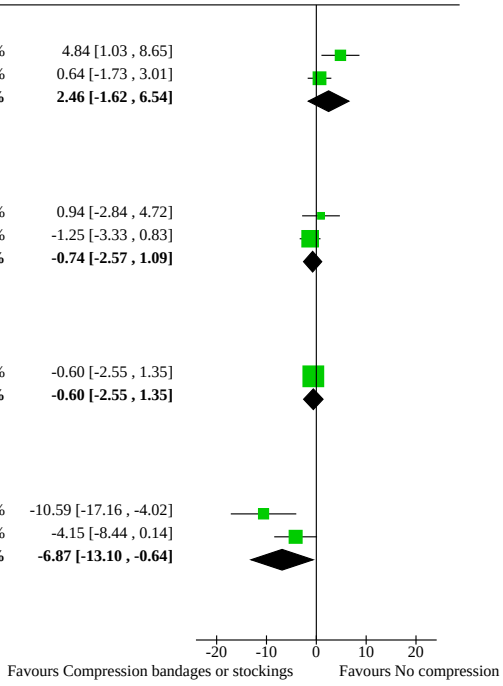


Footnotes

(1) The study reported ulcer-level data that were treated as participant-level data for this analysis (i.e. using participant as the unit of analysis) as the number of ulcers (n = 87) ≈ the number
(2) Multiple reports of Wong 2012 presented different results of adverse events. The result presented in this table was from based on Table 2 of the study report published on The Journal of

Analysis 1.4. Comparison 1: Compression bandages or stockings compared with no compression, Outcome 4: Participant health-related quality of life/health status

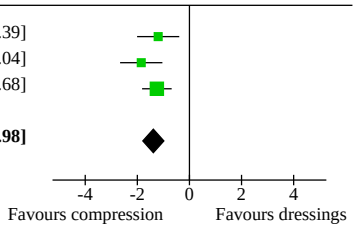
Study or Subgroup	Compression bandages or stockings Mean	SD	Total	No compression Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.4.1 SF-12 (physical component)								
Wong 2008b	46.14	11.67	96	41.3	11.3	54	43.4%	4.84 [1.03 , 8.65]
Wong 2012	53.74	9.23	182	53.1	9.68	94	56.6%	0.64 [-1.73 , 3.01]
Subtotal (95% CI)			**278**			**148**	**100.0%**	**2.46 [-1.62 , 6.54]**
Heterogeneity: Tau² = 6.20; Chi² = 3.36, df = 1 (P = 0.07); I² = 70%								
Test for overall effect: Z = 1.18 (P = 0.24)								
1.4.2 SF-12 (mental component)								
Wong 2008b	48.64	8.16	96	47.7	12.8	54	23.3%	0.94 [-2.84 , 4.72]
Wong 2012	55.25	8.51	182	56.5	8.3	94	76.7%	-1.25 [-3.33 , 0.83]
Subtotal (95% CI)			**278**			**148**	**100.0%**	**-0.74 [-2.57 , 1.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.99, df = 1 (P = 0.32); I² = 0%								
Test for overall effect: Z = 0.79 (P = 0.43)								
1.4.3 SF-12 (functional status)								
Wong 2012	39.7	8.33	182	40.3	7.57	94	100.0%	-0.60 [-2.55 , 1.35]
Subtotal (95% CI)			**182**			**94**	**100.0%**	**-0.60 [-2.55 , 1.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.60 (P = 0.55)								
1.4.4 Charing Cross Venous Ulcer Questionnaire (total score)								
Wong 2008b	35.41	18.01	96	46	20.6	54	42.2%	-10.59 [-17.16 , -4.02]
Wong 2012	20.95	15.47	182	25.1	18.1	94	57.8%	-4.15 [-8.44 , 0.14]
Subtotal (95% CI)			**278**			**148**	**100.0%**	**-6.87 [-13.10 , -0.64]**
Heterogeneity: Tau² = 12.72; Chi² = 2.59, df = 1 (P = 0.11); I² = 61%								
Test for overall effect: Z = 2.16 (P = 0.03)								



Analysis 1.5. Comparison 1: Compression bandages or stockings compared with no compression, Outcome 5: Mean pain score

Study or Subgroup	Compression Mean	SD	Total	Dressings Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kikta 1988 (1)	1.2	0.55	30	2.4	2.5	39	24.8%	-1.20 [-2.01 , -0.39]
Wong 2008b	1.15	1.59	96	3	2.8	54	24.7%	-1.85 [-2.66 , -1.04]
Wong 2012	1.31	1.88	182	2.56	2.46	94	50.5%	-1.25 [-1.82 , -0.68]
Total (95% CI)			**308**			**187**	**100.0%**	**-1.39 [-1.79 , -0.98]**

Heterogeneity: Tau² = 0.00; Chi² = 1.68, df = 2 (P = 0.43); I² = 0%
Test for overall effect: Z = 6.74 (P < 0.00001)
Test for subgroup differences: Not applicable



Footnotes

(1) The study reported clustered data but the participant was treated as the unit of analysis as the number of ulcers (n = 87) ≈ the number of participants (n = 84)

ADDITIONAL TABLES

Table 1. Details of compression bandages or stockings and comparators applied

Study ID	Compression bandages or stockings	No compression	Comment
Compression unspecified			
Daróczy 2006	Undefined compression plus local povidone-iodine (Betadine)	Local povidone-iodine (Betadine)	-
Short-stretch bandages			
Charles 1991	Short-stretch compression bandages (Rosidal, with the spiral technique and 1 - 3 times of changes per week) that was expected to achieve mean pressure of 33 mmHg	Usual care, without further details	-
Taradaj 2007	Elastic short-stretch bandages (Sigvaris) plus unspecified pharmacotherapy • Applied for 7 weeks and claimed to reach the ankle pressure of approximately 30 or 40 mmHg	Unspecified pharmacotherapy	Taradaj 2007 applied compression bandages and the control treatments only after removing affected veins on legs via operations in participants with venous leg ulcers.
Wong 2008a	Short-stretch bandage (Rosidal) • Sub-bandage resting pressure between 40 and 50 mmHg changed weekly for 24 weeks	A variety of dressings	-
Wong 2008b	Short-stretch bandage (Rosidal) • Sub-bandage resting pressure between 40 and 50 mmHg changed weekly for 24 weeks	A variety of dressings	-
Wong 2012	Short-stretch bandage (Rosidal) • Sub-bandage resting pressure between 40 and 50 mmHg changed weekly for 24 weeks	A variety of dressings	-

Table 1. Details of compression bandages or stockings and comparators applied *(Continued)*

Four-layer bandage			
Morrell 1998	Four-layer bandage following the Charing Cross bandaging technique (with a weekly treatment) • Compression levels and the duration of application unspecified	A wide variety of treatments • Not preclude the use of compression therapies	In the comparator, 53% of 3433 visits at home used some form of compression treatment but not the same compression as the intervention group (4-layer compression).
O'Brien 2003	Four-layer compression bandage (with a natural padding bandage, a light conformable bandage, a light compression bandage and a flexible cohesive bandage) • Sustained external pressure of 40 mmHg at the ankle	A variety of dressings	O'Brien 2003 stated that 5 participants in the control had compression applied at some stage during 3-months interval.
Taylor 1998	Four-layer bandage following the Charing Cross bandaging technique (with a weekly treatment) • Compression levels and the duration of application unspecified	A wide variety of treatments applied without restriction other than the use of high-compression bandaging	-
Wong 2008a	Four-layer bandage (Profore) • Sub-bandage resting pressure between 40 and 50 mmHg changed weekly for 24 weeks	A variety of dressings	-
Wong 2008b	Four-layer bandage (Profore) • Sub-bandage resting pressure between 40 and 50 mmHg changed weekly for 24 weeks	A variety of dressings	-
Wong 2012	Four-layer bandage (Profore) • Sub-bandage resting pressure between 40 and 50 mmHg changed weekly for 24 weeks	A variety of dressings	-
Unna's boot			
Cardoso 2019	Unna's boot • Compression level of 18 to 24 mmHg, the duration of applications unspecified	Dressings unspecified	-
Eriksson 1984a	Unna's boot • Compression level unspecified; changed once per 1 or 2 weeks; the duration of applications unspecified	• Porcine skin dressing (Skintec) • Aluminium foil dressing (Metallina)	Based on descriptions of compression therapies, the review authors considered the compression used was Unna's boots. Eriksson 1984a replaced porcine skin dressings - due to its unavailability - with double-layer bandage

Table 1. Details of compression bandages or stockings and comparators applied *(Continued)*

			(i.e. Unna's boot) during the study period.
Groenewald 1984	Unna's boot • Compression level unspecified; changed once per 1 or 2 weeks; the duration of applications unspecified	Hydrocolloid dressing	Based on descriptions of compression therapies, the review authors considered the compression used was Unna's boots.
Kikta 1988	Unna's boot • Compression level unspecified; changed once per 1 or 2 weeks; the duration of applications unspecified	Hydroactive dressing (DuoDERM)	-
Rubin 1990	Unna's boot • Compression level unspecified; changed once per 1 or 2 weeks; the duration of applications unspecified	Polyurethane foam dressing	-

Table 2. Results for adverse events reported in the included studies

Study ID	Adverse events in compression bandages or stockings	Adverse events in no compression	Inference
Eriksson 1984a	No case abandoned; No symptoms of peripheral arterial circulatory insufficiency	6 participants stopped using ***Metallina(R) aluminium foil dressing*** earlier because of poor effect (ulcer size increase or infections, or both)	Not relevant
Groenewald 1984	6 of 36 withdrew due to treatment changes required (overwhelming sepsis and ulcer size increase)	7 of 36 withdrew in hydrocolloid dressing due to non-compliance (n = 2) and treatment stopped (n = 5 including 2 having pain and irritation and 3 with overwhelming sepsis); Few unfavourable effects recorded for those using hydrocolloid dressings; An increased tendency toward fungus infections noted in some cases treated with hydrocolloid dressings	Not relevant
Kikta 1988	0 of 30 (0%) in Unna's boot	10 of 39 ulcers (26%) in hydroactive dressing including 8 with a reddish-green exudate; 1 with cellulitis; and 1 with circumferential ulcers and cellulitis	Fisher's exact test P-value = 0.004
Morrell 1998	9 deaths of 120 participants using 4-layer bandages	7 of 113 using usual care	Not relevant
O'Brien 2003	1 death in 4-layer bandage	Information not reported	Not relevant
Rubin 1990	No wound complications necessitating hospital admission of cessation of therapy	No wound complications necessitating hospital admission of cessation of therapy; 9 of 17 participants withdrew due to wound odour	Not relevant

Table 2. Results for adverse events reported in the included studies *(Continued)*

Taylor 1998	1 death, and 1 postponed to apply compression due to scabies	1 death; and 1 developed cellulitis in conventional care	Not relevant
Wong 2008a	See **Inference**	See **Inference**	Not relevant; 1 was reported having wound infection at week 4, and 1 with ankle movement restriction. However, the study authors did not specify which group these participants were from
Wong 2008b	Short-stretch bandages: 8 of 60 4-layer bandages: 13 of 60	Usual care without compression: 4 of 60	Not relevant
Wong 2012	4-layer compression bandages: 16 of 107; Short-stretch bandages: 10 of 107	Usual care without compression: 11 of 107	Not relevant

Multiple publications of the same study (Wong 2012) reported different results of adverse events. The result used in this table was from the Table 5 of the study report published in the Journal of the European Academy of Dermatology and Venereology.

Table 3. Results of participant health-related quality of life/health status reported in the included studies

Study ID	Questionnaires	Domains	Compression	Dressings	Inference
Morrell 1998	• SF-36 (higher score = better health) • EuroQol	Not relevant	Data at 12 weeks and 12 months were not presented	Data at 12 weeks and 12 months were not presented	The study authors stated that "for most dimensions of the SF-36 and EuroQol, health status deteriorated over time, with no difference between the groups"
O'Brien 2003	SF-36 (higher score = better health)	Physical function	Median 70 (IQR 45 to 85) at 6 weeks (n = 79)	Median 50 (IQR 25 to 80) at 6 weeks (n = 91)	Mann-Whitney U test P = 0.001
		Role-physical	100 (0 to 100)	25 (0 to 100)	P = 0.006
		Bodily pain	84 (61 to 100)	72 (51 to 100)	P = 0.840
		General health	77 (62 to 87)	72 (62 to 82)	P = 0.202
		Vitality	75 (60 to 80)	60 (55 to 75)	P = 0.160

Table 3. Results of participant health-related quality of life/health status reported in the included studies *(Continued)*

		Social function	100 (75 to 100)	87.5 (62.5 to 100)	P = 0.322
		Role-emotional	100 (100 to 100)	100 (33.3 to 100)	P = 0.150
		Mental health	88 (80 to 92)	88 (76 to 92)	P = 0.030
	Disease-specific quality of life instrument for chronic lower limb venous insufficiency (CIVIQ) (lower score = better status)	Pain	Median 18.8 (IQR 6.3 to 37.5) at 6 weeks (n = 79)	Median 31.3 (IQR 18.8 to 43.8) at 6 weeks (n = 91)	P = 0.140
		Physical	12.5 (6.3 to 37.5)	37.5 (12.5 to 62.5)	P = 0.006
		Social	33.3 (16.7 to 41.7)	41.7 (25 to 58.3)	P = 0.001
		Psychological	13.9 (11.1 to 25)	19.4 (11.1 to 27.8)	P = 0.488
		Global	18.8 (12.5 to 31.3)	28.8 (18.8 to 43.8)	P = 0.006
Wong 2008b	SF-12 (higher score = better health)	Mental component	Short-stretch bandages: mean 48.7 (SD 11.5) at 6 weeks; 47.2 (8.7) at 12 weeks Four-layer bandages: 47.3 (9.7) at 6 weeks; 50.2 (7.3) at 12 weeks	No compression: 47.6 (13.3) at 6 weeks; 47.7 (12.8) at 12 weeks	-
		Physical component	Short-stretch bandages: mean 40.8 (SD 11.2) at 6 weeks; 47.0 (SD 11.5) at 12 weeks; Four-layer bandages: 41.3 (10.0) at 6 weeks; 45.2 (11.9) at 12 weeks	No compression: 40.7 (10.7) at 6 weeks; 41.3 (11.3) at 12 weeks	-
	Charing Cross Venous Ulcer Questionnaire (lower score = better health)	Total scores	Short-stretch bandages: mean 48.8 (SD 12.6) at 6 weeks; 34.5 (17.2) at 12 weeks; Four-layer bandages: 49.1 (13.0) at 6 weeks; 36.4 (19.0) at 12 weeks	No compression: 46.7 (14.1) at 6 weeks; 46.0 (20.6) at 12 weeks	-
Wong 2012	SF-12 (higher score = better health)	Functional status	Short-stretch bandages: mean 40.5 (SD 7.31) at 12 weeks; 40.7 (7.15) at 24 weeks; Four-layer bandages: 38.4 (9.19) at 12 weeks; 38.6 (9.38) at 24 weeks	Dressings: mean 40.8 (SD 7.51) at 12 weeks; 40.3 (7.57) at 24 weeks	RMANOVA test for pre- and post-treatment scores at 12 weeks: P < 0.003 for short-stretch bandages; P < 0.007 for 4-layer bandages;

Table 3. Results of participant health-related quality of life/health status reported in the included studies *(Continued)*

				P = 0.060 for dressings Inference pre- vs post-treatment scores at 24 weeks not presented
	Mental component	Short-stretch bandages: mean 47.3 (SD 8.82) at 12 weeks; 55.3 (8.58) at 24 weeks; Four-layer bandages: 50.0 (8.17) at 12 weeks; 55.2 (8.48) at 24 weeks	Dressings: mean 47.2 (SD 12.4) at 12 weeks; 56.5 (8.30) at 24 weeks	Pre- and post-treatment scores at 12 weeks: all 3 groups P < 0.001 At 24 weeks: all P < 0.001
	Physical component	Short-stretch bandages: mean 47.5 (SD 11.1) at 12 weeks; 53.5 (9.37) at 24 weeks; Four-layer bandages: 47.7 (10.9) at 12 weeks; 54.0 (9.12) at 24 weeks	Dressings: mean 44.1 (SD 11.8) at 12 weeks; 53.1 (9.68) at 24 weeks	Pre- and post-treatment scores at 12 weeks: all 3 groups P ≤ 0.001 At 24 weeks: all P < 0.001
Charing Cross Venous Ulcer Questionnaire (lower score = better health)	Total scores	Short-stretch bandages: mean 21.6 (SD 16.4) at 12 weeks; 21.0 (15.8) at 24 weeks; Four-layer bandages: 22.4 (16.5) at 12 weeks; 20.9 (15.2) at 24 weeks	Dressings: mean 25.1 (SD 18.9) at 12 weeks; 25.1 (18.1) at 24 weeks	Pre- and post-treatment scores at 12 weeks: short-stretch bandages and 4-layer bandages: P < 0.001. Dressing P = 0.047 At 24 weeks: short-stretch bandages and four-layer bandages P < 0.035. Dressing not significant

Table 4. Results of mean pain scores reported in the included studies

Study ID	Pain measurement instruments	Compression bandages or stockings	No compression	Comments
Kikta 1988	Not specified; using a scale with grades from 1 to 10 (1 = the least painful)	Mean 2.4 (SEM 0.4) in Unna's boot	Mean 1.2 (SEM 0.1) in hydroactive dressing	Clustered data; Student's t test P value 0.007
Morrell 1998	Leg ulcer pain using the short-form McGill Pain Questionnaire (SF-MPQ)	Data were not presented	Data were not presented	Participants treated with 4-layer bandages were more likely to experience a reduction in leg ulcer pain

Table 4. Results of mean pain scores reported in the included studies *(Continued)*

				per month than those using usual care
O'Brien 2003	Pain measured using the domain of the quality of life questionnaire CIVIO (a lower score = less pain)	Median 18.8 (IQR 6.3 to 37.5)	Median 31.3 (IQR 18.8 to 43.8)	P value 0.140
Wong 2008b	Brief Pain Inventory instrument with a 10-point VAS scale (0 to 10; 0 = least painful)	• Week 6 Mean 1.9 (SD 1.8) for short-stretch bandages (n = 50) 2.1 (2.1) for 4-layer bandages (n = 46) • Week 12 1.1 (1.5) for short-stretch bandages (n = 50) 1.2 (1.7) for 4-layer bandages (n = 46)	• Week 6 3.1 (2.5) for usual care (n = 54) • Week 12 3.0 (2.8) for usual care (n = 54)	-
Wong 2012	Brief Pain Inventory instrument with a 10-point VAS scale (0 to 10; 0 = least painful)	• Week 12 Mean 1.25 (SD 1.84) in short-stretch bandages (n = 95) 1.43 (1.77) in 4-layer bandages (n = 87) • Week 24 Mean 1.25 (SD 1.90) in short-stretch bandages; 1.38 (1.87) in 4-layer bandages	• Week 12 2.61 (2.40) in usual care (n = 94) • Week 24 2.56 (2.46) in usual care	-

IQR: interquartile range; SD: standard deviation; SEM: standard error of the mean; VAS: visual analogue scale

APPENDICES

Appendix 1. Search strategies

Cochrane Wounds Specialised Register

1 MESH DESCRIPTOR Leg Ulcer EXPLODE ALL AND INREGISTER

2 ((varicose next ulcer*) or (venous next ulcer*) or (leg next ulcer*) or (stasis next ulcer*) or (crural next ulcer*) or (ulcus next cruris) or (ulcer* next cruris)) AND INREGISTER

3 #1 OR #2

4 MESH DESCRIPTOR Compression Bandages EXPLODE ALL AND INREGISTER

5 compression* AND INREGISTER

6 stocking* or hosiery AND INREGISTER

7 sock or socks or tights AND INREGISTER

8 bandag* AND INREGISTER

9 wrapp* AND INREGISTER

10 #4 OR #5 OR #6 OR #7 OR #8 OR #9

11 #3 AND #10

The Cochrane Central Register of Controlled Clinical Trials (CENTRAL)

#1 MeSH descriptor: [Leg Ulcer] explode all trees

#2 ((varicose next ulcer*) or (venous next ulcer*) or (leg next ulcer*) or (stasis next ulcer*) or (crural next ulcer*) or (ulcus next cruris) or (ulcer* next cruris)):ti,ab,kw

#3 #1 or #2

#4 MeSH descriptor: [Compression Bandages] explode all trees

#5 compression*:ti,ab,kw

#6 stocking* or hosiery:ti,ab,kw

#7 sock or socks or tights:ti,ab,kw

#8 bandag*:ti,ab,kw

#9 wrapp*:ti,ab,kw

#10 #4 or #5 or #6 or #7 or #8 or #9

#11 #3 and #10 in Trials

Ovid MEDLINE

1 exp Leg Ulcer/

2 (varicose ulcer* or venous ulcer* or leg ulcer* or stasis ulcer* or (lower extremit* adj ulcer*) or crural ulcer* or ulcus cruris or ulcer* cruris).tw.

3 1 or 2

4 exp Compression Bandages/

5 compression*.tw.

6 (stocking* or hosiery).tw.

7 (sock or socks or tights).tw.

8 bandag*.tw.

9 wrapp*.tw.

10 or/4-9

11 3 and 10

12 randomized controlled trial.pt.

13 controlled clinical trial.pt.

14 randomi?ed.ab.

15 placebo.ab.

16 clinical trials as topic.sh.

17 randomly.ab.

18 trial.ti.

19 or/12-18

20 exp animals/ not humans.sh.

21 19 not 20

22 11 and 21

Ovid Embase

1 exp Leg Ulcer/

2 (varicose ulcer* or venous ulcer* or leg ulcer* or stasis ulcer* or (lower extremit* adj ulcer*) or crural ulcer* or ulcus cruris or ulcer* cruris).tw.

3 1 or 2

4 exp Compression Therapy/

5 exp Compression Bandage/

6 exp Compression Garment/

7 compression*.tw.

8 (stocking* or hosiery).tw.

9 (sock or socks or tights).tw.

10 bandag*.tw.

11 wrapp*.tw.

12 or/4-11

13 3 and 12

14 Randomized controlled trial/

15 Controlled clinical study/

16 Random$.ti,ab.

17 randomization/

18 intermethod comparison/

19 placebo.ti,ab.

20 (compare or compared or comparison).ti.

21 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.

22 (open adj label).ti,ab.

23 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.

24 double blind procedure/

25 parallel group$1.ti,ab.

26 (crossover or cross over).ti,ab.

27 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 orintervention$1 or patient$1 or subject$1 or participant $1)).ti,ab.

28 (assigned or allocated).ti,ab.

29 (controlled adj7 (study or design or trial)).ti,ab.

30 (volunteer or volunteers).ti,ab.

31 trial.ti.

32 or/14-31

33 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)

34 32 not 33

35 13 and 34

EBSCO CINAHL Plus

S37 S13 AND S36

S36 S35 NOT S34

S35 S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28

S34 S32 NOT S33

S33 MH (human)

S32 S29 OR S30 OR S31

S31 TI (animal model*)

S30 MH (animal studies)

S29 MH animals+

S28 AB (cluster W3 RCT)

S27 MH (crossover design) OR MH (comparative studies)

S26 AB (control W5 group)

S25 PT (randomized controlled trial)

S24 MH (placebos)

S23 MH (sample size) AND AB (assigned OR allocated OR control)

S22 TI (trial)

S21 AB (random*)

S20 TI (randomised OR randomized)

S19 MH cluster sample

S18 MH pretest-posttest design

S17 MH random assignment

S16 MH single-blind studies

S15 MH double-blind studies

S14 MH randomized controlled trials

S13 S3 AND S12

S12 S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11

S11 TI wrapp* OR AB wrap

S10 TI bandag* OR AB bandag*

S9 TI (sock or socks or tights) OR AB (sock or socks or tights)

S8 TI (stocking* or hosiery) OR AB (stocking* or hosiery)

S7 TI compression* OR AB compression*

S6 (MH "Elastic Bandages")

S5 (MH "Compression Therapy")

S4 (MH "Compression Garments")

S3 S1 OR S2

S2 TI (((varicose ulcer*) or (venous ulcer*) or (leg ulcer*) or (stasis ulcer*) or (crural ulcer*) or (ulcus cruris) or (ulcer* cruris))) OR AB (((varicose ulcer*) or (venous ulcer*) or (leg ulcer*) or (stasis ulcer*) or (crural ulcer*) or (ulcus cruris) or (ulcer* cruris)))

S1 (MH "Leg Ulcer+")

US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov)

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Leg Ulcer

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Ulcer Venous

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Varicose Ulcer

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Stasis Ulcer

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Ulceration

World Health Organization International Clinical Trials Registry Platform

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping [Intervention] | Venous Leg Ulcer [Title]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Leg Ulcer [Condition]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Ulcer Venous [Title]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Ulcer Venous [Condition]

compression OR stockins OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Varicose Ulcer [Title]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Varicose Ulcer [Condition]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Stasis Ulcer [Title]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Stasis Ulcer [Condition]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Ulceration [Title]

compression OR stockings OR tights OR hosiery OR sock OR socks OR bandage OR wrap OR wrapping | Venous Ulceration [Condition]

Appendix 2. Risk of bias

1 Risk-of-bias assessment (individually randomised controlled trials)

1. Was the allocation sequence randomly generated?

Low risk of bias

The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots.

High risk of bias

The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day) of admission; sequence generated by some rule based on hospital or clinic record number.

Unclear

Insufficient information about the sequence generation process to permit judgement of low or high risk of bias.

2. Was the treatment allocation adequately concealed?

Low risk of bias

Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomisation); sequentially-numbered drug containers of identical appearance; sequentially-numbered, opaque, sealed envelopes.

High risk of bias

Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: using an open random-allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.

Unclear

Insufficient information to permit judgement of low or high risk of bias. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement, for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

3. Blinding - was knowledge of the allocated interventions adequately prevented during the study?

Low risk of bias

Any one of the following.

- No blinding, but the review authors judge that the outcome and the outcome measurement are not likely to be influenced by lack of blinding.
- Blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, but outcome assessment was blinded and the non-blinding of others unlikely to introduce bias.

High risk of bias

Any one of the following.

- No blinding or incomplete blinding, and the outcome or outcome measurement is likely to be influenced by lack of blinding.
- Blinding of key study participants and personnel attempted, but likely that the blinding could have been broken.
- Either participants or some key study personnel were not blinded, and the non-blinding of others likely to introduce bias.

Unclear

Any one of the following.

- Insufficient information to permit judgement of low or high risk of bias.
- The study did not address this outcome.

4. Were incomplete outcome data adequately addressed?

Low risk of bias

Any one of the following.

- No missing outcome data.
- Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias).
- Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically-relevant impact on the intervention effect estimate.

- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically-relevant impact on observed effect size.
- Missing data have been imputed using appropriate methods.

High risk of bias

Any one of the following.

- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups.
- For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically-relevant bias in intervention effect estimate.
- For continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes enough to induce clinically-relevant bias in observed effect size.
- 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation.
- Potentially inappropriate application of simple imputation.

Unclear

Any one of the following.

- Insufficient reporting of attrition/exclusions to permit judgement of low or high risk of bias (e.g. number randomised not stated, no reasons for missing data provided).
- The study did not address this outcome.

5. Are reports of the study free of suggestion of selective outcome reporting?

Low risk of bias

Any of the following.

- The study protocol is available and all of the study's prespecified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way.
- The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were prespecified (convincing text of this nature may be uncommon).

High risk of bias

Any one of the following.

- Not all of the study's prespecified primary outcomes have been reported.
- One or more primary outcomes are reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not prespecified.
- One or more reported primary outcomes were not prespecified (unless clear justification for their reporting is provided, such as an unexpected adverse effect).
- One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis.
- The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear

Insufficient information to permit judgement of low or high risk of bias. It is likely that most studies will fall into this category.

6. Other sources of potential bias

Low risk of bias

The study appears to be free of other sources of bias.

High risk of bias

There is at least one important risk of bias. For example, the study:

- had a potential source of bias related to the specific study design used; or
- has been claimed to have been fraudulent; or
- had some other problem.

Unclear

There may be a risk of bias, but there is either:

- insufficient information to assess whether an important risk of bias exists; or
- insufficient rationale or evidence that an identified problem will introduce bias

2 Risk-of-bias assessment (cluster-randomised controlled trials)

1. Recruitment bias

Recruitment bias (or identification bias) is the bias that occurs in cluster-RCTs if the personnel recruiting participants know individuals' allocation, even when the allocation of clusters has been concealed appropriately. The knowledge of the allocation of clusters may lead to bias because the individuals' recruitment in cluster trials is often behind the clusters' allocation to different interventions; and the knowledge of allocation can determine whether individuals are recruited selectively.

This bias can be judged through considering the following questions.

- Were all the individual participants identified/recruited before randomisation of clusters?
- Is it likely that selection of participants was affected by knowledge of the intervention?
- Were there baseline imbalances that suggest differential identification or recruitment of individual participants between arms?

2. Baseline imbalance

Baseline imbalance between intervention groups can occur due to chance, problems with randomisation, or identification/recruitment bias. The issue of recruitment bias has been considered above.

In terms of study design, the risk of chance baseline imbalance can be reduced by the use of stratified or pair-matched randomisation. Minimisation — an equivalent technique to randomisation — can be used to achieve better balance in cluster characteristics between intervention groups if there is a small number of clusters.

Concern about the influence of baseline imbalance can be reduced if trials report the baseline comparability of clusters, or statistical adjustment for baseline characteristics.

3. Loss of clusters

Similar to missing outcome data in individually-randomised trials, bias can occur if clusters are completely lost from a cluster trial, and are omitted from the analysis.

The amount of missing data, the reasons for missingness and the way of analysing data given the missingness should be considered in assessing the possibility of bias.

4. Incorrect analysis

Data analyses which do not take the clustering into account, in cluster trials will be incorrect. Such analyses lead to a 'unit of analysis error' and over-precise results (too small standard error) and too small P values. Although these analyses will not result in biased estimates of effect, if not correctly adjusted they will lead to too much weight allocated to cluster trials in a meta-analysis.

Note that the issue of analysis may not lead to concern any more and will not be considered substantial if approximate methods are used by review authors to address clustering in data analysis.

5. Comparability with individually-randomised trials

In the case that a meta-analysis includes, for example, both cluster- and individually-randomised trials, potential differences in the intervention effects between different trial designs should be considered. This is because the 'contamination' of intervention effects may occur in cluster-randomised trials, which would lead to underestimates of effect. The contamination could be known as a 'herd effect', i.e. within clusters, individuals' compliance with using an intervention may be enhanced, which in turn affects the estimation of effect.

Appendix 3. Data for complete wound healing outcomes

Study	Comparison	Time-to-complete wound healing	Proportion of wounds completely healed	Comments

(Continued)

Charles 1991	Group 1. Compression (short-stretch bandage) Group 2. No compression	-	Leg ulcers completely healed Group 1. 71% Group 2. 25%	Unit of analysis is probably ulcers. The authors concluded "the leg ulcers treated with the short-stretch compression bandage had a statistically significant (chi-square test) higher healing rate than those treated in the control group."
Daróczy 2006	Group 1. Compression (topical povidone-iodine plus compression) Group 2. No compression (topical povidone-iodine without compression)	-	Group 1. 82% of 21 patients Group 2. 62% of 21 patients	
Kikta 1988	Group 1. Compression (Unna's boot) Group 2. No compression (hydroactive dressing)	Estimated results using Tierney 2007 methods: HR 2.38 95% CI 1.23 to 4.60 (lnHR 0.87 and selnHR 0.34)	Data included in Analysis 1.2 Group 1. 33/42 ulcers healed Group 2. 21/45 ulcers healed Data included in the associated sensitivity analysis of assuming missing data had unhealed leg ulcers Group 1. 21/42 ulcers healed Group 2. 15/45 ulcers healed.	Regarding the proportion of wounds completely healed, the difference in the data is due to the different assumptions applied for data analysis (see Sensitivity analysis).
Morrell 1998	Group 1. Compression (4-layer bandaging) Group 2. No compression (usual care)	Group 1 compared with Group 2. Log rank test statistic 4.90 (df =1, P = 0.03); Univariate Cox analysis: HR 1.45 (95% CI 1.04 to 2.03); Multivariate Cox analysis: HR 1.65 (95% CI 1.15 to 2.35). Median healing time: Group 1. 20 weeks Group 2. 43 weeks Mean number of weeks the participants were free from ulcers: Group 1. 20.1 weeks	Number (%) patients with complete healing at 12 months Group 1. 78/120 (65%) Group 2. 62/113 (55%)	

(Continued)

		Group 2. 14.2 (difference 5.9; 95% CI 1.2 to 10.5)		
O'Brien 2003	Group 1. Compression (4-layer bandage) Group 2. No compression	Group 1 compared with Group 2 HR 1.8 (95% CI 1.2 to 2.9)	Kaplan–Meier estimate of the proportion healed at 3 months Group 1. 54% Group 2. 34% (P < 0·001).	
Rubin 1990	Group 1. Compression (Unna's boot) Group 2. No compression (polyurethane foam dressing)	-	ITT analysis: Group 1. 18/19 (94.7%) patients with ulcers healed Group 2. 7/17 (41.2%). Complete cases: Group 1. 18/19 (94.7%) Group 2. 7/8 (87.5%) (Chi-squared = 8.2, P < 0.005).	
Taradaj 2007	Group 1. Compression Group 2. No compression	-	Narratives: No statistical difference in the pre- and post-treatment changes of total surface area, volume, length, width, field, and granulation surface area among groups (P-values of all between-group comparisons > 0.05); the percentage of weekly wound surface change rates; and the percentage of weekly ulcer volume change rates.	
Taylor 1998	Group 1. Compression Group 2.	Results calculated using the methods in Tierney 2007: HR 4.54 (95% CI 1.65 to 12.49); lnHR 1.51 and selnHR 0.52. Median healing time Group 1. 55 days Group 2. 84 days. (Lee-Desu statistic 8.603, P = 0.0034).	Data used in Analysis 1.2 Group 1. 14/18 Group 2. 7/18 Data used in the associated sensitivity analysis of assuming missing data had unhealed leg ulcers Group 1. 12/18 Group 2. 3/18	Regarding the proportion of wounds completely healed, the difference in the data is due to the different assumptions applied for data analysis (see Sensitivity analysis).
Wong 2008a	Group 1. Compression (short-stretch bandage, and 4-layer bandage)	-	Data used in Analysis 1.2 Group 1. 15/20 Group 2. 5/10	Regarding the proportion of wounds completely healed, the difference in the data

(Continued)

	Group 2. No compression		Data used in the associated sensitivity analysis of assuming missing data had unhealed leg ulcers Group 1. 13/20 Group 2. 3/10.	is due to the different assumptions applied for data analysis (see Sensitivity analysis).
Wong 2008b	Group 1. Compression (short-stretch bandage) Group 2. Compression (4-layer bandage) Group 3. No compression	Cox regression adjusted for age, initial ulcer size, and ulcer duration (hazard ratios for healing for Group 1 and Group 2 relative to Group 3) HR 2.72 (95% CI= 1.53-4.86); 3.14 (95% CI= 1.74-5.67) Survival time Mean 7.831 weeks (SE 0.489) for SSB, 8.557 (0.430) for 4LB, 10.378 (0.383) for control.	Data analysed in Analysis 1.2: Group 1. 48/60 Group 2. 50/60 Group 3. 23/60. Data used in the associated sensitivity analysis of assuming missing data had unhealed leg ulcers Group 1. 38/60 Group 2. 36/60 Group 3. 17/60.	Regarding the proportion of wounds completely healed, the difference in the data is due to the different assumptions applied for data analysis (see Sensitivity analysis).
Wong 2012	Group 1. Compression (short-stretch bandage) Group 2. Compression (4-layer bandage) Group 3. No compression	Time-to-complete wound healing Group 1. mean 9.8 (SD 0.77) weeks Group 2. 10.4 (0.80) Group 3. 18.3 (0.86)	Week 12: Group 1. 66.4% (71/107) Group 2. 59.8% (64/107) Group 3. 28.0% (30/107). Week 24: Group 1. 72.0% (77/107) Group 2. 67.3% (72/107) Group 3. 29.0% (31/107)	

Appendix 4. Sensitivity analyses

Sensitivity analysis	Studies	Participants	Effect estimate
Outcome: Time-to-complete wound healing			
• Sensitivity analysis of removing unpublished data (i.e. abstracts and dissertations)	4	553	• 4 studies (553 participants): HR 1.93 (95% CI 1.34 to 2.77; I^2 = 45%)
• Sensitivity analysis using fixed-effect model	5	733	• 5 studies (733 participants) with data reported by participant: HR 2.00 (95% CI 1.62 to 2.46; I^2 = 59%)

(Continued)

• Post hoc sensitivity analysis of removing clustered data	4	649	• 4 studies (649 participants): HR 2.16, 95% CI 1.41 to 3.31; I^2 = 68%
Outcome: Proportion of wounds completely healed			
• Sensitivity analysis of considering participants with missing data as having unhealed leg ulcers	10	1215	• 8 studies (1120 participants) with data reported by participant: RR 1.81 (95% CI 1.38 to 2.36; I^2 = 65%) • 2 studies (95 participants) without analysable data: both reporting a higher proportion of leg ulcers completed healed when using compression bandages or stockings than using no compression
• Sensitivity analysis of removing unpublished data (i.e. abstracts and dissertations)	8	1005	• 6 studies (910 participants) with data reported by participants: RR 1.57 (95% CI 1.24 to 1.99; I^2 = 50%) • 2 studies (95 participants) without analysable data: both reporting a higher proportion of leg ulcers completed healed when using compression bandages or stockings than using no compression
• Sensitivity analysis using a fixed-effect model	10	1215	• 8 studies (1120 participants) with data reported by participant: RR 1.75 (95% CI 1.54 to 1.98; I^2 = 65%) • 2 studies (95 participants) without analysable data: both reporting a higher proportion of leg ulcers completed healed when using compression bandages or stockings than using no compression
• Post hoc sensitivity analysis of removing clustered data	9	1131	• 7 studies (1036 participants) with analysable data:pooled RR 1.79 (95%CI 1.38 to 2.33; I^2 = 70%) • 2 studies (95 participants) without analysable data: both reporting a higher proportion of leg ulcers completed healed when using compression bandages or stockings than using no compression

HISTORY

Protocol first published: Issue 8, 2019

CONTRIBUTIONS OF AUTHORS

Chunhu Shi: designed the review; co-ordinated the review; extracted data; analysed or interpreted data; undertook quality assessment; performed statistical analysis; produced the first draft of the review; contributed to writing or editing the review; wrote to study authors/experts/companies; approved the final review prior to publication.

Jo Dumville: conceived the review; designed the review; co-ordinated the review; analysed or interpreted data; checked quality of statistical analysis; contributed to writing or editing the review; advised on the review; performed previous work that was the foundation of the current review; approved the final review prior to publication.

Nicky Cullum: conceived the review; designed the review; checked quality of statistical analysis; contributed to writing or editing the review; advised on the review; performed previous work that was the foundation of the current review; approved the final review prior to publication.

Emma Connaughton: checked quality of data extraction; undertook quality assessment; checked quality assessment; contributed to writing or editing the review; approved the final review prior to publication.

Gill Norman: checked quality of data extraction; checked quality assessment; contributed to writing or editing the review; advised on the review; approved the final review prior to publication.

Contributions of the editorial base

Tanya Walsh (Editor): edited the protocol of this review; advised on methodology, interpretation and content; approved the final protocol prior to publication.

Gill Rizzello (Managing Editor): co-ordinated the editorial process; advised on content; edited the protocol and the review.

Sophie Bishop (Information Specialist): designed the search strategy and edited the search methods section.

Ursula Gonthier (former Editorial Assistant): edited the reference section of the protocol of this review.

Tom Patterson (Editorial Assistant): edited the reference section of the review.

DECLARATIONS OF INTEREST

Chunhu Shi: I received support from the Tissue Viability Society to attend conferences unrelated to this work. The Doctoral Scholar Awards Scholarship and Doctoral Academy Conference Support Fund (University of Manchester) also supported a PhD and conference attendance respectively; both were unrelated to this work.

Jo Dumville: this research was co-funded by the National Institute for Health Research Manchester Biomedical Research Centre, and partly funded by the National Institute for Health Research Applied Research Collaboration Greater Manchester.

Nicky Cullum: this research was co-funded by the National Institute for Health Research Manchester Biomedical Research Centre, and partly funded by the National Institute for Health Research Applied Research Collaboration Greater Manchester.

My previous and current employers received research grant funding from the NHS Research and Development programme and the Health Technology Assessment Programme for systematic reviews on compression, and for two randomised controlled trials of compression. These RCTs were not eligible for inclusion in this review. The funders had no role in the conduct of this review.

Emma Connaughton: none known.

Gill Norman: this research was co-funded by the National Institute for Health Research Manchester Biomedical Research Centre.

Clifford Richardson (peer reviewer for the protocol for this review) declares that one of the review authors was the Head of the department in which he works, although he himself is not involved with the wound care research team within this department and has not been involved with the preparation or writing of this review.

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- NIHR Manchester Biomedical Research Centre (BRC), UK

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- We deleted the outcomes 'ulcer recurrence' and 'participant adherence to compression treatment', as the comparison of recurrence rates after initial healing is observational and the adherence outcome was only relevant to the compression arm of the included studies.
- We applied the trial filter developed by Glanville 2019 for the CINAHL Plus search, prepared by the Cochrane Centralised Search Service (CSS), rather than the Scottish Intercollegiate Guidelines Network (SIGN 2019) filter documented in the protocol.
- We involved one review author for independent data extraction and another review author to double-check.
- We assessed risk of bias in included studies using the tool with seven specific domains that separated the blinding of participants and personnel from blinding of outcome assessment, rather than a tool with six domains that considered the two domains of blinding together.
- We judged overall risk of bias using all seven domains rather than only three domains (sequence generation, allocation concealment, and blinding of outcome assessment) as pre-planned.
- We included mean pain score in our Summary-of-findings table together with the other outcomes listed.

INDEX TERMS

Medical Subject Headings (MeSH)

Bandages, Hydrocolloid; Bias; *Compression Bandages [adverse effects]; Dermatologic Agents [therapeutic use]; Pain Management; Quality of Life; Randomized Controlled Trials as Topic; *Stockings, Compression [adverse effects]; Time Factors; Varicose Ulcer [pathology] [*therapy]; *Wound Healing; Zinc Oxide [therapeutic use]

MeSH check words

Aged; Humans; Middle Aged