

Compression for venous leg ulcers (Review)

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Compression for venous leg ulcers

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ABSTRACT

Background

Around one percent of people in industrialised countries will suffer from a leg ulcer at some time. The majority of these leg ulcers are due to problems in the veins, resulting in an accumulation of blood in the legs. Leg ulcers arising from venous problems are called venous (varicose or stasis) ulcers. The main treatment has been a firm compression garment (bandage or stocking) in order to aid venous return. There is a large number of compression garments available and it is unclear whether they are effective in treating venous ulcers and which compression garment is the most effective.

Objectives

To undertake a systematic review of all randomised controlled trials of the clinical effectiveness of compression bandage or stocking systems in the treatment of venous leg ulceration.

Specific questions addressed by the review are:

1. Does the application of compression bandages or stockings aid venous ulcer healing?
2. Which compression bandage or stocking system is the most effective?

Search methods

For this update we searched the Cochrane Wounds Group Specialised Register (14/10/08); The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4 2008); Ovid MEDLINE (1950 to October Week 1 2008); Ovid EMBASE (1980 to 2008 Week 41) and Ovid CINAHL (1982 to October Week 1 2008). No date or language restrictions were applied.

Selection criteria

Randomised controlled trials recruiting people with venous leg ulceration that evaluated any type of compression bandage system or compression hosiery were eligible for inclusion. Comparators included no compression (e.g. primary dressing alone, non-compressive bandage) or an alternative type of compression. Trials had to report an objective measure of ulcer healing in order to be included (primary outcome for the review). Secondary outcomes of the review included ulcer recurrence, costs, quality of life, pain, adverse events and withdrawals. There was no restriction on date, language or publication status of trials.

Data collection and analysis

Details of eligible studies were extracted and summarised using a data extraction table. Data extraction was performed by one review author and verified independently by a second review author.

Main results

Overall, 39 RCTs reporting 47 comparisons were included.

Review question 1: there was reasonable evidence from seven RCTs that venous ulcers heal more rapidly with compression than without.

Review question 2: findings from six trials of single-component compression suggested that this strategy was less effective than multi-component compression. Evidence from compression systems with two components (3 trials) and three components (4 trials) suggested better outcomes when an elastic component was included. Different versions of compression with four-components (based on the Charing Cross four-layer bandage system) have similar effectiveness (3 trials). Compression with four components (variants of the Charing Cross four-layer bandage) is more effective than multi-component compression that includes a short-stretch bandage (6 trials). It is difficult to determine the relative effectiveness of the four-layer bandage compared with paste bandage systems because of differences in the paste systems (5 trials). There was no difference in effectiveness between the adjustable compression boot and compression bandages (2 trials) or between single-layer compression stockings and paste bandages (2 trials). Two-layer stockings appeared more effective than the short-stretch bandage (2 trials). The relative effectiveness of tubular compression when compared with compression bandages was not clear from current evidence (2 trials).

Three trials reported ulcer recurrence; because of sparseness of data and trials not being primarily designed to assess this outcome, firm conclusions could not be drawn. Although several trials included cost data, only one reported a rigorously conducted cost-effectiveness analysis with findings suggesting that the four-layer bandage was more cost-effective than multi-component compression comprising a short-stretch bandage. Seven trials assessed health-related quality of life and none observed significant differences between treatment groups. Several trials evaluated pain either as a stand-alone outcome, or as part of the assessment of adverse events. In general, the data did not indicate clear differences between treatment groups. It is possible that stockings could be associated with less pain than bandages but in view of scarcity of available data this requires further evaluation. Many of the trials reported adverse events and / or withdrawals. Overall, these outcomes appeared similar across different treatment groups.

Authors' conclusions

Compression increases ulcer healing rates compared with no compression. Multi-component systems are more effective than single-component systems. Multi-component systems containing an elastic bandage appear more effective than those composed mainly of inelastic constituents.

PLAIN LANGUAGE SUMMARY

Compression bandages and stockings to aid the healing of venous leg ulcers

Venous leg ulcers occur when the blood returning from the veins in the legs to the heart is slow or obstructed. These ulcers can take a long time to heal (weeks or months) and can cause distress to patients as well as being very costly for the health service. Compression bandages help to aid venous return and there is a number of types of bandages available, some of which are just a single type of bandage whilst others involve the application of several different bandages to the leg. Compression stockings are sometimes used as an alternative to compression bandages. This review examines the effectiveness of compression bandages versus no compression, and compares different types of compression bandages and stockings. We have looked at how well these different treatments work in terms of ulcer healing. We found that applying compression was better than not using compression and that multi-component bandages worked better than single-component systems. Multi-component systems (bandages or stockings) appear to perform better when one part is an elastic (stretchy) bandage.

Venous leg ulcers: the extent of the problem and management with compression

BACKGROUND

The point prevalence of active leg ulceration in the UK has been

estimated at 1.5/1000 (Callam 1992a; Lees 1992) and a similar rate was reported in Australia (Baker 1991). Prevalence increases with age, and is higher among women (Callam 1992a). Leg ulceration is typically a chronic recurring condition, with duration of episodes of ulceration ranging from a matter of weeks to more than 10 years (Callam 1985; Moffatt 1995; Noonan 1998). There is a considerable cost both to the patient in terms of pain, restricted mobility and social isolation (Charles 1995; Hareendran 2005) and to the health service. The estimated annual cost of leg ulcer treatment to the National Health Service (NHS) in the UK was between £230 million and £400 million during 1990-1991 (Bosanquet 1992). A more recent study estimated the cost of leg ulcer care within individual UK district health authorities at £212,700 to £333,400 annually (price year 1999) (Ellison 2002). Another evaluation estimated the average cost of treating a venous leg ulcer in the UK as varying between 814 and 1,994 Euros (price year 2002), with higher costs associated with larger and more chronic wounds (Ragnarson Tennvall 2005). Most leg ulcers are associated with venous disease, and history of a deep vein thrombosis is widely regarded as a predisposing factor to venous insufficiency and hence venous ulceration, however the aetiology of leg ulceration remains poorly understood. Venous insufficiency has been shown to be associated with increased hydrostatic pressure in the veins of the leg, and it is in an attempt to reverse this and aid venous return that external compression, in various forms, is applied as a therapy for venous leg ulcers.

Various forms of bandaging have been applied over the years. In the 17th Century, compression was applied as rigid lace-up stockings, and elasticated bandages were first produced in the middle of the 19th Century (Thomas 1995). At the beginning of the 21st century there remains wide variation in the management of venous leg ulcers. In the USA, Unna's boot (a non-compliant, plaster-type bandage) is favoured; in the UK the four-layer bandage (4LB) (which includes elastic components) is widely used whilst in mainland Europe and Australia the short stretch bandage (SSB) is standard practice. This review summarises the evidence for the effectiveness of the different forms of compression bandaging and compression stockings for venous leg ulcers. Devices that apply intermittent or pulsed compression to the limb were specifically excluded from this review and have been assessed in a separate Cochrane review (Nelson 2008).

Classification of different types of compression

There are many ways of applying compression, including single components (i.e. one type of bandage or stocking) and systems consisting of multiple components (different types of bandages and / or stockings used together). The interpretation of comparisons between compression systems has been hindered by the lack of internationally agreed performance standards, for example the UK and European classification systems for compression stockings are different. In the UK, performance indicators for bandages

and compression stockings have been developed (BS7505:1995). Bandages are categorised as retention, support or compression, depending on their performance in standardised laboratory tests. Compression bandages are further sub-divided according to the amount of force required to extend them and therefore the level of compression which they can apply to a limb. Furthermore, the laboratory performance of a bandage may not reflect its performance in clinical use as this might depend upon application technique and operator training. Compression systems commonly used for venous leg ulcers are listed below (from Thomas 1995).

Classification of Bandages:

- Class 1: retention bandages. Used to retain dressings.
- Class 2: support bandages. Used to support strains and sprains, e.g. crepe. Other bandages in this category can apply mild to moderate compression, e.g. Elastocrepe (Smith and Nephew), Rosidal K (Lohmann), Comprilan (Beiersdorf), when particular application techniques are used and the bandages are reapplied frequently.
- Class 3a: light compression. These bandages exert 14 to 17 mmHg at the ankle when applied in a simple spiral, e.g. Elset (Seton Scholl).
- Class 3b: moderate compression. These bandages apply 18 to 24 mmHg at the ankle when applied as a simple spiral, e.g. Granuflex Adhesive Compression Bandage (ConvaTec).
- Class 3c: high compression. These bandages apply 25 to 35 mmHg at the ankle when applied as a simple spiral, e.g. Setopress (Seton Scholl), and Tensopress (Smith and Nephew).
- Class 3d: extra high compression. These bandages apply up to 60 mmHg at the ankle when applied as a simple spiral, e.g. blue line webbing.

Hosiery can be used to both treat open ulceration and reduce the risk of recurrence post-healing and is similarly classified according to the level of compression applied to the limb. Importantly, hosiery is subject to less operator variability than stockings:

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

Recent developments in the classification of compression systems

A recent report from an international expert consensus group has debated the validity of the bandage classification described above and has recommended classification based on alternative criteria (Partsch 2008). In particular, they make a distinction between layers and components of compression bandage systems. Whereas

previously, different compression systems have been described as 'single-layer', two-layer', 'four-layer' and so on, this report proposes that application of all bandages involves some degree of overlap and therefore it is misleading to categorise any bandage system as 'single-layer'. The group recommended that the components of compression should be described, such as orthopaedic wool, crepe bandage or cohesive elastic bandages. Other recommended classification criteria include sub-bandage pressure (measured in the medial gaiter area with the patient supine) and the elastic property of the overall compression system. In terms of sub-bandage pressure, alternative categories to those described by the British Standards Institute (BS7505:1995) have been proposed, based on *in vivo* measurements. Overall, the ranges of pressure proposed by the consensus group are higher than those from the British Standards Institute. The recommendation to assess the elastic property of the compression system overall has arisen from the notion that although individual parts of a compression bandage system may be elastic, the interaction between different components might result in a system that is inelastic. In order to assess this, a measurement called the 'static stiffness index' (SSI) has been proposed; defined as the difference in sub-bandage pressures measured in standing and supine positions. A pressure increase of > 10 mmHg when the patient moves from supine to standing has been suggested to define inelasticity (high stiffness), and an increase of < 10 mmHg corresponds to elasticity (low stiffness) (Partsch 2008). Findings from a study of haemodynamics in 42 patients with chronic venous insufficiency treated with class II compression stockings suggested that the quotient of maximum working pressure to resting pressure (a measure of stiffness) is closely related to haemodynamic improvement, with increasing quotient representing reduced venous reflux (Häfner 2001). Where compression bandages are used as a single component, they can still be defined as 'elastic' and 'inelastic' (Partsch 2008).

Commonly used multi-component systems include:

- Short stretch/inelastic: orthopaedic wool plus 1-3 rolls of short-stretch bandage
- Inelastic paste system: paste bandage plus support bandage, e.g. Elastocrepe (Smith and Nephew)
- Unna's boot: non-compliant paste bandage
- Three layer elastic multi-layer: orthopaedic wool plus class 3c bandage, e.g. Tensopress (Smith and Nephew) plus shaped tubular bandage, e.g. Shaped Tubigrip (Seton Scholl)
- Four layer elastic multi-layer: orthopaedic wool plus support bandage (crepe) plus class 3a bandage (e.g. Elset, Seton Scholl) plus cohesive bandage (e.g. Coban, 3M).

The previous version of this review defined different compression systems in terms of the number of layers whereas, in line with the recommendations of the consensus group outlined above, this version refers to components. However, 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 or the SSI 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 experts in tissue viability at the outset of this review, and invited them to complete a survey. 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. As far as possible, the information gleaned from this exercise has been used in classifying and grouping different types of compression therapy in this review, and in aiding interpretation of findings.

Risks associated with use of compression

The use of compression to enhance venous return and aid the healing of venous ulcers is not without risk. The application of external compression at very high pressures will reduce blood supply to the skin and may lead to pressure damage. Similarly, the application of moderate pressures to patients with impaired arterial blood supply to the legs may also result in pressure damage. National clinical guidelines in the UK recommend that all patients presenting with a leg ulcer be screened for arterial disease using Doppler measurement of the ankle-brachial pressure index (ABPI) by suitably trained staff (Royal College of Nursing 2006). Clinically significant arterial disease is often defined using a cut-off of the ABPI of below 0.8. Patients with venous leg ulceration who have ABPI between 0.5 and 0.7 may be eligible to receive modified compression (Moffatt 2007). As part of this review, data on baseline ABPI and adverse events related to treatment have been recorded where available.

OBJECTIVES

To undertake a systematic review of all reliable evaluations of the clinical effectiveness of compression bandage or stocking systems in the treatment of venous leg ulceration.

Specific questions addressed by the review, and the comparisons made to answer this are:

Question 1: Does the application of compression bandages or stockings aid venous ulcer healing?

- 1.1 Compression compared with primary dressing alone
- 1.2 Compression compared with non-compressive bandages
- 1.3 Compression compared with usual care

Question 2: Which compression bandage or stocking system is the most clinically effective?

- 2.1 Single-component compression systems
 - 2.1.1 Single-component inelastic compression
 - 2.1.2 Single-component elastic compression
- 2.2 Compression systems comprising two components
- 2.3 Compression systems comprising three components
- 2.4 Compression systems comprising four components that includes an elastic component (the 'four-layer bandage')
 - 2.4.1 Comparison between different versions of the four-layer bandage
 - 2.4.2 Comparison between the four-layer bandage and multi-component systems that include an inelastic bandage
 - 2.4.3 Comparison between the four-layer bandage and compression systems with a paste bandage as the base
- 2.5 Adjustable compression boots compared with other types of compression
- 2.6 Compression stockings or tubular devices compared with compression bandage systems

METHODS

Criteria for considering studies for this review

Types of studies

Prospective, randomised controlled trials (RCTs) evaluating compression bandaging or stockings in the treatment of venous ulceration were eligible for inclusion. Studies using quasi-randomisation methods to allocate treatment (e.g. alternation or odd/even case numbers) were excluded. Trials were included if: the compression therapies under investigation were the only systematic difference between study arms; and if they reported an objective measure of ulcer healing such as time to complete healing, frequency of complete healing, change in wound size or healing rate. Trials reporting only subjective assessments of improvement/deterioration of the wound were excluded. There was no restriction on articles on the basis of language or publication status.

Types of participants

Trials recruiting people of any age with venous leg ulceration (may also be described as stasis or varicose ulceration) in any care setting were eligible for inclusion. As the method of diagnosis of venous ulceration may vary between studies there is no standardised definition applied but each study must refer to the use of compression

for venous rather than other types of leg ulcers e.g. arterial, mixed or vasculitic.

Types of interventions

Trials evaluating any form of compression bandage or compression stockings in patients with venous leg ulcers were eligible, including those assessing the following: single-component elastic or inelastic bandage systems; multi-component bandage systems; tubular compression devices; compression boots; and compression hosiery (stockings). Comparators included no compression (e.g. primary dressing alone or non-compressive bandages) or an alternative type of compression. Since the focus of Review Question Two was to assess the relative effectiveness of different types of compression therapy, trials comparing compression with other therapies (e.g. surgery, pharmacological treatment) were excluded. In addition, trials reporting the use of intermittent pneumatic compression were excluded as this therapy is the focus of another Cochrane review (Nelson 2008).

Types of outcome measures

In order to be eligible for inclusion, trials must report at least one primary outcome.

Primary outcomes

Objective measures of healing such as:

- Time to complete healing
- Proportion of ulcers healed within trial period
- Change in ulcer size (surface area or volume)
- Rate of change in ulcer size (surface area or volume)

Secondary outcomes

- Ulcer recurrence
- Costs
- Quality of life
- Pain
- Adverse events
- Patient withdrawals

Search methods for identification of studies

Electronic searches

Details of the search strategy for the original version of this review are available in [Appendix 1](#).

The following electronic databases were searched to identify RCTs on the use of bandages or stockings for the treatment of venous leg ulcers without date or language restrictions:

Cochrane Wounds Group Specialised Register (Searched 14/10/08)

The Cochrane Central Register of Controlled Trials (CENTRAL) - Issue 4 2008

Ovid MEDLINE - 1950 to October Week 1 2008

Ovid EMBASE - 1980 to 2008 Week 41

Ovid CINAHL - 1982 to October Week 1 2008

The following search strategy was used in the The Cochrane Central Register of Controlled Trials (CENTRAL):

#1 MeSH descriptor Occlusive Dressings explode all trees

#2 MeSH descriptor Stockings, Compression explode all trees

#3 (compression or bandag* or stocking* or hosiery or wrapp*):ti,ab,kw

#4 (#1 OR #2 OR #3)

#5 MeSH descriptor Leg Ulcer explode all trees

#6 (varicose NEXT ulcer*) or (venous NEXT ulcer*) or (leg NEXT ulcer*) or (foot NEXT ulcer*) or (stasis NEXT ulcer*):ti,ab,kw

#7 (#5 OR #6)

#8 (#4 AND #7)

The search strategies for Ovid MEDLINE, Ovid EMBASE and Ovid CINAHL can be found in [Appendix 2](#), [Appendix 3](#) and [Appendix 4](#) respectively. The Ovid MEDLINE search was combined with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision); Ovid format ([Lefebvre 2008](#)). The EMBASE and CINAHL searches were combined with the trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN) ([SIGN 2008](#)).

Searching other resources

The reference lists of all new studies identified in this update were searched to reveal any further studies not identified through the electronic searches.

For the first version of this review, experts in wound care and pharmaceutical companies were contacted to enquire about unpublished, ongoing and recently published trials. An Advisory Panel was also established; they assisted by checking our reference lists for any omissions, and they informed us of any unpublished, ongoing or recently completed trials.

Data collection and analysis

Data extraction and management

References identified from searches were entered into a bibliographic software package (ProCite). Two review authors worked independently and screened the references. If either review author considered a reference to be potentially relevant, the full report

was retrieved for further scrutiny. The two review authors made independent decisions about inclusion and exclusion of studies by referring each retrieved report to the selection criteria described above. Disagreements were resolved by discussion.

Details of eligible studies were extracted and summarised using a data extraction sheet. The following data were extracted:

- source population
- patient inclusion / exclusion criteria
- care setting
- baseline variables by group, e.g. age, sex, baseline area of ulcers, duration of ulceration
- description of the interventions and numbers of patients randomised to each intervention
- descriptions of any co-interventions / standard care
- follow-up period
- primary and secondary outcomes

Attempts were made to obtain data missing from reports by contacting the authors. Studies that have been published in duplicate were included only once and all relevant data were extracted. Data extraction was performed by one review author and verified independently by a second review author. Disagreements were resolved by discussion.

Assessment of risk of bias in included studies

Each study was individually critically appraised using the following quality criteria:

- adequacy of method of randomisation (sequence generation)
- allocation concealment at randomisation
- whether incomplete outcome data addressed
- blinded outcome assessment of healing
- baseline comparability of groups for important prognostic factors (ulcer surface area and duration)

The methodological quality of trials in the review overall is discussed narratively (see 'Risk of bias in included studies' below). In addition, validity assessment information is used in the summary sections for each type of comparison in an attempt to distinguish between different trials in terms of their methodological quality and summarise the body of evidence.

Data synthesis

Included trials were grouped in the narrative synthesis according to the types of compression being evaluated. For example, evaluations of single-component systems were described separately to those focusing on multi-component compression. Within each comparison group, studies were pooled when they appeared similar in terms of methods, participant characteristics, interventions and outcomes. A test of statistical heterogeneity was generated for each pooled outcome. Statistical heterogeneity was defined as a Chi-

squared P value of 0.1 or greater and the I^2 test was undertaken in order to estimate the percentage of the variability in estimates of effect due to heterogeneity rather than chance (Higgins 2003). It has been suggested that when the I^2 estimation is greater than zero, both fixed effect and random effects analyses should be undertaken and any difference in estimates noted (Sterne 2008). Where clinical, methodological and statistical heterogeneity were not apparent, similar studies were pooled using a fixed effect model. A random effects model was additionally applied where I^2 was greater than zero in the absence of apparent clinical or methodological heterogeneity. Where pooling was not possible or appropriate, individual estimates from trials were reported in the narrative synthesis.

For dichotomous outcomes (e.g. frequency of complete healing during the trial period), relative risk (RR) estimates with 95% confidence interval (CI) were calculated for each trial individually and pooled if considered appropriate. The RR was presented in preference to the odds ratio (OR) as the latter gives an inflated impression of the size of effect when event rates are high, as is the case for most trials reporting healing of chronic wounds.

For continuous outcomes (e.g. percentage change in ulcer surface area, healing rate in cm^2 per week), the mean difference (MD) with 95% CI was calculated for each trial individually. Where appropriate, trials were pooled using the weighted mean difference (WMD). When trials assessed the same outcome using different scales (e.g. change in ulcer area in cm^2 and as a percentage) but otherwise did not appear to be methodologically, clinically or statistically heterogeneous, estimates were pooled using the standardised mean difference (SMD).

In terms of time-to-event outcomes, estimates of hazard ratio (HR) and 95% CI as presented in the trial reports were converted into the log rank observed minus expected events and variance of this statistic (Tierney 2007). Where appropriate, estimates were pooled using a fixed effect model (random effects model not available for this analysis). When I^2 was greater than zero, sources of heterogeneity were investigated using sub-group analysis.

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#); [Characteristics of studies awaiting classification](#).

Thirty nine RCTs reporting 47 comparisons are included in this review. Three evaluations are published as conference proceedings only (Colgan 1995; Kralj 1996; Knight 1996).

The number of patients in the included trials ranged from 10 to 387. Just over one-third (36%) had sample sizes of 50 patients or fewer and over half (62%) recruited 100 patients or fewer. Twelve trials reported an a priori sample size estimation; generally these

were the more recent evaluations (Morrell 1998; Moffatt 1999; Partsch 2001; Meyer 2003; Moffatt 2003a; O'Brien 2003; Ukat 2003; Franks 2004; Iglesias 2004; Jünger 2004a; Jünger 2004b). Three of these evaluations were designed as non-inferiority trials and presented a proposed non-inferiority limit (Moffatt 1999; Jünger 2004a; Jünger 2004b). Two more studies included some information about the intended sample size but did not show the full details of the estimation (Polignano 2004a; Milic 2007) and one included a post hoc assessment of statistical power (Meyer 2002). The remaining 24 trials (62%) did not report any information about sample size estimation.

All patients were deemed to have venous ulceration and most trials (33/39) specified a cut-off value of ABPI to exclude clinically significant arterial disease at baseline. The cut-off point for application of compression was 0.8 in the majority of these studies (23/33), other values being 0.7 and 0.75 in one trial each, 0.9 in seven trials and 1.0 in one trial.

Most of the trial reports provided some information on patient selection criteria. Four trials presented minimal details, describing only the cut-off value for ABPI (Charles 1991; Duby 1993; Taylor 1998; Ukat 2003) and three trials did not include any details at all relating to inclusion and exclusion of patients, apart from the stipulation of having a venous leg ulcer (Hendricks 1985; Eriksson 1986; Knight 1996).

The amount of pressure applied to a leg depends on bandage application or stocking fitting technique. Overall, few details were reported relating to the techniques used for applying compression or relevant staff experience and training. Some reports stated that compression devices were applied according to the manufacturers' instructions (Hendricks 1985; Kikta 1988; Moody 1999; Franks 2004; Jünger 2004a; Polignano 2004a). In some evaluations, nurses with prior experience of leg ulcer management provided care (Callam 1992b; Scriven 1998; Taylor 1998; Vowden 2000; Meyer 2002; Meyer 2003; Jünger 2004a; Nelson 2007a) whilst in others, training was provided for the purposes of the trial (Wilkinson 1997; Morrell 1998; Moody 1999; O'Brien 2003; Iglesias 2004; Jünger 2004b).

Information on the techniques used for bandage application were seldom presented but when available these included a spiral technique (Charles 1991; Callam 1992b; Moody 1999), figure of eight application (Meyer 2002; Meyer 2003) and Putter technique (two bandages applied in opposite directions) (Partsch 2001). In some trials, patients or their relatives were involved in the application of compression devices. In a trial of compression boots, patients adjusted the straps between clinic visits in order to help maintain the original degree of compression (DePalma 1999). In other trials, patients or relatives were instructed to reapply bandages between clinic visits (Eriksson 1986; Ukat 2003; Jünger 2004b).

Seven RCTs were identified that compared compression with no compression (Review Question 1). Specific comparators included primary dressing only (Eriksson 1984; Kikta 1988), non-compressive bandages (Rubin 1990) and usual care that did not routinely

include compression (Charles 1991; Taylor 1998; Morrell 1998; O'Brien 2003).

For Review Question 2 (Which compression bandage or stocking system is the most clinically effective?), trials were grouped to reflect comparisons between different types of compression. Eight broad comparison groups were formed, as follows:

1. Single-component compression (elastic or inelastic) versus other types of compression (six trials). One trial compared single-component inelastic compression with the 4LB (Kralj 1996). The other trials compared single-component elastic compression with: an alternative single-compression system (paste bandage) (Cordts 1992), two-components (Eriksson 1986), three components (Travers 1992) and four components (Colgan 1995; Nelson 2007a).
2. Two-component compression systems versus other types of compression (three trials). Comparators included alternative two-component systems (Danielsen 1998; Moody 1999) and the 4LB (Moffatt 2003a).
3. Three-component compression systems versus other types of compression (four trials), the comparison in each case being a competing system comprising three components (Callam 1992b; DUBY 1993; Gould 1998; Meyer 2002).
4. The original 4LB versus alternative versions of the 4LB (three trials) (Wilkinson 1997; Moffatt 1999; Vowden 2000).
5. The 4LB versus multi-component systems based on the short-stretch bandage (six trials) (DUBY 1993; Scriven 1998; Partsch 2001; Ukat 2003; Franks 2004; Iglesias 2004).
6. The 4LB versus compression systems with a paste bandage as the basis (five trials) (DUBY 1993; Colgan 1995; Knight 1996; Meyer 2003; Polignano 2004a).
7. Adjustable compression boots compared with compression bandages (two trials); comparators being a paste bandage system (DePalma 1999) and four-component compression (Blecken 2005).
8. Compression stockings or tubular devices compared with compression bandages (six trials). Specific comparisons included: single-layer stocking versus paste bandage (Hendricks 1985; Koksall 2003), two-layer stocking versus a short-stretch bandage (Jünger 2004b; Polignano 2004b), tubular compression versus short-stretch bandage (Jünger 2004a) and a three-component system incorporating a tubular device versus a three-component bandage system (Milic 2007).

Just under half of the trials (18/39) were conducted in the UK (Charles 1991; Callam 1992b; Travers 1992; DUBY 1993; Wilkinson 1997; Gould 1998; Morrell 1998; Scriven 1998; Taylor 1998; Moffatt 1999; Moody 1999; Vowden 2000; Meyer 2002; Meyer 2003; Moffatt 2003a; Franks 2004; Iglesias 2004; Nelson 2007a). Two were performed in Ireland (Colgan 1995; O'Brien 2003), 11 in mainland Europe (Eriksson 1984; Eriksson 1986; Kralj 1996; Danielsen 1998; Partsch 2001; Ukat 2003; Jünger 2004a; Jünger 2004b; Polignano 2004a; Polignano 2004b; Milic 2007), one in Turkey (Koksall 2003) and seven in the USA

(Hendricks 1985; Kikta 1988; Rubin 1990; Cordts 1992; Knight 1996; DePalma 1999; Blecken 2005). In terms of the type of setting, all studies (where described) were conducted in outpatient and community settings, with three recruiting some hospitalised patients as part of the sample (Kralj 1996; Ukat 2003; Polignano 2004a).

Risk of bias in included studies

Seven trials employed computer-generated randomisation lists (Meyer 2002; Meyer 2003; Moffatt 2003a; O'Brien 2003; Iglesias 2004; Polignano 2004a; Milic 2007) and one used random number tables to generate the randomisation sequence (Wilkinson 1997). Other trials deemed likely to have used a satisfactory randomisation method were Morrell 1998; Taylor 1998; Moffatt 1999 and Jünger 2004a. Six trials used block randomisation (Wilkinson 1997; Scriven 1998; Jünger 2004b; Polignano 2004a; Iglesias 2004; Nelson 2007a). In an attempt to promote adequate balance of baseline variables across groups (e.g. ulcer area and duration), several studies used stratified randomisation (Wilkinson 1997; Danielsen 1998; Morrell 1998; Scriven 1998; Moffatt 1999; Partsch 2001; Meyer 2002; Meyer 2003; Moffatt 2003a; Franks 2004; Iglesias 2004; Jünger 2004a; Nelson 2007a) or minimisation (Taylor 1998). Three trials were factorial and included additional randomised comparisons of other interventions used concurrently with compression: knitted viscose dressing versus foam dressing (Callam 1992b), two different foam dressings (Franks 2004) and knitted viscose dressing versus hydrocolloid dressing and oral oxypentifylline versus placebo (Nelson 2007a). In the majority of trials, the patient was the unit of study but in five studies limbs were randomised and analysed (Kikta 1988; DUBY 1993; Wilkinson 1997; Scriven 1998; Blecken 2005). The methods of analysis used in these trials ignored the highly correlated healing data from patients with both limbs included, with one exception that used within-individual randomisation and employed an appropriate method for analysis of healing rate (Blecken 2005). Overall, 16 out of 39 trials were deemed to have incorporated adequate allocation concealment. These included three that used a remote telephone randomisation service (Wilkinson 1997; Iglesias 2004; Jünger 2004a) and one that used a minimisation programme which we assume would be computerised and so include allocation concealment (Taylor 1998). In addition, nine studies reported the use of sealed envelopes with some other detail about this method (i.e. opaque envelopes and / or opened in sequential order) and we assumed that this would amount to adequate allocation concealment (Morrell 1998; Scriven 1998; Vowden 2000; O'Brien 2003; Ukat 2003; Jünger 2004b; Polignano 2004a; Franks 2004; Nelson 2007a). A further three trials described randomisation as concealed but did not provide details of the methods used to achieve this; again, we assumed that the methods used were satisfactory (Rubin 1990; Danielsen 1998; Meyer 2003). In one evaluation, the trial authors confirmed that allocation was unconcealed (Moffatt

2003a). In the remaining 22 trials, allocation concealment was either by sealed envelopes with no further description of the exact procedures followed (Kralj 1996; Partsch 2001), or more commonly, not mentioned at all (Eriksson 1984; Hendricks 1985; Eriksson 1986; Kikta 1988; Charles 1991; Callam 1992b; Cordts 1992; Travers 1992; Duby 1993; Colgan 1995; Knight 1996; Gould 1998; DePalma 1999; Moffatt 1999; Moody 1999; Meyer 2002; Koksall 2003; Polignano 2004b; Blecken 2005; Milic 2007). We have labelled these 22 trials as 'unclear' in terms of adequacy of allocation concealment.

Three trials reported using blinded outcome assessment (Gould 1998; Koksall 2003; Jünger 2004b) and one incorporated blinded confirmation of healing (Iglesias 2004). For eight trials, outcome assessment was not blind (Colgan 1995; Wilkinson 1997; Morrell 1998; Scriven 1998; Partsch 2001; Ukat 2003; Franks 2004; Nelson 2007a) and for all other studies, either the relevant information was not clear or not mentioned at all.

Just under half of the trials (18/39) conducted analysis by intention to treat (Callam 1992b; Travers 1992; Duby 1993; Colgan 1995; Morrell 1998; Scriven 1998; Moffatt 1999; Partsch 2001; Meyer 2002; Meyer 2003; Moffatt 2003a; O'Brien 2003; Franks 2004; Iglesias 2004; Polignano 2004a; Polignano 2004b; Blecken 2005; Nelson 2007a) and one presented raw data so that the review authors could generate such an analysis (Hendricks 1985). It was sometimes possible for the review authors to re-calculate estimates of complete healing (dichotomous outcome) based on a denominator comprising all patients originally randomised to treatment (Danielsen 1998). For the remaining trials, it was either unclear whether the intention to treat principle had been employed, or else it was obvious that this was not the case.

Several prognostic studies have suggested that baseline ulcer area and duration are significant independent predictors of delayed healing of venous leg ulcers (Skene 1992; Franks 1995; Margolis

2000; Margolis 2004; Brown 2004). Therefore, each included trial was examined with reference to the balance of these variables across treatment groups. In four trials, treatment groups appeared to be comparable at baseline (Partsch 2001; Franks 2004; Iglesias 2004; Nelson 2007a). Overall, 21 evaluations were rated as 'unclear' for this criterion for the following reasons: no data or very limited information provided (n=8) (Eriksson 1984; Eriksson 1986; Kikta 1988; Knight 1996; Gould 1998; Moody 1999; Meyer 2002; Polignano 2004b); mean rather than median values presented (medians preferable since baseline ulcer area and duration data are usually positively skewed) (n=9) (Charles 1991; Callam 1992b; Cordts 1992; Travers 1992; Kralj 1996; Morrell 1998; Koksall 2003; Jünger 2004a; Blecken 2005); and insufficient information provided for at least one of the prognostic variables (e.g. data presented in categorical format which is less useful for group comparisons) (n=4) (Moffatt 1999; Meyer 2003; Moffatt 2003a; Ukat 2003). Scrutiny of baseline ulcer area and duration suggested imbalances which could confound the treatment effect in the 14 remaining studies (Hendricks 1985; Rubin 1990; Duby 1993; Colgan 1995; Wilkinson 1997; Danielsen 1998; Scriven 1998; Taylor 1998; DePalma 1999; Vowden 2000; O'Brien 2003; Jünger 2004b; Polignano 2004a; Milic 2007).

In some respects, the methodological quality of clinical trials of compression appears to be improving over time, with evaluations published within the last ten years being more likely to include a proper method of randomisation with attempts to generate balanced groups at baseline, allocation concealment and analysis by intention to treat. Most trials do not use blinded outcome assessment. An overall summary of the methodological quality of the included trials can be found in Figure 1 and a graphical breakdown per trial is shown in Figure 2. Figure 3 presents the trials in chronological order, illustrating improving methodological quality over time.

Figure 1. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

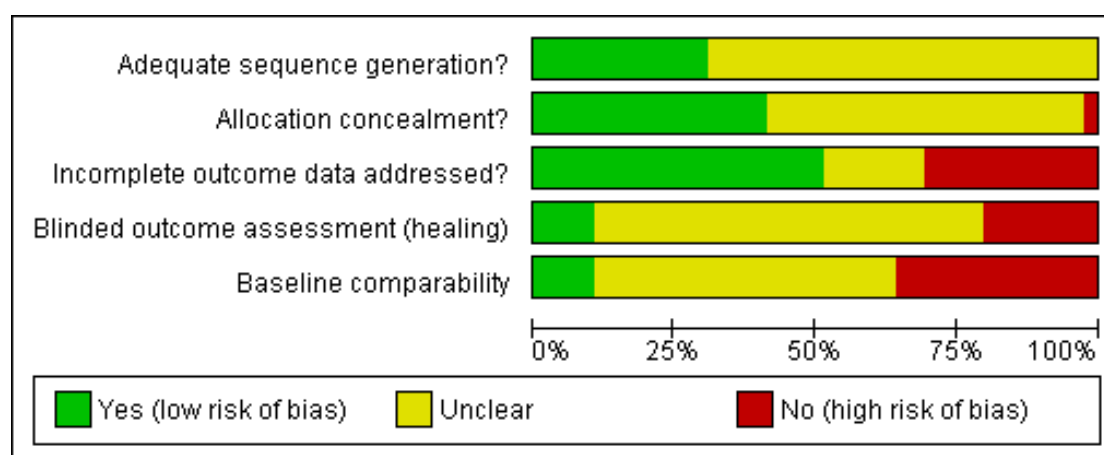


Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Adequate sequence generation?	Allocation concealment?	Incomplete outcome data addressed?	Blinded outcome assessment (healing)	Baseline comparability
Blecken 2005	?	?	+	?	?
Callam 1992b	?	?	+	?	?
Charles 1991	?	?	?	?	?
Colgan 1995	?	?	+	+	+
Cordts 1992	?	?	+	?	?
Danielsen 1998	?	+	+	?	+
DePalma 1999	?	?	+	?	+
Duby 1993	?	?	+	?	+
Eriksson 1984	?	?	+	?	?
Eriksson 1986	?	?	?	?	?
Franks 2004	?	+	+	+	+
Gould 1998	?	?	+	+	?
Hendricks 1985	?	?	+	?	+
Iglesias 2004	+	+	+	+	+
Jünger 2004a	+	+	+	?	?
Jünger 2004b	?	+	+	+	+
Kikta 1988	?	?	+	?	?
Knight 1996	?	?	?	?	?
Koksal 2003	?	?	+	+	?
Kralj 1996	?	?	+	?	?
Meyer 2002	+	?	+	?	?
Meyer 2003	+	+	+	?	?
Milic 2007	+	?	+	?	+
Moffatt 1999	+	?	+	?	?
Moffatt 2003a	+	+	+	?	?
Moody 1999	?	?	?	?	?
Morrell 1998	+	+	+	+	?
Nelson 2007a	?	+	+	+	+
O'Brien 2003	+	+	+	?	+
Partsch 2001	?	?	+	+	+
Polignano 2004a	+	+	+	?	+
Polignano 2004b	?	?	+	?	?
Rubin 1990	?	+	?	?	+
Scriven 1998	?	+	+	+	+
Taylor 1998	+	+	+	?	+
Travers 1992	?	?	+	?	?
Ukat 2003	?	+	?	+	?
Vowden 2000	?	+	+	?	+
Wilkinson 1997	+	+	?	+	+

Figure 3. Methodological quality summary with trials presented in chronological order

	Adequate sequence generation?	Allocation concealment?	Incomplete outcome data addressed?	Blinded outcome assessment (healing)?	Baseline comparability?
Eriksson 1984	?	?	?	?	?
Hendricks 1985	?	?	?	?	?
Eriksson 1986	?	?	?	?	?
Kikta 1988	?	?	?	?	?
Rubin 1990	?	?	?	?	?
Charles 1991	?	?	?	?	?
Callam 1992b	?	?	?	?	?
Corbett 1992	?	?	?	?	?
Travers 1992	?	?	?	?	?
Duby 1993	?	?	?	?	?
Colgan 1995	?	?	?	?	?
Knight 1996	?	?	?	?	?
Kralj 1996	?	?	?	?	?
Wilkinson 1997	?	?	?	?	?
Danielson 1998	?	?	?	?	?
Gould 1998	?	?	?	?	?
Morrell 1998	?	?	?	?	?
Scriven 1998	?	?	?	?	?
Taylor 1998	?	?	?	?	?
DePalma 1999	?	?	?	?	?
Moffatt 1999	?	?	?	?	?
Moody 1999	?	?	?	?	?
Vowden 2000	?	?	?	?	?
Partsch 2001	?	?	?	?	?
Meyer 2002	?	?	?	?	?
Kokosz 2003	?	?	?	?	?
Meyer 2003	?	?	?	?	?
Moffatt 2003a	?	?	?	?	?
O'Brien 2003	?	?	?	?	?
Ukai 2003	?	?	?	?	?
Frank 2004	?	?	?	?	?
Iglesias 2004	?	?	?	?	?
Junger 2004a	?	?	?	?	?
Junger 2004b	?	?	?	?	?
Pollignano 2004a	?	?	?	?	?
Pollignano 2004b	?	?	?	?	?
Breckan 2005	?	?	?	?	?
Milic 2007	?	?	?	?	?
Nelson 2007	?	?	?	?	?

Effects of interventions

Review Question 1: Does the application of compression bandages or stockings aid venous ulcer healing?

Overall, seven RCTs were identified comparing compression with no compression. These studies have been grouped according to the type of comparator: primary dressing only (Eriksson 1984; Kikta 1988); non-compressive bandages (Rubin 1990); and usual care that did not routinely include compression (Charles 1991; Taylor 1998; Morrell 1998; O'Brien 2003).

1.1 Compression compared with primary dressing alone (2 RCTs)

Two trials compared the use of compression (both with a paste impregnated device as the basis) with primary dressings alone

(Eriksson 1984; Kikta 1988). In the earlier study, based in Sweden, 44 patients were allocated to receive one of the following for eight weeks: freeze-dried porcine skin dressing with no compression; non-adherent aluminium foil dressing with no compression; or compression therapy consisting of zinc oxide paste inner stocking plus outer elastic bandage (Eriksson 1984). Frequency of complete healing was not reported, the primary outcomes being percentage decrease in ulcer area and volume at eight weeks. The respective values (as read from a figure with no available variability estimates) were: porcine skin dressing 65% and 75%; aluminium foil dressing 10% and 0%; and compression 80% and 90%. The estimates for the group receiving the porcine skin dressing are difficult to interpret as the randomised intervention ceased mid-study because of lack of availability. At this point, patients in this group crossed over to the compression treatment. Six patients receiving the aluminium foil dressing discontinued treatment because of ulcer deterioration (increase in size and/or infection). None of

the patients randomised to compression discontinued treatment. Baseline ulcer area and duration were not reported.

The second study was conducted in the USA and recruited 84 patients with 87 venous leg ulcers (Kikta 1988). Allocated treatments were as follows: hydrocolloid dressing (n=45 ulcers); and Unna's boot (no description of exact components) (n=42 ulcers). When frequency of complete healing at six months was analysed on an intention-to-treat basis (by review author), the estimated between-group difference was not statistically significant: RR 1.50 (95% CI 0.90 to 2.50), $P = 0.12$ (Analysis 1.1). The authors reported that 18 ulcers were withdrawn from the study within two weeks of randomisation (6 in hydrocolloid group, 12 in compression group, reasons not given), therefore other analyses (conducted by the authors) were based on 66 patients with 69 ulcers. None of the patients receiving compression discontinued treatment because of adverse events compared with ten patients in the hydrocolloid group, eight because of wound exudate and two because of cellulitis ($P = 0.004$ for between-group difference). It was difficult to fully assess baseline comparability because mean values were reported rather than medians, however baseline ulcer duration appeared longer in the compression group (mean±sem 51±17 versus 45±12 weeks). Caution is required in interpreting findings because healing data on multiple ulcers from the same patient will be highly correlated and should not be assumed to be independent. Inappropriate analysis of such data may generate biased estimates of effect (Altman 1997).

Both trials used a patient exclusion criterion relating to presence of arterial disease that is less stringent relative to most other trials of compression therapy (commonly ABPI < 0.8): ABPI < 0.75 (Eriksson 1984); and ABPI < 0.7 (Kikta 1988).

1.2 Compression compared with non-compressive bandages (1 RCT)

A multicentre trial conducted in the USA compared Unna's boot (zinc and calamine paste bandage) with polyurethane foam dressing (n=36 patients) (Rubin 1990). All patients received elastic bandages as a retaining layer that did not provide compression. The estimate for the number of patients with complete healing at 12 months was in favour of compression: RR 2.30 (95% CI 1.29 to 4.10), $P = 0.005$ (Analysis 2.1). The mean healing rate (cm² per day) was also significantly better for the compression group: 0.5 versus 0.07 ($P = 0.004$, variability not reported). None of the patients randomised to compression withdrew from treatment whereas nine of those allocated to the non-compressive regimen withdrew because of malodorous wound exudate. Six of these nine patients experienced increase in ulcer size during the trial. Baseline ulcer duration was not reported. The mean (range) baseline ulcer area appeared larger in the group receiving compression: 76.0 (0.02 to 600.0) versus 32.2 (6.0 to 270.0) cm² (median values not reported).

1.3 Compression compared with usual care (4 RCTs)

One trial compared a short-stretch bandage (SSB) with usual district nurse care (not involving compression) (Charles 1991). The other three studies compared a package of specialised leg ulcer care that included provision of the 4LB, with usual primary care management which generally did not involve compression (Taylor 1998; Morrell 1998; O'Brien 2003). Three trials were conducted in the UK (Charles 1991; Taylor 1998; Morrell 1998) and one was performed in Ireland (O'Brien 2003).

In the evaluation of SSB versus usual care (N=53 patients), more patients achieved complete healing at three months in the SSB group (71% versus 25%) (Charles 1991). The authors stated that this difference was statistically significant but did not report the P value. As raw numbers for this outcome were not clear from the trial report, these data have not been plotted. Twenty one per cent of the usual care group experienced an increase in ulcer area during the trial versus none in the SSB group. Three patients withdrew from each group.

Three trials compared four component compression (the 4LB) in the context of a specialist leg ulcer community service with usual management by the general practitioner (GP) and district nurse (Taylor 1998; Morrell 1998; O'Brien 2003). In one trial (N=36 patients), significantly more patients experienced complete healing at three months in the compression group: RR 4.0 (95% CI 1.35 to 11.82), $P = 0.01$ (Analysis 3.1) (Taylor 1998). Further analyses reported in the paper suggested that healing occurred more rapidly with the 4LB. Two patients withdrew from this treatment, compared with four in the usual care group. Cost analyses based on consumables, district nurse time and mileage estimated significantly lower values for the 4LB both per week and for the whole trial duration.

The second trial (N=233 patients) found no statistically significant difference in complete healing at one year (Morrell 1998): RR 1.18 (95% CI 0.96 to 1.47), $P = 0.12$ (Analysis 3.2). However, survival analyses conducted by the trial authors suggested significantly faster time to healing for the compression group. Kaplan-Meier analysis estimated median weeks to healing as 20 versus 43 ($P = 0.03$, log rank test). A Cox proportional hazards model adjusted for patient age, baseline ulcer area, baseline ulcer duration and history of deep vein thrombosis, estimated the following in favour of the 4LB: HR 1.65 (95% CI 1.15 to 2.35) ($P < 0.05$, exact value not reported). Ulcer recurrence during the one-year trial period was not significantly different between groups: RR 1.53 (95% CI 0.88 to 2.66), $P = 0.13$ (Analysis 3.3) and the log rank test of difference in time to recurrence was also not significantly different between groups ($P = 0.38$). No significant differences were detected between groups for change in health status during the trial nor for mean NHS cost per patients per year. Seventeen patients withdrew from the 4LB group and 23 from usual care. Since mean values were reported, it was difficult to assess group comparability but the usual care group appeared to have included people with larger and more chronic ulcers at baseline.

The third trial (N=200 patients) found a shorter healing time with compression ($P = 0.006$, log rank test and $P = 0.015$ from Cox model adjusting for patient age, baseline ulcer area, baseline ulcer duration, history of deep vein thrombosis, diabetes and rheumatoid arthritis) (O'Brien 2003). Costs per leg healed were significantly lower for the compression group: median (interquartile range) cost (presume price year 1999-2000) EURO209.7 (137.5 - 269.4) versus EURO234.6 (168.2 - 345.1), $P = 0.04$. In addition, the compression group experienced statistically significant increases in some domains of health-related quality of life at six weeks relative to the usual care group, detected in both disease-specific (including global score) and generic instruments. Findings from the three evaluations of four-component compression are slightly difficult to interpret because some patients in the usual care group could have received compression but full details (e.g. number of patients, type of compression) are not always documented. In addition, the bandage application is not the only systematic difference between the two groups; other aspects of the provision of specialist care to the compression groups could have influenced the outcomes.

Summary of evidence for Review Question 1: Does the application of compression bandages or stockings aid venous ulcer healing?

Overall, there is reasonable evidence that venous ulcers heal more rapidly with compression than without. Some of the observed benefits for patients receiving a specialised package of care that included application of the 4LB when compared with usual care could be explained by aspects other than compression, for example, a higher level of staff expertise resulting in better clinical management of leg ulceration overall. The data suggest that costs associated with compression treatment are lower than those for strategies not involving compression.

Review Question 2: Which compression bandage or stocking system is the most clinically effective?

2.1 Single-component compression systems (6 RCTs)

This section summarises the evidence from clinical trials evaluating single-component compression systems compared with other types of compression. For the purposes of this review, it has been assumed that a single-component compression system consists of one type of compression bandage that may be used with or without a primary dressing. When used, primary dressings have been described, but are not be considered as part of the compression system. Six trials were identified overall. One compared a single-component inelastic system with the 4LB (Kralj 1996) whilst the other five compared a single-component elastic system with various types of alternative compression treatments (Eriksson 1986; Cordts 1992; Travers 1992; Colgan 1995; Nelson 2007a).

2.1.1 Single-component inelastic compression (1 RCT)

A small trial (N=40 patients) conducted in Slovenia found similar rates of complete healing at six months with an inelastic bandage (used with a hydrocolloid primary dressing) and the 4LB (Kralj 1996): RR 1.14 (95% CI 0.51 to 2.55), $P = 0.74$ (Analysis 4.1). Information from the author suggested that not all patients were in the trial for the full six-month period. Data on time to healing suggested faster wound closure for the group receiving the 4LB: mean values 57.6 versus 84.9 days (method of deriving these values not stated). Four patients withdrew from the 4LB group and two from the single-component group. As some patients were recruited from an in-patient setting (number not known) the source population may have had a greater degree of comorbidity compared with other trials of venous leg ulcer treatment recruiting only community-based patients. However, exclusion criteria included severe concurrent disease.

2.1.2 Single-component elastic compression (5 RCTs)

Five trials were identified that compared a single-component elastic compression system with other types of compression. The latter included an alternative single-component system (Cordts 1992), two components (Eriksson 1986), three components (Travers 1992) and four components (Colgan 1995; Nelson 2007a).

One trial compared two different single-component compression systems: a cohesive elastic bandage used in conjunction with a hydrocolloid primary dressing versus a zinc oxide and calamine paste impregnated bandage (described as Unna's boot with no other components mentioned) (Cordts 1992). Analyses were based on those who had completed the study (there were seven withdrawals in the elastic bandage group and six for the paste bandage) (N=43 patients randomised; n=30 analysed). No statistically significant differences were found between the treatments for the following outcomes: complete healing at 12 weeks (RR 1.17, 95% CI 0.54 to 2.54) (Analysis 5.1); mean percentage change in ulcer area relative to baseline (MD -65.00%, 95% CI -163.44 to 33.44, values read from graph) (Analysis 5.2); mean healing rate per week (MD 0.03 cm²/week, 95% CI -0.01 to 0.07) (Analysis 5.3) and pain score (not plotted). Adverse events were reported in two patients receiving the elastic bandage and in three patients allocated the paste bandage but none of these necessitated withdrawal from treatment.

A second trial compared single-component compression (elastic bandage plus hydrocolloid dressing) with two components (zinc oxide paste impregnated stocking plus an outer elastic bandage) (N=34 patients) (Eriksson 1986). In the single-component group, the elastic bandage was removed at night and reapplied in the morning by the patient. There was no significant difference between groups at 12 weeks for complete healing: RR 1.29 (95% CI 0.62 to 2.65) (Analysis 5.1). The mean percentage decreases in ulcer area and volume at 12 weeks (read from a figure) were 70% and 55% respectively for single-component compression and 75%

and 75% for the system comprising two components. Two patients receiving the single-component system withdrew compared with three from the other group.

When a single-component system (elastic cohesive bandage) was compared with three components (paste bandage, non-cohesive elastic bandage and elastic tubular overlay) there was no statistically significant difference detected at seven weeks for percentage change relative to baseline ulcer area (MD -7.0%, 95% CI -18.38 to 4.38, based on values read from graph) ([Analysis 5.2](#)) ([Travers 1992](#)). Twenty-seven patients were recruited and all completed the trial. Assessment of ankle sub-bandage pressures showed no significant difference between groups at the start of treatment but after one week the three component system had better maintenance of compression: 23 mmHg versus 35 mmHg ($P < 0.01$). All patients in this trial had baseline ABPI > 0.9 , a more stringent threshold than that seen in many other trials of venous leg ulcer treatment (usually > 0.8). The recruited sample appeared to be relatively young (mean ages 54 for single-component and 59 for three components). Comparability between treatment groups at baseline could not be easily judged because of reporting of mean rather than median values. However, the available data suggested that larger ulcers on average were treated with the single-component system and more chronic ulcers were allocated to three components.

Another trial ($N=30$ patients) evaluated three types of compression: a single-component compression system consisting of polyurethane foam primary dressing plus elastic bandage; the 4LB (Profore); and a modified Unna's boot which consisted of four components (paste bandage, cotton crepe bandage, elastic adhesive bandage and class II compression sock) ([Colgan 1995](#)). In terms of complete healing at 12 weeks, no significant difference was found between groups for the comparison between single-component compression and the 4LB, RR 0.33 (95% CI 0.09 to 1.27) ([Analysis 6.1](#)), nor for single-component versus modified Unna's boot RR 0.29 (95% CI 0.08 to 1.05) ([Analysis 5.1](#)). There were no cases of ulcer recurrence during a six month follow-up period (starting from the end of the 12 week treatment period). Three patients withdrew from the single-component group because of inability to tolerate the bandage. One patient receiving Unna's boot withdrew because of an allergy and there were no reported withdrawals from the 4LB group. The average cost of the bandages per patient over 12 weeks in Irish £ (price year not stated) was: single-component 58.33, Unna's boot 66.24, and 4LB 82.54.

A large trial ($N=245$ patients) with 2x2x2 factorial design evaluated pentoxifylline versus placebo, knitted viscose versus hydrocolloid dressings as well as single-component compression (hydrocolloid-lined elastic adhesive bandage) versus the 4LB (wool, crepe, support bandage, cohesive elastic bandage) ([Nelson 2007a](#)). Analyses were conducted initially on all patients, i.e. those with both simple and non-simple venous ulceration (non-simple defined as serologically confirmed rheumatoid arthritis or venous

pathology not confirmed with hand-held Doppler). The estimate for complete healing at 24 weeks suggested a statistically significant difference in favour of the 4LB over the single component, adhesive bandage: RR 0.74 (95% CI 0.59 to 0.92) ([Analysis 6.1](#)). A Kaplan-Meier estimate of median days to healing showed faster wound closure for the 4LB group (78 versus 168 days, log rank test not reported) and a HR estimate from a Cox proportional hazards model adjusting for drug, dressing, study centre, simple / non-simple ulcer aetiology, baseline ulcer area, baseline ulcer duration and years since first ulcer was 2.0 (95% CI 1.4 to 2.9), $P < 0.0005$, indicating a greater probability of healing with the 4LB. The proportion of patients who changed bandage during the trial because of an adverse event was 28% for the single-component compression and 15% for the 4LB. Further analyses (complete healing, withdrawal rate and quality of life) were conducted on a subset of patients with simple venous ulceration ($n=200$). For people with simple ulcers, complete healing at 24 weeks was less likely with the single component bandage than the 4LB: RR 0.70 (95% CI 0.55 to 0.89) (not plotted). The proportion of patients who withdrew from the bandage system with or without simultaneous withdrawal from the randomised drug and dressing treatment was 20% for the single-component group and 5% for the 4LB. Health-related quality of life was assessed using the Nottingham Health Profile and showed significantly greater improvements in some domains for the 4LB group at 24 weeks.

Analysis graphs 5 and 6 show plots of outcomes for individual trials; data have not been pooled, with reasons for this outlined as follows. [Analysis 5.1](#) shows three trials comparing single-component compression with compression based on a paste bandage for the outcome of complete healing at three months ([Colgan 1995](#); [Cordts 1992](#); [Eriksson 1986](#)). There were both clinical and methodological differences between these trials. In one, the single-component system consisted of a cohesive elastic bandage ([Cordts 1992](#)) whereas the other two trials used non-cohesive devices ([Colgan 1995](#); [Eriksson 1986](#)). In addition, the comparators differed and consisted of: a single-component paste bandage ([Cordts 1992](#)), paste bandage plus elastic bandage ([Eriksson 1986](#)) and a four-component system ([Colgan 1995](#)). The outcome in one trial was based on those who had completed the study ([Cordts 1992](#)) whereas the other two reported on all recruited patients ([Eriksson 1986](#); [Colgan 1995](#)). [Analysis 6.1](#) shows complete healing during the study period for two trials of single-component compression versus four components ([Colgan 1995](#); [Nelson 2007a](#)). The single-component systems differed, one being adhesive ([Nelson 2007a](#)) and the other non-cohesive ([Colgan 1995](#)). In addition, the trial durations differed: three months ([Colgan 1995](#)) and six months ([Nelson 2007a](#)). [Analysis 5.2](#) displays two trials comparing single-component compression with a paste-based system for the outcome of percentage reduction in ulcer area during the trial period ([Cordts 1992](#); [Travers 1992](#)). The outcome was assessed at different time points: seven weeks ([Travers 1992](#)) and 12 weeks ([Cordts 1992](#)).

Summary of evidence for Section 2.1: Single component compression systems

Findings from the largest and highest quality trial suggest better healing outcomes for the 4LB compared with single-component compression in terms of frequency of complete healing and time to healing. In addition, adverse event rates were lower and quality of life scores higher for the multi-component system. Estimates for complete healing were in favour of the 4LB whether analyses were based on all patients (i.e. those with both simple and non-simple venous ulceration) or a sub-group with simple venous ulceration (Nelson 2007a). The other five trials did not detect significant differences between groups for healing outcomes. Sample sizes were small in these four studies (range 27 to 43 patients) and therefore unlikely to have sufficient statistical power to detect true treatment effects. One of the trials reported better maintenance of compression with a three-component system when compared with a single component (Travers 1992).

2.2 Compression systems comprising two components (3 RCTs)

Three trials were identified: two compared alternative two-component systems (Danielsen 1998; Moody 1999) and the third compared two components with four components (the 4LB) (Moffatt 2003a).

Two trials compared elastic and inelastic (short-stretch) outer bandages, all preceded by padding of the lower limb (Danielsen 1998; Moody 1999). When data were pooled for complete healing at 3-6 months (N=95), there was no statistically significant difference between groups: RR 1.23 (95% CI 0.67 to 2.25), $P = 0.51$ (test for heterogeneity $P = 0.47$, $I^2=0\%$) (Analysis 7.2).

In the earlier trial (N=43 patients), complete healing was additionally reported at one month and one year (Danielsen 1998). At one month, there was no statistically significant difference between the alternative two component systems (RR 3.48, 95% CI 0.42 to 28.63, Analysis 7.1) however at one year more people had healed in the system with the elastic outer bandage: RR 3.48 (95% CI 1.14 to 10.60), $P = 0.03$ (Analysis 7.3). Additional analyses conducted by the trial authors at one year also suggested a better outcome for the elastic bandage: Kaplan-Meier estimate of proportions healed were 81% versus 31%, $P = 0.03$; and median values for relative ulcer area 0.00 versus 0.77 ($P < 0.01$). It is assumed that the latter outcome represents the percentage of original ulcer area remaining although this is not explained in the trial report. Several different dressings and topical applications were used within groups making the results difficult to interpret. It should also be noted that the numbers of patients with complete healing reported at each time point represented those who had healed and recurred since the previous assessment; this is reflected in the larger proportion of patients with complete healing at 6 months relative to one year in the inelastic group (15% versus 25%). Analysis of ankle sub-bandage pressures indicated better maintenance of compression

for the system including an elastic component. Withdrawal rates were 30% from the elastic group and 50% from the inelastic group (this includes three patients who were deemed ineligible by the trial authors post-randomisation). The patient selection criteria appeared stringent compared with some other trials (exclusions: ABPI < 0.9 , diabetes and inability to walk unassisted).

The second trial (N=52 patients) reported mean times to healing of 9.3 weeks for the group receiving an elastic bandage and 9.9 weeks for the inelastic bandage, and mean percentage reduction in ulcer area at 3 months as 52% versus 73% respectively (no variability data reported for either outcome) (Moody 1999). The percentages of patients with increased ulcer size / clinical infection during the study period were 23% / 15% for those receiving an elastic bandage and 15% / 12% for the inelastic bandage. One patient receiving the inelastic bandage withdrew because of difficulties in performing the necessary frequency of bandage re-application; there were no other reports of withdrawals. Baseline ulcer area was not reported; patients receiving the inelastic bandage had ulcers of longer duration at baseline, on average (assessment based on mean values with no variability data).

The third trial in this section compared a two-component system comprising padding plus elastic bandage (Surepress) with the 4LB (Profore) (N=112 patients) (Moffatt 2003a). The frequency of complete healing did not differ significantly between groups at three months: RR 0.82 (95% CI 0.62 to 1.10) (Analysis 8.1). At six months, a statistically significant difference was detected in favour of the 4LB when patients were analysed up to end of the randomised treatment: RR 0.56 (95% CI 0.41 to 0.77), $P = 0.0003$ (Analysis 8.2). This analysis was repeated including patients who had healed following withdrawal from the randomised treatment, some of whom switched bandage systems; the between group difference was not statistically significant (RR 0.88, 95% CI 0.73 to 1.05) (Analysis 8.3). The reported HR adjusted for sex, baseline ulcer area, ulcer duration, ankle circumference, medication use, previous ulceration and limb ABPI was 1.18 (95% CI 0.69 to 2.02), $P = 0.55$. In the group receiving the two-component system, 19 patients reported 21 bandage-related adverse events versus seven patients with eight events in the group allocated the 4LB. In both groups the types of adverse events included irritation, pain, slippage, tissue breakdown and excessive pressure. Withdrawal rates were 54% for two components and 12% for four components. The mean weekly cost of treatment per patient (clinic costs and home care costs) was lower in the 4LB group (£79.91 versus £83.56) and the same trend was observed for mean cost per patient over the six-month trial (£876 versus £916). Prices were in UK £ Sterling with 2000 as the price year. The trial authors proposed that the lower costs in the group receiving the 4LB were explained by fewer dressing changes relative to the group receiving two components (1.1 versus 1.5 per week, $P = 0.0002$). Assessment of health-related quality of life using SF-36 data at baseline, 24 weeks and at healing / withdrawal suggested no significant differences between the two bandage systems. The analysis

was adjusted for baseline score. There may have been a baseline imbalance between groups in terms of ulcer duration as, although median and minimum values were the same (six weeks and two weeks), the maximum value was substantially higher in the group receiving two components (1040 weeks versus 104 weeks) introducing a possible bias in favour of the 4LB.

Summary of evidence for Section 2.2: Compression systems comprising two components

There was no evidence of a between-group difference for complete healing at 3-6 months when data were pooled from two small trials comparing elastic and inelastic outer bandages, both being preceded by padding (Danielsen 1998; Moody 1999). Further findings from one of these trials suggested a better performance for the system including an elastic bandage in terms of complete healing at one year, maintenance of compression and withdrawal rates (Danielsen 1998). The largest trial in this group suggested that the 4LB out-performed two component compression in terms of complete healing at six months, however there was no evidence of a difference between groups in healing outcomes at three months, nor from a hazard ratio estimate; fewer adverse events and withdrawals were observed in the group receiving the 4LB (Moffatt 2003a). This was the strongest trial methodologically, incorporating computer-generated randomisation, stratification at randomisation for study centre and baseline ulcer area and analysis by intention-to-treat, however, treatment allocation was unconcealed.

2.3 Compression systems comprising three components (4 RCTs)

Four trials compared alternative three component compression systems (Duby 1993; Callam 1992b; Gould 1998; Meyer 2002). For three trials, whether the middle bandage was elastic or inelastic was the main distinguishing feature (Callam 1992b; Gould 1998; Meyer 2002). Of these three trials, one used orthopaedic wool as the first component in both arms (Callam 1992b), whilst the other two used a paste bandage (Gould 1998; Meyer 2002). The third component varied between trials and consisted of: an elastic graduated tubular bandage for the arm receiving the elastic middle component and an inelastic cohesive bandage for the group allocated the inelastic middle component (Callam 1992b); an elasticated viscose stockinette for both groups (Gould 1998); and an elastic graduated tubular bandage for both groups (Meyer 2002). Analysis 9.1 shows the data from these trials in terms of complete healing. Significantly more patients (Callam 1992b) and ulcers (Gould 1998) completely healed by 3 to 4 months when patients received a compression system incorporating an elastic rather than inelastic bandage (N=171 patient / ulcers): RR 1.83 (95% CI 1.26 to 2.67), P = 0.002 (test for heterogeneity P = 0.75, I²=0%). The possibility of highly correlated healing data influencing the estimate of effect should be noted in the trial using

ulcers as the unit of randomisation / analysis; some patients had both limbs studied (using the largest wound available), the first limb being randomised and the second receiving the alternative compression system (Gould 1998). The third study had a longer follow up period and did not detect a statistically significant difference in healing at six months (N=112 patients): RR 0.94 (95% CI 0.69 to 1.27), P = 0.67 (Analysis 9.1) (Meyer 2002). This trial also conducted survival analyses and reported similar median time to healing for both groups: 9.0 versus 9.5 weeks for groups receiving elastic and inelastic middle components respectively. Larger ulcer area was identified as a statistically significant independent predictor of delayed healing (P < 0.001) (Meyer 2002). In terms of adverse events, one trial reported that two patients in each group had a minor degree of damage related to the bandage (Callam 1992b). This trial also assessed patient-reported pain and reported that a greater proportion of those receiving the inelastic component complained of ulcer pain at all clinic visits (48% versus 29%, P = 0.03). In terms of withdrawals, one trial reported more patients discontinuing treatment in the group receiving the inelastic middle component (30% versus 12%) (Callam 1992b), another reported similar rates for both groups (around 14%) (Meyer 2002) whilst the third reported the overall withdrawal rate as 18% but did not provide data per group (Gould 1998).

One trial had possible imbalances between groups at baseline with larger ulcers in the group receiving the inelastic middle component and more ulcers of longer duration in the group receiving the elastic middle component. In view of the types of data presented (mean values for ulcer area and categorical data for wound duration) it was difficult to assess baseline comparability with certainty (Callam 1992b). In another trial, baseline data were not presented by treatment group but the trial authors reported that groups were similar (Gould 1998). The third trial presented categorical data suggesting that groups were comparable for baseline ulcer area; this was the only baseline variable shown (Meyer 2002).

The fourth trial compared the following compression systems: orthopaedic wool, short-stretch bandage and net covering versus zinc and ichthammol paste bandage, cotton crepe bandage, and elastic tubular bandage (N=51 limbs) (Duby 1993). There was no statistically significant difference between the groups in complete healing at three months: RR 1.73 (95% CI 0.74 to 4.06), P = 0.20 (Analysis 11.1). Findings appeared to be more favourable for the short-stretch group in terms of mean percentage reduction in ulcer area at three months (60% versus 43%), but variability data were not reported, precluding generation of a plot, and the P value was not presented. The group receiving the paste bandage system included more male patients and had a longer mean baseline ulcer duration compared with the group receiving the short-stretch bandage. Since limbs rather than patients were allocated, and this was not adjusted for in any analyses, the possibility of biased estimates of treatment effect should be considered.

Summary of evidence for Section 2.3: Compression systems

comprising three components

Four trials compared different compression systems that comprised three components (Duby 1993; Callam 1992b; Gould 1998; Meyer 2002). In three trials, the main difference between study arms was whether the middle component was elastic or inelastic (Callam 1992b; Gould 1998; Meyer 2002). A pooled estimate from two trials for frequency of complete healing at 3–4 months suggested a better outcome for the system including an elastic bandage. Individual estimates from both trials might be biased because of potentially poor balance of prognostic factors at baseline (Callam 1992b) and correlated healing data arising from the same individuals being regarded as independent (Gould 1998); however the latter included blinded outcome assessment, a procedure which should help to reduce bias. The third trial found no difference between groups in terms of complete healing at six months and median times to healing; this study was the only one in this group to report a proper method of randomisation (Meyer 2002). Overall, these data could suggest that the differences between treatment groups diminish over time, but this notion should be regarded with caution because estimates at different time points did not come from the same evaluations.

A fourth trial comparing short-stretch and paste bandage systems did not report any significant differences between groups but was probably too small to detect clinically meaningful differences (Duby 1993).

2.4 Compression systems comprising four components that includes an elastic component (the 'four-layer bandage')

2.4.1 Comparison between different versions of the four-layer bandage (3 RCTs)

Three trials compared variants of the 4LB (Wilkinson 1997; Moffatt 1999; Vowden 2000). Data from two trials were plotted for the comparison of the original Charing Cross 4LB with an alternative system but studies were not pooled as the comparators differed. The estimates showed no statistically significant differences at three months for complete healing (patients or limbs) (Analysis 10.1) (Wilkinson 1997; Moffatt 1999) or at six months in one evaluation (N=232): RR 0.96 (95% CI 0.83 to 1.12), $P = 0.6$ (Analysis 10.1) (Moffatt 1999). The components of the alternative system used in the earlier trial (Wilkinson 1997) differed from most proprietary kits (elasticated viscose stockinette to retain the primary dressing, lint applied in separate strips horizontally around the leg, elastic bandage and elasticated viscose stockinette as the final retaining component for the whole system). The third trial compared three different four-component systems: the original Charing Cross 4LB; a modified 4LB (alternative devices were substituted for the two middle components but appeared to have similar characteristics to the originals); and a proprietary kit (Robinson Ultra-Four) (Vowden 2000). Frequency of complete healing was reported at three months and five months but

since raw numbers were not clear from the trial report, data have not been plotted. No statistically significant differences between groups were reported for complete healing, respective rates being 60%, 76% and 60% at three months, and 87%, 84% and 83% at five months.

Two of the trials reported additional outcomes. There was no statistically significant difference in the mean reduction in ulcer area during the three-month trial period based on limbs that were unhealed and completed the trial: 39% for the original 4LB system ($n=5$ limbs) and 34% for the alternative system ($n=8$), $P = 0.89$ (Wilkinson 1997). Another trial reported that the Kaplan-Meier estimate of proportions of patients healed at six months was 82% for the original 4LB system and 84% for the alternative; the HR estimate was 1.18 (95% CI 0.87 to 1.59), $P = 0.28$ (stated as adjusted for baseline variables but unclear exactly which ones) (Moffatt 1999). This trial assessed quality of life using the Nottingham Health Profile and found similar scores between groups for all domains at six months. A small number of withdrawals because of bandage discomfort were noted for all three trials and there were no apparent differences between treatment groups. Two trials reported pressure damage arising from the bandage: this affected one patient in each of the two arms receiving alternatives to the original Charing Cross system (Vowden 2000) and one patient receiving the Charing Cross system (Wilkinson 1997).

Summary of evidence from Section 2.4.1: Comparison between different versions of the four-layer bandage

Overall, there is no evidence of a difference in outcomes between different versions of the 4LB system. The smallest trial in the group (N=35 limbs) used a proper method of randomisation and allocation concealment (Wilkinson 1997). The other two trials were larger but some aspects of methodological quality were difficult to assess because of lack of information in the trial reports (Moffatt 1999; Vowden 2000).

2.4.2 Comparison between the four-layer bandage and multi-component systems that include an inelastic bandage (6 RCTs)

Six trials were identified comparing the 4LB with a multi-component system that included a short-stretch (inelastic) bandage (SSB) (Duby 1993; Scriven 1998; Partsch 2001; Ukat 2003; Franks 2004; Iglesias 2004). The 4LB systems all comprised: an initial layer of orthopaedic wool, a crepe bandage to smooth the wool layer, an elastic bandage and an elastic cohesive bandage as the outer layer. The comparator systems usually consisted of orthopaedic wool, one or two SSBs and sometimes a retaining layer (e.g. cohesive bandage or tubular device). When data from four trials were pooled, there was no significant difference between treatment groups in frequency of complete healing at 3 to 4 months: RR 1.12 (95% CI 0.96 to 1.31), $P = 0.15$ (test for heterogeneity

$P = 0.16$, $I^2 = 41\%$) (Analysis 12.1) (Duby 1993; Partsch 2001; Ukat 2003; Iglesias 2004). Since the I^2 estimation was greater than zero, this analysis was repeated using a random effects model which showed a similar estimate of effect: RR 1.07 (95% CI 0.85 to 1.36) (Analysis 12.2). Data from one trial indicated no differences in complete healing at six months when analysed according to both intention to treat (RR 1.05, 95% CI 0.89 to 1.25) and when the analysis was limited to those treated as randomised (i.e. excluding those who switched treatments after withdrawal from the randomised bandage) (RR 0.94, 95% CI 0.77 to 1.15) (Franks 2004). The estimate from another trial for complete healing at one year also showed no difference between bandage types: RR 1.08 (95% CI 0.97 to 1.22) (Iglesias 2004) (Analysis 12.1).

Five trials reported estimates derived from Kaplan-Meier survival analyses, for either cumulative proportions of patients healed, median time to healing, or both (Scriven 1998; Partsch 2001; Ukat 2003; Franks 2004; Iglesias 2004). Data from one trial suggested more patients treated with SSB healed at four months (but P value not reported): 78% versus 85% (Partsch 2001). In another trial, the proportion healed was 56% in both groups at three months, and values remained similar at six months: 4LB 85% and SSB 83% (Franks 2004). The third trial found similar values between groups at three months (46% for the 4LB and 37% for the SSB, $P = 0.1$) but by six months the between-group difference was significant and in favour of the 4LB (68% versus 55%, $P = 0.02$) (Iglesias 2004). The fourth trial reporting this outcome did not detect a statistically significant difference between groups at one year: 55% for the 4LB and 57% for SSB, $P = 0.1$ (Scriven 1998). With respect to median times to healing, one trial showed no significant difference between groups (4LB 92 days versus SSB 126 days, $P = 0.117$) (Iglesias 2004) whilst a second evaluation reported a significant difference in favour of the 4LB ($P = 0.03$) but did not report the estimates (Ukat 2003).

Four trials reported HR estimates of treatment effect (Partsch 2001; Ukat 2003; Franks 2004; Iglesias 2004). All four trials included type of bandage, study centre and baseline ulcer area as covariates and three included baseline ulcer duration (Partsch 2001; Ukat 2003; Iglesias 2004). The trials varied in the addition of other prognostic factors, indicating that the hazard ratio for each trial had been estimated in a different way. Pooling the trials indicated a higher probability of healing with the 4LB: HR 0.80 (95% CI 0.66 to 0.97), $P = 0.02$, however, statistically significant heterogeneity was detected ($P = 0.06$, $I^2 = 60\%$) (Analysis 12.3). In order to explore possible sources of heterogeneity, each trial was omitted in turn from the meta-analysis and the effect on the pooled estimate observed. In addition, trials were grouped according to the geographical location of the study (UK or continental Europe) in order to investigate whether the compression system used locally appeared to perform better when evaluations were split in this way (Analysis 12.3). It can be observed from Analysis 12.3 that heterogeneity persisted in each sub-group analysis. Overall, the treatment effect remained in favour of the 4LB except in analyses

where the largest trial was omitted (Iglesias 2004, 67.4% weight in the initial analysis), reducing statistical power.

Two trials reported on the reduction in ulcer area during the trial period (Duby 1993; Ukat 2003). Since no data were provided on variability, neither estimate could not be plotted. In one trial, the mean percentage reduction at 12 weeks was 76% for the 4LB and 60% for the SSB (between-group difference reported as not statistically significant by the trial authors but P value not shown) (Duby 1993). In the second trial, the respective mean and median values were: 4LB 58% and 77%; and SSB 46% and 56% (P values for between-group differences not reported) (Ukat 2003).

Two trials included an assessment of quality of life (Franks 2004; Iglesias 2004). One used the Nottingham Health Profile and observed no statistically significant differences between treatment groups for scores for any domain at six months (Franks 2004). The other trial had a large amount of missing data for this outcome and so reported a descriptive analysis of findings obtained using the SF-12 and the Hyland Leg and Foot Ulcer Questionnaire (Iglesias 2004). Overall, there did not appear to be marked differences between treatment groups.

Three trials included an analysis of costs (Scriven 1998; Ukat 2003; Iglesias 2004) but only one comprised a rigorously conducted cost-effectiveness analysis (Iglesias 2004). Cost estimates were based on NHS and Personal Social Services costs and health benefits were measured as differences in ulcer free days and quality adjusted life years. The following estimates were reported, all in favour of the 4LB: mean between-group difference in healing time 10.9 days (95% CI -6.8 to 29.1); MD in QALYs -0.02 (95% CI -0.08 to 0.04); and MD in total cost (£ sterling, price year 2001): £227.32 (95% CI 16.53 to 448.30) per patient per year. Sensitivity analyses showed the cost-effectiveness estimate to be robust to variation in the number of bandages used and unit costs of compression systems. The 4LB emerged as the dominant treatment strategy. The second trial calculated the cost per patient and cost per ulcer healed, based on costs of bandages and other disposables (e.g. primary dressings, wadding) and 30 minutes of nursing time per bandage change (Ukat 2003). Costs per patient (EURO) were 587 for the 4LB and 1,345 for the SSB; and per ulcer healed 1,845 and 5,502 respectively. Statistical tests for between group differences and price year were not reported. The third trial estimated the cost of treatment over six months as (£ Sterling) 392.60 for the 4LB and 184.56 for the SSB (estimates based on cost of bandage systems only, price year not stated) (Scriven 1998).

Two trials reported adverse events in detail, including presentation of those considered to be possibly or definitely related to compression (Franks 2004; Iglesias 2004). One trial reported that out of 30 adverse events reported by 23 patients, 12 (40%) were possibly or definitely related to the bandage in the 4LB group, compared with 36 adverse events in total reported by 22 patients, nine (25%) could have been device-related for the SSB group (Franks 2004). The second trial reported the number of patients with adverse events possibly related to compression as 39% for the 4LB and

47% for the SSB (Iglesias 2004).

Five trials reported on withdrawals (Scriven 1998; Partsch 2001; Ukat 2003; Franks 2004; Iglesias 2004). Two found similar withdrawal rates for both treatment groups: 18% (Ukat 2003) and around 22% (Franks 2004). Two others found higher withdrawal rates in patients allocated to the SSB: 3% versus 6% (represents proportion of limbs withdrawn) (Scriven 1998); and 24% versus 34% (Iglesias 2004). The fifth trial reported more withdrawals in the group receiving the 4LB, 12% versus 23% (Partsch 2001).

Summary of evidence from Section 2.4.2: Comparison between the four-layer bandage and multi-component systems that include an inelastic bandage

Most unadjusted analyses of healing (complete healing at fixed time points and cumulative proportions healed) did not show differences between treatment groups, with the exception of the largest trial in this group which detected significantly more ulcer healing in those treated with the 4LB for cumulative proportions healed at six months (Iglesias 2004). Pooled HRs (4 trials) adjusted for baseline ulcer area and other covariates also suggested an estimate in favour of the 4LB (Partsch 2001; Ukat 2003; Franks 2004; Iglesias 2004). One trial included a rigorous cost-effectiveness analysis which indicated that the 4LB was the dominant treatment strategy (Iglesias 2004). Two trials assessing quality of life found no difference between the two bandage systems (Franks 2004; Iglesias 2004). Two trials reported adverse events in detail; one found more device related adverse events in the group receiving the 4LB (Franks 2004) whilst the other found more in the SSB (Iglesias 2004). The evidence overall suggested roughly similar withdrawal rates for the two bandage systems.

2.4.3 Comparison between the four-layer bandage and compression systems with a paste bandage as the base (5 RCTs)

Five trials were identified for this comparison (Duby 1993; Colgan 1995; Knight 1996; Meyer 2003; Polignano 2004a). In all studies, the 4LB consisted of orthopaedic wool, a crepe bandage, an elastic bandage and an elastic cohesive bandage as the final retaining component. Three trials used a proprietary 4LB kit (Profore) (Colgan 1995; Knight 1996; Polignano 2004a). The paste bandage system (sometimes referred to as Unna's Boot) varied between trials, consisting of: paste bandage applied over a foam primary dressing with no other compression components (Knight 1996); a two-component system with an elastic cohesive bandage applied after the paste bandage (Polignano 2004a); three component systems comprising paste / crepe / elastic tubular bandage (Duby 1993) and paste / elastic / elastic tubular bandage (Meyer 2003); and finally, a four-component system consisting of paste / crepe / elastic cohesive / and class II compression sock (Colgan 1995).

Four trials reported complete healing at different time points: three months (N = 71 patients / limbs) (Duby 1993; Colgan 1995); six

months (N = 68 patients) (Polignano 2004a); and one year (N = 133 patients) (Meyer 2003). Data were pooled for the two trials with a three-month endpoint (fixed effect model) suggesting no significant difference in complete healing between the 4LB and paste-based compression: RR 1.34 (95% CI 0.78 to 2.28), P = 0.29 (test for heterogeneity P = 0.11, I²=60%) (Analysis 13.1) (Duby 1993; Colgan 1995). The estimate generated from a random effects model was similar: RR 1.23 (95% CI 0.54 to 2.82) (Analysis 13.2). Likewise, the observed between-group difference for complete healing at other time points did not suggest a statistically significant difference: RR 1.13 (0.82 to 1.57) at six months (Polignano 2004a) (Analysis 13.1); and RR 0.82 (95% CI 0.66 to 1.01) at one year (Meyer 2003) (Analysis 13.1).

Survival analysis was undertaken for two trials (Meyer 2003; Polignano 2004a). Data from one evaluation suggested shorter time to healing with paste bandage (median values 12 versus 16 weeks, P = 0.04), with the difference in probability of healing becoming significant after 20 weeks post-randomisation (P = 0.036) (Meyer 2003). Larger baseline ulcer area was a significant independent predictor of delayed healing (statistics not presented) but baseline ulcer duration was not found to be a prognostic factor. The second trial estimated similar values for median days to healing for each study arm (53 for the four-layer bandage and 56 for the paste bandage) (Polignano 2004a). This trial also presented a HR estimate that suggested no significant difference between groups: 1.62 (95% CI 0.87 to 3.02), P = 0.13 and found that larger ulcers at baseline were associated with longer time to healing (P = 0.01). Baseline ulcer duration did not emerge as a significant predictor of delayed healing.

Two trials presented the mean percentage reduction in ulcer area during the trial (Duby 1993; Polignano 2004a). For the earlier study, variability data were not provided and so the estimate of treatment effect could not be plotted. The mean percentage reduction at three months appeared to be higher in the group receiving the 4LB (76% versus 43%) but the P value for the between-group difference was not reported (Duby 1993). Data from the second trial were converted into a MD estimate of treatment effect, indicating no significant difference between groups: 54.50% (95% CI -9.17 to 118.17), P = 0.09 (Analysis 13.3) (Polignano 2004a). Two trials reported rate of healing as follows: percentage daily healing rate (Polignano 2004a); and the absolute rate in cm² per week (Knight 1996). These data were pooled using standardised mean difference (SMD), and suggested a significant treatment effect in favour of the 4LB: SMD 0.52 (95% CI 0.06 to 0.97), P = 0.03 (test for heterogeneity P = 0.47, I²=0%) (Analysis 13.4).

One trial reported recurrence, stating that there were no cases of ulcer recurrence during a six month follow-up period (starting from the end of the 12 week treatment period) (Colgan 1995).

One trial included a cost analysis based on the costs of bandages per patient over the 12-week trial period (Colgan 1995). Nursing time was not included in the estimate. The estimates for average values in Irish £ (price year not stated) were 82.54 for the 4LB and

66.24 for the paste bandage (statistical tests not reported).

One trial reported on change in patient-reported pain during the trial and found no significant difference between groups in pain score assessed by visual analogue scale from baseline to final assessment ($P = 0.32$) (Polignano 2004a).

Three trials reported withdrawal rates and observed similar rates for both study groups, with a small number due to adverse events (Colgan 1995; Meyer 2003; Polignano 2004a).

Instances of possible baseline imbalance were observed in some trials where statistical adjustment was not described. Ulcers in the paste bandage groups appeared larger and more chronic at baseline in the trials by DUBY 1993 (mean values presented) and Colgan 1995 (medians reported), possibly biasing the results in favour of the 4LB. One trial provided no information about baseline characteristics (Knight 1996). Estimates from one trial may have been further biased because of highly correlated healing data where limbs, rather than patients, were the unit of study (DUBY 1993).

Summary of evidence for Section 2.4 3 Comparison between the four-layer bandage and compression systems with a paste bandage as the base

The two largest and most recent trials in this group were at a lower risk of bias than the others, having used computerised randomisation, allocation concealment and analysis by intention to treat (Meyer 2003; Polignano 2004a). Based on these high quality data, there were no statistically significant differences in frequency of complete healing between the 4LB and paste-based systems at six months (Polignano 2004a) or one year (Meyer 2003). Estimates of time to healing showed no difference between groups in one trial (Polignano 2004a) and a significant difference in favour of the paste bandage system in the other (Meyer 2003). This difference in outcome could be explained by differences in the components of the paste bandage systems, two components being used in one trial (Polignano 2004a) and three components in the other (Meyer 2003); different systems could exert different amounts of compression. A pooled standardised mean difference in healing rate suggested a better outcome for patients receiving the 4LB (Knight 1996; Polignano 2004a) but this estimate should be viewed with caution because of unknown factors such as skewness of data and differences in data collection between the two studies. One of these trials assessed pain during the trial and found no difference between groups (Polignano 2004a).

Findings from one trial suggested lower costs for the paste bandage system (Colgan 1995) but this trial, along with the other two in this group (DUBY 1993; Knight 1996) was small and of poor methodological quality.

The evidence overall suggested that withdrawal rates were similar for the two types of compression.

2.5 Adjustable compression boots compared with other types of compression (2 RCTs)

Two small trials were identified for this comparison (DePalma 1999; Blecken 2005). Both studies described the adjustable boot as an inelastic compression garment, and both evaluated different versions of the CircAid proprietary device.

The first trial ($n=38$ patients) evaluated an adjustable compression boot consisting of a series of interlocking, non-elastic bands that encircled the leg, held in place by hook and loop fasteners, together with a foot-piece made of very low stretch bands (DePalma 1999). Patients were instructed to adjust the straps in order to maintain compression. The comparison regimen comprised a paste bandage covered by an elastic bandage, the overall system being described as Unna's Boot. All patients received a gauze primary dressing retained with a conforming gauze wrap. Three different estimates of healing rate were reported: mean area healed (cm^2) per day; mean area healed (%) per day; and the linear healing rate of the wound edge towards the wound centre (mean cm per day). No statistically significant differences were observed for any of these outcomes (Analysis 14.2). The mean total cost per patient completing the trial based on costs of clinician time and materials suggested a lower cost for patients receiving the adjustable compression boot: US\$ 559.41 versus US\$ 901.73, $P = 0.05$ (price year not stated). Two patients withdrew from the group receiving the adjustable boot, and five withdrew from those allocated the paste bandage. Patients allocated the adjustable boot were younger on average and had a shorter mean baseline ulcer duration compared with the paste bandage group. Since only participants with ulcers smaller than 5 cm diameter at baseline were eligible for inclusion, the estimates from this study may have limited generalisability relative to patients seen in clinical practice, some of whom may present with larger wounds.

The second study entailed within-individual randomisation whereby 12 patients with bilateral venous leg ulcers were recruited (Blecken 2005). One limb per patient was randomised to receive the adjustable compression boot, similar to the device used in the above study except that the adjustable bands were made of velcro. Application of the boot was preceded by a paraffin-impregnated gauze primary dressing, sterile absorbent gauze, and a felt pad cushion, all retained with a cotton stockinette. An elastic anklet was applied over the boot. The second limb was allocated a four-component compression system; this differed from the traditional 4LB, consisting of paraffin-impregnated gauze primary dressing, sterile absorbent gauze, felt pad, gauze bandage and elastic bandage. At 12 weeks, four limbs out of 12 healed in each group, these limbs belonging to the same patients in each group (Analysis 14.1). The trial authors claimed a significantly higher mean healing rate in cm^2 per week for the group receiving the adjustable compression boot but this difference was not apparent when the MD was plotted: 0.63 (95% CI -1.18 to 2.44) (Analysis 14.2). The trial authors also reported a HR estimate of the difference between groups in healing rate, reporting a statistically significant difference in favour of the group receiving the adjustable compression boot; however this analysis is not appropriate with a contin-

uous outcome variable. The patient inclusion criterion of ABPI ≥ 1.0 was stricter than for other trials of compression therapy (eligibility threshold normally 0.8). There were no withdrawals from the trial.

Summary of evidence from Section 2.5: Adjustable compression boots compared with other types of compression

Overall, evidence from two trials does not suggest a difference in healing between adjustable compression boots and compression bandage systems. Both trials are small and the quality of evidence is poor. Data from one trial suggest that the compression boot may be a less costly option (DePalma 1999) but a more rigorous evaluation alongside a good quality clinical trial is required. The second trial used within-individual randomisation and findings indicated that the same individuals healed within each group, irrespective of treatment (Blecken 2005).

2.6 Compression stockings or tubular devices compared with compression bandage systems (6 RCTs)

Four trials compared compression stockings with compression bandages (Hendricks 1985; Koksai 2003; Jünger 2004b; Polignano 2004b) and two compared tubular compression devices with compression bandage systems (Jünger 2004a; Milic 2007). Two trials compared a single-layer compression stocking with a paste bandage (Hendricks 1985; Koksai 2003). In both cases, the stocking was used over a primary dressing: gauze or foam (Hendricks 1985) and hydrocolloid (Koksai 2003). In one trial, the stocking was removed by the patient at night and reapplied in the morning (Hendricks 1985), in the other study this was not described (Koksai 2003). The comparator systems consisted of a zinc oxide and calamine paste bandage with no other components described (Koksai 2003) and a zinc oxide / calamine paste bandage used with an outer elastic bandage and a gauze or foam primary dressing (Hendricks 1985). Two trials compared a two-layer stocking system with a short-stretch bandage (Jünger 2004b; Polignano 2004b). The other two trials compared a heel-less, open-toed graduated tubular compression device with the SSB (Jünger 2004a), and two three-component compression systems, with a final layer of either tubular compression or elastic bandage (Milic 2007). Few other details of regimens were provided in the papers, such as use of primary dressings, or whether stockings were removed at night. For the comparison of single-layer stocking versus paste bandage no significant differences were detected between groups in terms of complete healing at four months (N=60 patients) (Koksai 2003) and 18 months (N=21 patients) (Hendricks 1985) (Analysis 15.1). One trial report included presentation of raw data, allowing the review author to calculate estimates from Kaplan-Meier survival analysis (Hendricks 1985). The estimated cumulative proportions healed at 18 months were 73% for patients randomised to the

stocking and 90% for those allocated to the paste bandage system. The estimates for median time to healing were 18 weeks versus seven weeks respectively ($P = 0.39$, log rank test). The other trial reported no significant difference between groups for mean weeks to healing: 6.65 for stocking and 6.85 for the paste bandage ($P > 0.05$) (Koksai 2003). This trial also reported the healing rate (cm^2 / week) and again found no significant difference between groups (Analysis 15.2). In terms of secondary outcomes, one trial assessed mean pain score during bandage application and at home using a visual analogue scale from zero to 10 where zero represented no pain and 10 the worst pain imaginable (Koksai 2003). For both outcomes, patients receiving the stocking had significantly lower mean pain scores: during bandage application 1.88 versus 3.69, $P < 0.0001$; and at home 1.88 versus 3.27, $P < 0.0001$. One treatment-related adverse event was reported in the group receiving the stocking; there were no further details relating to the nature of the adverse event. Four patients allocated the stocking withdrew compared with three from the paste bandage group, one of these having a severe reaction to the dressing. In the other trial, there were no withdrawals from the paste bandage group and one from the stocking group, reason not described (Hendricks 1985). Findings from the oldest trial are difficult to interpret because of some patients swapping treatments several times during the trial period. In addition, there were baseline imbalances for ulcer area and ulcer duration with median values showing that wounds were larger but of shorter duration in the group randomised to receive the stocking (Hendricks 1985).

Data from two trials comparing a two-layer stocking system with the SSB were pooled using a fixed effect model and showed that significantly more patients achieved complete healing with stockings at three months than with the SSB: (N=177 patients) RR 1.72 (95% CI 1.14 to 2.58), $P = 0.009$ (test for heterogeneity $P = 0.29$, $I^2=10\%$) (Analysis 16.1) (Jünger 2004b; Polignano 2004b). The between-group difference remained statistically significant when the analysis was repeated using a random effects model: RR 1.70 (95% CI 1.08 to 2.67), $P = 0.02$ (Analysis 16.2). At three months, the cumulative proportions healed as read from a plot of survival curves were 51% for the group receiving the two-layer stocking versus 30% for the SSB ($P = 0.057$, log rank test) (Jünger 2004b). For this trial, no significant difference was detected between groups for median days to healing: 47 for stockings versus 52 for bandages ($P = 0.82$, Mann-Whitney U-test). The other trial reported a significantly shorter mean time to healing for the group receiving the stockings: 72 days versus 101 days ($P = 0.027$, log rank test) (Polignano 2004b). In terms of other healing outcomes, no significant between-group differences were detected for mean percentage change in ulcer size at three months (Analysis 16.3) (Jünger 2004b). In the other trial, 2/29 (7%) patients randomised to the SSB developed new venous leg ulcers during the trial compared with 3/27 (11%) for the group receiving stockings (Polignano 2004b).

These two trials reported a variety of secondary outcomes (Jünger

2004b; Polignano 2004b). In one, both decrease in ulcer pain during the trial and comfort while wearing compression were significantly better for the group receiving stockings ($P = 0.017$ and $P = 0.038$ respectively) (Polignano 2004b). A higher withdrawal rate was noted in the SSB group in this trial (38% versus 15%). Of five patients withdrawing from the SSB group, one was considered by the original investigators to be potentially related to compression (bullous dermatitis); there were no reported withdrawals due to adverse events in the group receiving stockings. The second trial reported significantly more favourable outcomes for some aspects of comfort of compression assessed by questionnaire in the group receiving stockings (constriction $P = 0.003$, restricted freedom of movement $P = 0.0009$, sweating under the dressing $P = 0.04$, itching of skin on leg $P = 0.006$), and no significant differences between groups for the remaining aspects (tightness, leg pain, burning in leg, heat sensation in leg and prickling of leg) (Jünger 2004b). In terms of adverse events, this trial reported 29 adverse events (two serious) in 20/65 (31%) patients receiving stockings and 42 adverse events (four serious) in 26/67 (39%) patients receiving the SSB. Withdrawal rates were similar between groups. This trial also included a cost analysis based on cost of procedures and associated resources including application of stockings or bandages, primary dressings, debridement, skin care, physiotherapy and lymphatic drainage. Labour costs were included but overheads were excluded. The estimated mean cost per percentage reduction in wound area (EURO, price year 2003) was 2.57 for the group receiving stockings and 4.58 for the SSB group.

In one trial, ulcers were larger (based on report of median values) and of longer duration (mean values) at baseline in the SSB group (Jünger 2004b). This trial was the largest of this comparison group ($N=134$ patients) and was the highest quality, including block randomisation, allocation concealment, and blinded outcome assessment. In the other trial, the group receiving the SSB had a larger proportion of female patients (72% versus 52% in the group randomised to stockings) and had larger proportions of patients with a major clinical condition or abnormalities present at baseline (Polignano 2004b). As no further details of these diseases were provided, it is difficult to assess whether the observed imbalance between groups could have influenced the estimated treatment effect.

Two trials compared tubular compression devices with compression bandage systems (Jünger 2004a; Milic 2007). One compared a heel-less, open-toed graduated tubular compression device providing 30 to 40 mmHg at the ankle with the SSB (Jünger 2004a). The second evaluated two three-component compression systems, the first two components in each group consisting of cotton gauze bandage and cotton crepe bandage and the competing third components consisting of graduated tubular compression (ankle pressure 35 to 40 mmHg) versus elastic bandage (Milic 2007).

One trial reported no statistically significant difference in rates of complete healing at three months: ($N=178$) RR 0.98 (95% CI 0.76 to 1.26), $P = 0.86$ (Analysis 17.1) (Jünger 2004a). Both trials

reported findings from survival analyses. Kaplan-Meier analysis from the first trial suggested a median estimate of 42 days to healing in both groups and found no significant difference in probability of healing derived from survival curves ($P = 0.41$) (Jünger 2004a). In this trial, findings from Cox regression indicated that baseline ulcer area was a significant independent predictor of delayed healing ($P = 0.002$), but baseline ulcer duration and patient age were not prognostic ($P = 0.35$ and $P = 0.82$ respectively). In the other trial, the cumulative proportions of patients healed at 16 months were 93% for tubular compression and 51% for the system including an elastic bandage ($P < 0.001$) (Milic 2007). This trial also reported shorter median time to healing for the group receiving tubular compression (133 versus 211 days, P value not reported) and reported that no baseline variables emerged as significant predictors of healing using Cox regression. This trial reported significantly lower recurrence rates at one year for the group receiving tubular compression (24% versus 53%, $P < 0.05$). Both trials reported more adverse events for the groups receiving tubular compression. In the earlier trial, 14% of patients receiving tubular compression complained of pain or tightness during treatment which was resolved in all cases by using a larger sized device; the patients receiving the SSB did not experience such problems and no other adverse events were reported (Jünger 2004a). In this trial 10 patients were excluded from the analysis, of whom 7 had compression for less than one week; the breakdown of numbers per group was not given. In the other trial, 17% of patients experienced skin excoriation of the ankle or leg and 47% experienced pressure or pain caused by slippage of the device, all of whom received tubular compression; details of adverse events were not provided for the group receiving compression bandages (Milic 2007). In this trial, more patients complained of pain at the start of treatment in the bandages group (29% versus 11%) and there were more withdrawals in the group receiving the bandage system (4% versus 12%), with the majority of withdrawals (8/9 patients) from the bandage group being due to patients requesting change to the alternative treatment.

One trial included an assessment of health-related quality of life using the Nottingham Health Profile. Findings suggested no difference between treatment groups (Jünger 2004a).

The generalisability of findings may be limited as patients were younger than usual in one trial (median age 55 and 57 for the two treatment groups) (Milic 2007) and in the other trial the ABPI was > 0.9 (Jünger 2004a).

Summary of evidence from Section 2.6: Compression stockings or tubular devices compared with compression bandage systems

Findings from two small trials suggested no significant differences between single-layer stockings and paste bandages for healing outcomes (Hendricks 1985; Koksai 2003). Rates for adverse events and withdrawals appeared similar across treatment groups. One

trial assessed pain and reported significantly better outcomes in the group receiving stockings (Koksal 2003). Both trials were small. One included blinded outcome assessment but did not analyse by intention to treat (Koksal 2003). The other trial analysed by intention to treat but baseline comparability was not adequate (Hendricks 1985). All other aspects of methodological quality were unclear for both trials.

When a two-layer stocking system was compared with the SSB, some healing outcomes favoured the stockings (Jünger 2004b; Polignano 2004b). In addition, better outcomes were observed for the stockings in terms of pain, comfort, costs and withdrawal rates. One trial was of better methodological quality, using allocation concealment and blinded outcome assessment (Jünger 2004b).

Of the two evaluations of tubular compression versus compression bandages, one found better outcomes for healing and recurrence for the tubular device (Milic 2007) whilst the other found no difference between groups (Jünger 2004a). The variation in outcome between the two trials could be explained by the different comparators used: SSB (Jünger 2004a) and a three-component bandage system comprising an outer elastic bandage (Milic 2007). One trial reported pain in 14% of patients receiving tubular compression which was resolved in all cases by using a larger sized device; there were no complaints of pain in the group receiving the SSB (Jünger 2004a). In the other trial, more patients complained of pain in the bandages group at the start of treatment (Milic 2007). Adverse events appeared more frequent in the tubular compression group in both trials. Withdrawals were not reported per group for one trial (Jünger 2004a) and in the other trial were higher in the group receiving bandages (Milic 2007). Both trials carried out proper methods of randomisation and one also used allocation concealment (Jünger 2004a).

DISCUSSION

Summary of main results

The evidence suggests that venous ulcers heal more rapidly with compression than without and that multi-component systems achieve better healing outcomes than single-component compression. When competing systems comprising two components were compared, there was some evidence suggesting that those including an elastic component may be more effective; a similar finding was noted for alternative three-component systems. The performance of two components and four components was similar in one trial. Variants of the original Charing Cross 4LB achieve similar outcomes. Estimates from survival analyses indicated better outcomes for the 4LB compared with multi-component systems comprising the SSB. Heterogeneity was detected in this analysis, possibly arising because of differences in methods of estimating individual hazard ratios. Geographical location may account for

heterogeneity if care providers are already skilled in the application of one type of bandage but require training as part of the study for the alternative system. However, heterogeneity persisted when trials were analysed in sub-groups according to the geographical region in which they were undertaken (UK or Continental Europe). An individual patient data meta-analysis is in progress for the comparison of 4LB versus multi-component systems comprising SSB and will be incorporated when this review is next updated. Differences between the 4LB and paste bandage systems were not clear and interpretation could have been hampered by differential performance of variants of the paste bandage. Other innovations in compression therapy include the adjustable compression boot, stockings and tubular devices. The available evidence did not suggest a difference in healing outcomes between the adjustable compression boot and compression bandages. No differences were observed between a single-layer stocking and a paste bandage system for healing outcomes. When a two-layer stocking system was compared with a SSB, some healing outcomes were in favour of the stockings. Better outcomes were observed for all types of stockings in terms of pain scores when compared with bandages. The evidence arising from comparison of tubular compression versus bandages is conflicting and hindered by differences in comparators. In terms of cost-effectiveness, most evaluations were of costs only. Only one trial conducted a rigorous cost-effectiveness analysis in which the 4LB emerged as the dominant treatment strategy when compared with the SSB.

There was limited evidence on ulcer recurrence, with only three trials reporting this outcome (Colgan 1995; Morrell 1998; Milic 2007). One reported no cases of recurrent ulceration in patients receiving single-component elastic compression, the 4LB or four-component compression comprising a paste bandage when rates were assessed during a six-month follow-up period following 12 weeks of treatment (Colgan 1995). Another trial comparing application of the 4LB in the context of a specialist clinic with usual care by the district nurse did not detect a statistically significant difference between groups for recurrence rates or time to recurrence during the one-year trial period (Morrell 1998). In an evaluation of tubular compression versus compression bandages, significantly lower recurrence rates were detected in the group receiving tubular compression at one year (Milic 2007). It is likely that the majority of included trials lacked the statistical power and duration of follow-up required to detect meaningful recurrence rates following treatment with compression therapy.

Importantly this review update has attempted to take account of recent recommendations concerning the classification and description of different systems of compression (Partsch 2008). This update refers to the numbers of components in compression systems rather than the number of layers, as it has been argued that the number of components is more meaningful.

Quality of the evidence

The methodological quality of evidence in this field is variable. A general observation is that quality appears to be improving over time, with trials published within the last ten years being more likely to take important steps to reduce bias in estimates of treatment effect, including using proper methods of randomisation (i.e. unpredictable allocation to treatment groups), allocation concealment, blinded outcome assessment and analysis by intention to treat. More recent trials are more likely to be larger and to have been based on prior estimation of the required sample size to detect a defined difference in outcome between groups. Interpretation of older trials is often difficult because of small sample sizes and problems with methodological quality. Furthermore small trials are more likely to result in chance but potentially important baseline differences between treatment groups for prognostic factors such as ulcer size or duration. The possible impact of such baseline imbalances is usually difficult to interpret post hoc, and ideally would be adjusted for in the primary analysis (an approach commonly taken in more recent, high quality studies). Shortcomings in the statistical analysis of trial data were frequently encountered. Some studies report the mean (rather than median) time to healing which could result in biased estimates as such analysis is based on all participants having healed and / or the survival curve having an assumed shape (the shape is not assumed in non-parametric survival analysis). For continuous outcomes such as healing rate and change in ulcer area, data are likely to be skewed but transformation is usually not mentioned. Again, this could have influenced the derived estimates of effect (Bland 2000). More recent trials include survival analyses for time to healing (for example Scriven 1998; Franks 2004; Iglesias 2004; Jünger 2004a; Jünger 2004b; Nelson 2007a), and this provides a more meaningful estimate of treatment effect, particularly if hazard ratio estimates are provided, adjusted for prognostic factors such as baseline ulcer area and ulcer duration. All future trials should incorporate such analyses.

Interventions are frequently not comprehensively described in trial reports and so it can be difficult to judge the degree of compression being applied and impossible for readers to apply the evidence directly. A typical example of this is term “Unna’s boot” which is used to characterise the compression system but is often not described further. It is clear from studying the trials included in this review that the definition of Unna’s boot varies and there does not appear to be an agreed definition in the literature. The basis for this type of compression is a paste impregnated bandage (usually zinc oxide and calamine) (Kikta 1988) and in some cases this is the sole component. However, the paste bandage can also be applied as part of a multi-component system comprising two, three or four components, all of which could perform differently. Trial reports should include details of the number and type of components, the material used, the dimensions of bandages and the technique of application (e.g. spiral, figure-of-eight), as recently recommended by an expert consensus group (Rabe 2008).

Co-Interventions

The study selection criteria stipulated that the bandages under study should be the only systematic difference between treatment groups. In practice, this criterion has been difficult to apply without excluding many trials of important types of compression therapy from the review. One example of this is where a specialised package of care incorporating multi-component compression is compared with usual care that does not routinely include compression (Charles 1991; Taylor 1998; Morrell 1998; O’Brien 2003). In these trials, application of the bandage is not the only difference between treatment arms since the characteristics of care providers vary between groups with compression in one arm being provided by staff with specialist training and experience who could advise patients more generally about the management of their venous leg ulcer, for example, regarding limb elevation and mobility. The evaluations of paste bandages and Unna’s boots also introduce an additional, non-bandage difference between groups (for example Duby 1993; Colgan 1995; Knight 1996; Meyer 2003; Polignano 2004a). These devices normally provide a primary wound contact layer as well as compression bandaging. The alternative study arm is likely to receive a different type of primary dressing (e.g. foam dressing or hydrocolloid) prior to application of bandages or stockings. Factors such as additional aspects of care used together with compression, or different primary dressings between treatment arms may obscure the treatment effect due to the compression and so hinder the interpretation of findings. In many of the included trials, the observed treatment effect may be further influenced by imbalance of treatment groups at baseline with respect to independent prognostic factors. The literature on healing prognosis has shown consistently that baseline ulcer area and ulcer duration are significant independent predictors of delayed healing (Skene 1992; Franks 1995; Margolis 2000; Margolis 2004; Brown 2004). Some of the more recent trials address this by using stratified randomisation and undertaking analyses that can adjust for covariates, such as Cox proportional hazards models (for example Franks 2004; Iglesias 2004). When trials do not incorporate such methods, and particularly when trials are small in size, the estimated treatment may be prone to bias because of chance differences in the baseline prognostic profiles of treatment groups.

Quality of bandage application

It has been suggested that the clinical effect of compression is partly dependent on the skill of the bandager in achieving the correct amount of sub-bandage pressure and a pressure graduated from toe to knee (Feben 2003). Depending on setting (i.e. country of study), the performance of one compression system may be advantaged over others by greater staff familiarity. In the absence of consistent and systematic data on the degree of staff expertise, it is difficult to estimate what effect staff skills may have had on the treatment effects observed in this review. Some trials indicate a

possible move towards compression systems that are less dependent on practitioner skill where patients and their relatives may contribute more to application of devices, namely compression hosiery (Koksal 2003; Jünger 2004b; Polignano 2004b).

Limitations of the review

Although the search strategy was comprehensive, it is possible that eligible unpublished trials could remain unidentified. One unpublished trial of compression came to light during a wound management conference (Nelson 2007b). Communication with the trial authors confirmed that: the trial was small (N=40 patients), compared the 4LB with SSB, and had terminated prematurely (personal communication, Professor Charles McCollum). Since no baseline or outcome data were available, it is not possible to judge the potential effect of including this trial in the review. Other eligible unpublished evaluations may exist that have not been identified by the review process. Therefore, the effect of publication bias on this review should not be discounted.

Comparison with other systematic reviews of compression therapy for venous leg ulceration

This updated review includes a substantial amount of new evidence in relation to the previous version (N=22 clinical trials), particularly concerning competing multi-component systems and alternative devices to bandages such as compression boots and hosiery. The findings of the earlier review are largely upheld and this version provides some additional evidence to indicate that multi-component systems that include an elastic bandage are more effective in terms of wound healing compared with multi-component systems with inelastic constituents. This finding conflicts with some aspects of recent, consensus based recommendations of compression classification, where it was suggested that multi-component systems including elastic constituents will perform similarly to inelastic systems overall because of friction between different elements (Partsch 2008).

This updated review, in contrast with its parent review, included only those trials where treatment allocation was described as random. Consequently two studies that were included in the original version of the review are excluded from this update. The comparisons involved were: compression (Unna's Boot) versus no compression (dressing alone) (Sikes 1985); and compression stockings versus short-stretch bandage (Horakova 1994). A third trial that evaluated two different three-component systems was excluded from this version because we became aware that participants in one treatment arm also received steroids (Northeast 1990).

One other systematic review of compression therapy for venous leg ulceration was identified (Palfreyman 1998). The study selection criteria of the Palfreyman review differed from this review in that quasi randomised studies, evaluations of intermittent pneu-

matic compression and those with recurrence as the primary outcome were included whereas studies where venous disease was not confirmed by vascular assessment were excluded. In addition, the literature search was restricted to English language articles. This resulted in eight trials being identified as eligible for inclusion and these were sub-grouped for meta-analysis purposes according to the type of compression evaluated. Some findings reflected those of the current review in terms of healing: multi-component compression was more effective than single-component systems (based on Nelson 1995, a secondary reference to Nelson 2007a in this Cochrane review); and multi-component compression comprising an elastic bandage performed better than that consisting of non-elastic devices (based on Callam 1992b, included as a primary reference in this review). However, the Palfreyman review included only one trial in the comparison of compression versus no compression (Kikta 1988), estimating no statistically significant difference between groups. Two further studies were described as comparing Unna's Boot with 'other therapies', whereas in the current review these were included within the following comparisons: compression versus no compression (non-compressive bandages) (Rubin 1990); and competing single-component compression systems (Cordts 1992). Of the remaining studies included in the Palfreyman review, one focused on ulcer recurrence and the other two evaluated the effectiveness of intermittent pneumatic compression. We took the view that it is not helpful to exclude those studies that do not report vascular assessment of venous disease since methods of diagnosis vary between studies and are also likely to vary in clinical practice, meaning that a standardised definition may not be realistic.

AUTHORS' CONCLUSIONS

Implications for practice

Compression increases the healing rates of venous leg ulcers compared with no compression. Multi-component compression systems are more effective than single-component systems. Multi-component systems containing an elastic bandage appear more effective than those composed mainly of inelastic constituents. Variants of the original Charing Cross four-layer bandage achieve similar outcomes. The four-layer bandage is more clinically and cost-effective than multi-component systems comprising a short-stretch bandage. The relative effects of the four-layer bandage and paste bandage systems are not clear from current evidence. There is currently no evidence of a difference in the effectiveness of adjustable compression boots and compression bandage systems or between single-layer stockings and paste bandage systems. Two-layer stockings might be more effective than the short-stretch bandage. The relative effectiveness of tubular compression and compression bandages is currently unclear. The limited evidence on

the effects of different compression systems on venous ulcer recurrence precludes definitive conclusions at the current time. The performance of any type of compression bandage might be influenced by operator skill; this is likely to be less of an issue for compression hosiery.

Implications for research

Some of the research concerning ulcer treatment is of poor quality but methodological improvements are seen in more recent trials, possibly as a result of the CONSORT Statement, a document that provides guidance as to the reporting of randomised controlled trials (Begg 1996). The following are recommended for future studies:

- Recommendations outlined in the CONSORT Statement should be adopted as far as possible.
- If possible, future trials should be conducted in collaboration with a clinical trials unit in order to provide the optimal infrastructure for trial design, conduct, data management and analysis.
- Recruitment numbers should be based on an *a priori* sample size calculation. In many trials the sample size is too small to detect clinically important differences between treatments as statistically significant. In order to recruit sufficient patient numbers, multicentre trials should be more frequently considered. When these trials are commissioned they require a strong infrastructure to provide support and promote collaboration.
- A proper method of randomisation should be used and reported (e.g. computer-generated list) and allocation to treatment should be concealed (e.g. remote telephone randomisation service).
- The primary endpoint of treatment trials should be complete ulcer healing and the primary outcome should preferably be time to healing. Assistance should be sought from a suitably qualified statistician regarding the design and analysis of the trial in relation to survival analysis. In addition, the length of follow-up needs to be of sufficient duration to capture a meaningful proportion of events. If time to event analysis is not feasible, other outcomes could include frequency of complete healing during the trial period or (less preferably) healing rate and change in ulcer surface area.
- For each patient a single reference ulcer should be selected. Multiple ulcers on a patient should not be studied unless the trial has been specifically designed to accommodate this, and appropriate statistical analysis, that accounts for clustering, prespecified.

- Treatment groups should be comparable at baseline. In small RCTs randomisation alone may not achieve balance for prognostic factors. Methods of statistical analysis should adjust for baseline imbalance.

- A complete and thorough description of concurrent treatments including primary dressings should be given in trial reports.

- Assessment of outcomes should be undertaken either by assessors masked to trial treatment or independently confirmed by assessors masked to treatment.

- Analysis should be according to intention-to-treat.

- Evaluations should provide sufficiently full details of the interventions used, including descriptions of all components of compression, such that readers would be able to apply the treatments described (with training where necessary).

- Evaluations should report the skill level of staff providing care.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Blecken 2005

Methods	RCT (within individual randomisation, no other details about method of randomisation) . Trial conducted in USA, type of setting not described
Participants	12 patients with post-thrombotic bilateral venous leg ulcers were recruited (7 men and 5 women). All had history of deep vein thrombosis. Inclusion criterion: ABPI ≥ 1.00 . Exclusion criteria: chronic or acute systemic disease; and impaired mobility secondary to rheumatoid arthritis. Mean patient age 61 years; range 45 to 82 (breakdown per group not reported). At baseline, patients had active ulcers from 1-6 years. Mean \pm se baseline ulcer area (cm ²): Group 1. 48.98 \pm 14.13; Group 2. 50.08 \pm 18.30 (95% CI of difference group 1. minus group 2. -27.25 to 25.07)
Interventions	All patients: prior to bandage application, ulcers were cleansed with neutral soap and water and the skin lubricated with lanolin. Compression reapplied every 72 hours Group 1. Adjustable compression boot system consisting of: fine mesh paraffin-impregnated gauze primary dressing (Aquafor); single layer of sterile absorbent gauze; 1 cm thick felt pad cushion; surgical cotton stockinette; non-elastic compression garment comprising a series of individually adjustable Velcro bands 5.1 cm wide extending from ankle to knee (CircAid); and elastic anklet (Medi) applied from the base of the toes to 5 cm above the malleolus (n=12 limbs) Group 2. Four-layer bandage comprising: fine mesh paraffin-impregnated gauze primary dressing (Aquafor); single layer of sterile absorbent gauze; 1 cm thick felt pad overlapping at least 3 cm of the ulcer area; thick gauze bandage (Kerlix); and 15 cm wide elastic bandage (n=12 limbs)
Outcomes	Number (%) limbs with complete healing at 12 weeks: Group 1. 4/12 (33%); Group 2. 4/12 (33%). Note: the same 4 individuals healed in each group Mean \pm SE ulcer area reduction rate (cm ² per week): Group 1. 2.93 \pm 0.60; Group 2. 2.30 \pm 0.70 (95% CI of difference Group 1. minus Group 2. 0.05 to 1.21), P = 0.037 (paired t-test) Hazard ratio for area reduction rate: 0.56 (95% CI 0.33 to 0.96), P = 0.017 (indicating faster healing rate in Group 1). The authors reported that patient age and sex were not associated with reduction rate but statistics for covariates were not shown Mean \pm SE patient satisfaction score, assessed with a scoring sheet at 12 weeks (1=not satisfied; 2=moderately satisfied; 3=very satisfied): Group 1. 2.92 \pm 0.08; 2. Group 2. 58 \pm 0.15 (95% CI of difference Group 1. minus Group 2. -0.08 to 0.75), P = 0.104
Notes	Ulcer area assessed at baseline then every 4 weeks by direct grid tracing combined with digital imaging. The four-layer bandage system used was not the traditional one. No withdrawals. Skill of care provider not explained. The hazard ratio for area reduction rate is difficult to interpret as the outcome variable is continuous rather than time-to-event

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"This was a randomized study..."
Allocation concealment?	Unclear	No details provided.
Incomplete outcome data addressed? All outcomes	Yes	Twelve people recruited and all appear in results (individual patient data)
Blinded outcome assessment (healing)?	Unclear	No details provided.
Baseline comparability?	Unclear	Mean values reported for baseline ulcer area and so difficult to judge comparability; no ulcer duration data presented

Callam 1992b

Methods	RCT, factorial design. Setting was two hospital outpatient clinics in Scotland, UK
Participants	<p>132 patients were recruited from those attending hospital-based leg ulcer clinics in two hospitals in Scotland, UK.</p> <p>Inclusion criteria: not stated.</p> <p>Exclusion criteria: ABPI < 0.8, diabetes, sero-positive rheumatoid arthritis, lived too far away, refused consent.</p> <p>Number of patients male/female: Group 1. 33/32; Group 2. 26/41</p> <p>Mean patient age in years: Group 1. 62; Group 2. 65</p> <p>Mean±sd baseline ulcer area in cm²: Group 1. 8.2±12.9; Group 2. 11.0±15.9</p> <p>Number of patients with baseline ulcer duration < 6 months / 6-11 months / 1-2 years / ≥3years: Group 1. 27 / 19 / 13 / 6; Group 2. 37 / 17 / 12 / 1</p> <p>Number (%) patients walking with difficulty: Group 1. 15/65 (23%); Group 2. 17/67 (25%)</p>
Interventions	<p>Group 1. Three-component compression system consisting of: orthopaedic wool (Soff-ban Natural), elastic bandage (Tensopress), and cotton-elastic graduated compression tubular support bandage (Tensoshape) (n=65 patients)</p> <p>Group 2. Three-component compression system consisting of: orthopaedic wool (Soff-ban Natural), non-elastic cotton-elastic bandage (Elastocrepe), and non-elastic cotton-lycra cohesive bandage (Tensoplus Forte) (n=67 patients)</p> <p>All bandages were applied by experienced research nurses using a spiral technique</p> <p>Patients were also randomised to a knitted viscose dressing (Tricotex) or a hydrocellular polyurethane foam dressing (Allevyn)</p>
Outcomes	<p>Number (%) patients with complete healing at 12 weeks: Group 1. 35/65 (54%); Group 2. 19/67 (28%), P = 0.01, Cox proportional hazards model</p> <p>No statistically significant interaction between dressings and bandages was detected (P</p>

Callam 1992b (Continued)

	<p>= 0.87, Cox proportional hazards model)</p> <p>Mean±sd number of bandage changes during the 12 week trial period: Group 1. 11.7±6.7; Group 2. 12.3±6.5 (reported as not significant but P value not shown)</p> <p>The trial authors reported that: 'two patients in each group sustained bandage damage although this was minor in all cases.'</p> <p>Proportion of patients reporting ulcer pain at all clinic visits: Group 1. 29%; Group 2. 48% (P = 0.03, Wilcoxon two-sample test)</p> <p>Number (%) patients who withdrew (reasons - can be more than one per patient): Group 1. 8/65 (12%) (2 sensitivity, 3 exudate, 7 deterioration of ulcer, 1 social, 3 other - includes bandage slippage and patient intolerance); Group 2. 20/67 (30%) (8 sensitivity, 10 exudate, 17 deterioration of ulcer, 1 social, 7 other - includes bandage slippage and patient intolerance), P = 0.025, Chi-squared test, for difference between groups in proportions of patients who withdrew</p>
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Notes	<p>Ulcer area was measured using transparency tracing and computerised planimetry at baseline, then every 4 weeks. Possible imbalance in baseline variables: larger ulcers in Group 2 but more ulcers of longer duration in Group 1</p>
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Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details provided.
Allocation concealment?	Unclear	No details provided.
Incomplete outcome data addressed? All outcomes	Yes	All patients randomised appear in the analysis.
Blinded outcome assessment (healing)?	Unclear	Not stated.
Baseline comparability?	Unclear	Difficult to assess from data presented. Mean ulcer area slightly greater in Group 2 but slightly more ulcers of longer duration in Group 1

Charles 1991

Methods	RCT, no details of methods. Outpatient setting in inner London, UK
Participants	<p>53 patients with venous leg ulcers were recruited.</p> <p>Inclusion criterion: ABPI > 0.8</p> <p>Mean (range) patient age in years: Group 1. 78 (55-99); Group 2. 75 (37-91)</p> <p>Mean (range) baseline ulcer area in cm²: Group 1. 12.0 (1.5 - 52.0); Group 2. 15.0 (1.0 - 88.0)</p> <p>Mean (range) baseline ulcer duration in months: Group 1. 32 (4 - 336); Group 2. 25 (4 - 120)</p>

Interventions	<p>Group 1: Compression system applied by project nurse. The application consisted of: primary dressing (not defined); foam padding covered with gauze; further padding (Cello-lona) to bony prominences as required; short-stretch bandage (Rosidal K) applied spirally with 50% overlap and no more than 90% stretch from toes to knee. One bandage (10 cm x 5 m) was used except for 5 patients with a higher degree of mobility who had 2 bandages. Bandages were changed 1-3 times per week; they were washed by the patient and reused (n=27 patients).</p> <p>Group 2: Continuation of usual care by district nurse (no patients received short-stretch bandage) (n=26 patients)</p>
Outcomes	<p>Proportion of patients with complete healing at 3 months: Group 1. 71%; Group 2. 25%. The authors reported that the between-group difference was statistically significant (Chi squared test) but did not report the P value. NB: Raw data for the number of patients experiencing complete healing were not provided in the paper and the review author has not extrapolated these values from the reported percentages as group denominators unclear</p> <p>Proportion of patients with increase in ulcer area during the 3 month trial: Group 1. 0%; Group 2. 21%</p> <p>Number (%) patients who withdrew during the trials (reasons): Group 1. 3/30 (10%) (2 refused treatment, 1 referred for surgery); Group 2. 3/29 (10%) (3 admitted to hospital for leg ulcer treatment). NB: it is unclear whether these 6 patients were included in the 53 patients described above</p>
Notes	Ulcer area was measured weekly using transparency tracing. Cost of one short-stretch bandage was £3.75. The mean pressure under the short stretch bandage was 33 mmHg (measured by Oxford monitor)

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Patients ... were randomly divided into a control and an experimental group"
Allocation concealment?	Unclear	"Patients ... were randomly divided into a control and an experimental group"
Incomplete outcome data addressed? All outcomes	Unclear	Six people withdrew from treatment but unclear if they were included in analysis; only % healed reported for outcome - no raw numbers
Blinded outcome assessment (healing)?	Unclear	No detail regarding outcome assessment however implies that the treating nurses assessed outcome
Baseline comparability?	Unclear	Only mean data presented but possible imbalance: larger ulcers in Group 2; longer

	duration in Group 1
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Colgan 1995

Methods	RCT (single-centre). Setting was outpatients in Ireland. Outcome assessment was non-blind
Participants	30 patients were recruited from routine venous ulcer out-patient clinics. Inclusion criteria: diagnosis of venous aetiology; ulcer size > 1cm ² . Exclusion criterion: arterial disease (no definition provided). Number of patients male/female: Group 1. 4/6; Group 2. 2/8; Group 3. 2/8 Mean patient age in years: Group 1. 65.5; Group 2. 67.5; Group 3. 56.0 Median (mean) baseline ulcer area in cm ² : Group 1. 9 (48.5); Group 2. 7 (27.5); Group 3. 20 (42.8) Median (mean) baseline ulcer duration in months: Group 1. 24 (66.5); Group 2. 10 (9.3); Group 3. 12 (53.5)
Interventions	Group 1. Modified Unna's boot, a compression system with four components: paste bandage; cotton crepe bandage (Elastocrepe); elastic adhesive bandage (Elastoplast); class II compression sock) (n=10 patients) Group 2. 4 layer bandage (Profore) (n=10 patients) Group 3. Polyurethane foam dressing (Lyof foam dressing) plus elastic bandage (Setopress) (n=10 patients) All patients: treatment was delivered by clinic nurse. Treatment duration was 12 weeks
Outcomes	Number (%) patients with complete healing at 12 weeks: Group 1. 7/10 (70%); Group 2. 6/10 (60%); Group 3. 2/10 (20%) (statistical tests not reported) Number (%) patients who withdrew (reasons): Group 1. 1/10 (10%) (allergy); Group 2. 0/10 (0%); Group 3. 3/10 (30%) (3 inability to tolerate bandage) There were no cases of ulcer recurrence in any group during a 6-month follow-up period following completion of the 12-week treatment period Costs of bandages were calculated but not did not include nursing time due to wide variation in services. Average (range) cost / patient / 12 weeks (Ir £): Group 1. 66.24 (18.14 to 108.84); Group 2. 82.54 (27.94 to 177.20); Group 3. 58.33 (19.11 to 83.24)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"We undertook a prospective randomized study..."
Allocation concealment?	Unclear	No details provided.

Colgan 1995 (Continued)

Incomplete outcome data addressed? All outcomes	Yes	Thirty patients randomised and 30 patients analysed.
Blinded outcome assessment (healing)?	No	Author correspondence: "...assessor was not blinded".
Baseline comparability?	No	Initial ulcer size larger in Group 3; duration greater in Group 1

Cordts 1992

Methods	RCT (no details about methods). Setting was out-patient clinic in Boston, USA
Participants	<p>43 patients with chronic venous insufficiency were recruited.</p> <p>Inclusion criteria: > 18 years, venous leg ulcer confirmed by duplex scanning</p> <p>Exclusion criteria: signs and symptoms of clinical infection, arterial ulcers, ulcer area > 50 cm², uncontrolled diabetes mellitus, venous surgery within one month on affected leg, ulcer with exposed muscle, tendon or bone, pregnancy, patients on antibiotics, steroids or chemotherapy, known HIV positive patients.</p> <p>Groups were stated to be comparable for patient age, sex, race, general health and associated medical problems (data not shown).</p> <p>Number (%) of patients with history of deep vein thrombosis: Group 1. 3/16 (19%); Group 2. 1/14 (7%)</p> <p>Mean±se baseline ulcer area in cm²: Group 1. 9.1±1.7; Group 2. 6.0±2.4</p> <p>Mean±se baseline ulcer duration in weeks: Group 1. 95±29; Group 2. 96±34</p>
Interventions	<p>Group 1. Hydrocolloid dressing (Duoderm) plus cohesive elastic bandage (Coban) (n=16 patients)</p> <p>Group 2. Unna's boot (Dome-Paste, a zinc oxide and calamine impregnated bandage) n=14</p> <p>All patients: dressings were changed weekly or more often if required</p>
Outcomes	<p>Analysis was based on 30/43 patients</p> <p>Number (%) of patients with complete healing at 12 weeks (data reported for study completers only): Group 1. 8/16 (50%); Group 2. 6/14 (43%), P = 0.18, Chi-squared test</p> <p>Mean±se days to healing (not derived from survival analysis): Group 1. 61.1±10.1; Group 2. 55.1±10.8 (P = 0.69, Student's t test)</p> <p>Mean±se percentage change relative to baseline ulcer area at 12 weeks (values read from figure): Group 1. -90±5; Group 2. -25±50 (P = 0.9, ANOVA)</p> <p>Mean±se healing rate in cm² per week adjusted for baseline ulcer perimeter in cm (i.e. healing rate divided by baseline ulcer perimeter): Group 1. 0.049±0.007; Group 2. 0.0201±0.017 (P = 0.11, Student's t test)</p> <p>Mean±se pain score based on 1-10 scale where 0=no pain: Group 1. 1.0±0.16; Group 2. 1.0±0.21 (authors reported no significant difference but did not show the P value)</p> <p>Number (%) of patients with adverse events not requiring withdrawal from treatment (description): Group 1. 2/16 (13%) (1 necrosis at ulcer edge, 1 wound infection) ; Group 2. 3/14 (21%) (all had wound infection)</p>

Cordts 1992 (Continued)

	Number (%) of patients who withdrew from the trial: Group 1: 7/16 (44%); Group 2: 6/14 (43%). All withdrawals were because of failure to attend clinic	
Notes	Ulcer area was determined using photography and computerised planimetry. Costs not reported. Patient acceptance of bandage was higher with Duoderm than Unna's boot	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Patients were randomly assigned to treatment..."
Allocation concealment?	Unclear	"Patients were randomly assigned to treatment..."
Incomplete outcome data addressed? All outcomes	No	43 people randomised; analysis of only 30 people. Withdrawal rates similar in both groups; reason for each was non-attendance at clinic
Blinded outcome assessment (healing)?	Unclear	Not stated.
Baseline comparability?	Unclear	Mean (not median) ulcer areas given and larger in Group 1; durations similar

Danielsen 1998

Methods	RCT (randomisation stratified by baseline ulcer area, larger or smaller than 20 cm ²). Setting was hospital outpatient clinic in Copenhagen, Denmark
Participants	<p>43 patients were randomised.</p> <p>Inclusion criteria: lipodermatosclerosis, leg ulcers and incompetent veins demonstrated by Doppler and/or clinical examination.</p> <p>Exclusion criteria: significant arterial insufficiency (systolic blood pressure in 1st toe < 60 mmHg or ABPI < 0.9), immunological aetiology of ulcer, diabetes, uncompensated heart disease, inability to walk unassisted.</p> <p>Number of patients male/female (of 40 patients included in authors' analyses): Group 1. 12/9; Group 2. 8/11</p> <p>Median (range) patient age in years: Group 1. 72 (38 to 85); Group 2. 71 (37 to 90)</p> <p>Mean [median] (range) baseline ulcer area in cm²: Group 1. 19.7 [2.4] (0.3 to 124.5); Group 2. 16.5 [6.3] (0.4 to 66.1)</p> <p>Mean [median] (range) baseline ulcer duration in months: Group 1. 22.2 [12] (2 to 120); Group 2. 27.8 [15] (2 to 84)</p>
Interventions	Group 1. Lower leg padded with gauze then long stretch, non-adhesive compression bandage (Setopress) applied in a spiral with 50% overlap and approximately 86% extension. Usually one bandage was used (3.5 m unstretched). The bandage was changed every 1-

	<p>7 days, according to wound exudate (but was left unchanged for as long as possible). All bandages applied by study nurse (n=23 patients)</p> <p>Group 2. Lower leg padded with gauze then short-stretch, non-adhesive compression bandage (Comprilan) applied in a spiral with 50% overlap, using similar tension to that in long stretch bandage. Usually 1½ short-stretch bandages were used (total unstretched length 4.5 m). Bandages were changed every 1-2 days and were usually applied by community nurse (n=20 patients)</p> <p>All patients: Hydrocolloid primary dressing (Comfeel) was used if possible. Patients with large ulcers or maceration of the surrounding skin were treated with an non-antibacterial ointment/gel. When local infection was suspected, mupirocin, silver sulphadiazine cream (Flamazine) or cadexomer iodine (Iodosorb) were used. Systemic antibiotics were given for cellulitis. Eczema of the per-ulcer skin was treated with a steroid ointment. Patients continued with randomised bandage system after healing</p>
Outcomes	<p>Note: The analyses of complete healing, incidence of cellulitis and withdrawals are as calculated by the review author, according to intention-to-treat (complete case analysis). All other analyses are as reported by the trial authors and are based on 40 patients overall (excluding 3 patients who were ineligible, Group 1. n=21 and Group 2. n=19)</p> <p>Number (%) patients with complete healing at 1 month: Group 1. 4/23 (17%); Group 2. 1/20 (5%)</p> <p>Number (%) patients with complete healing at 6 months: Group 1. 9/23 (39%); Group 2. 5/20 (25%)</p> <p>Number (%) patients with complete healing at 1 year: Group 1. 12/23 (52%); Group 2. 3/20 (15%)</p> <p>Kaplan-Meier estimate of the proportions of patients healed at 1 year: Group 1. 81%; Group 2. 31% (P = 0.03, log rank test)</p> <p>Mean [median] (range) relative ulcer area at 12 months: Group 1. 0.25 [0] (0 to 3.11); Group 2. 0.95 [0.77] (0 to 4.04) (P < 0.01 for between group difference, Mann-Whitney test)</p> <p>Number of patients who developed cellulitis: Group 1. 7/23 (30%); Group 2. 8/20 (40%)</p> <p>Number of patients using hydrocolloid / mupirocin / silver sulphadiazine / cadexomer iodine: Group 1. 6 / 5 / 3 / 1; Group 2. 3 / 2 / 5 / 2</p> <p>Number (%) of patients who withdrew during the trial period (reasons): Group 1. 7/23 (30%) (2 ineligible, 2 preferred compression stockings post-healing, 2 preferred other treatment, 1 knee pain/swelling because of bandage); Group 2. 10/20 (50%) (1 ineligible, 1 preferred compression stockings post-healing, 3 preferred other treatment, 3 had poor compliance, 1 changed addressed, 1 died)</p>
Notes	<p>Ulcer area was measured using transparency tracing and planimetry (instrument not stated) at baseline then at 1, 6 and 12 months. The authors stated that values for the total area of ulceration on the reference limb were studied</p> <p>Ankle sub-bandage pressure was measured using an Oxford pressure monitor. Group 1. maintained mean pressure of 40 mmHg at one week; Group 2. decreased mean pressure by 10 mmHg during first 24 hours. The between-group differences at 2 hours and 24 hours was significant (P < 0.001 and P < 0.017 respectively)</p> <p>This trial assessed incidence of healing and also maintenance of healing. Ulcers could have healed and recurred before the assessment points. It appears that 2 ulcers recurred after the 6 month assessment in Group 2</p>

Danielsen 1998 (Continued)

	The use of various primary dressings and topical agents could have confounded the treatment effect	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"... patients were randomized to receive treatment..."
Allocation concealment?	Yes	The authors reported that "randomisation was blind" but did not provide any other details
Incomplete outcome data addressed? All outcomes	Yes	Three patients were excluded by trial authors from analysis as deemed ineligible. These were re-instated in the denominators by review authors
Blinded outcome assessment (healing)?	Unclear	No detail.
Baseline comparability?	No	Baseline median ulcer area and duration greater in Group 2.

DePalma 1999

Methods	RCT (multicentre, method of randomisation not stated). Setting: outpatients, USA
Participants	<p>38 outpatients were recruited from 6 study centres.</p> <p>Inclusion criteria: patient age at least 18 years; unilateral venous leg ulcer diagnosed by duplex examination</p> <p>Exclusion criteria: ulcers of non-venous or mixed aetiology; ulcer diameter >5 cm; severe arterial, metabolic or neuropathic disease; not expected to heal with conservative treatment; poor general health; using medications inhibiting wound healing; acute deep venous thrombosis within last 3 months; venous surgery within the last month; allergy to study materials; pregnant; likely to be non-compliant; deemed by investigators to be better treated by methods other than those used in the study</p> <p>Mean±sd patient age (years): Group 1. 63.95±9.73; Group 2. 58.15±9.60.</p> <p>Mean±sd baseline ulcer area (cm squared): Group 1. 3.59±3.54; Group 2. 3.28±4.08.</p> <p>Mean±sd baseline ulcer duration (months): Group 1. 27.42±54.72; Group 2. 12.28±14.54</p> <p>Number of patients with chronic deep venous obstruction: Group 1. 4; Group 2. 5</p>
Interventions	<p>All patients: ulcers were cleansed and debrided (no further details given), dressed with paraffin-impregnated gauze (Adaptic) covered by 4x4 inch gauze pad (Curity), retained with a conforming gauze wrap (Kling)</p> <p>Group 1. Unna's Boot consisting of zinc oxide, glycerin and gelatin impregnated 10 cm x 9 m roller gauze bandage (Medicopaste) covered by an elastic Ace type bandage (n=19)</p>

	Group 2. Thera-Boot - a device consisting of a series of interlocking, non elastic bands encircling the leg and held in place by hook and loop fasteners plus a foot piece made of very low stretch bands. Patients were instructed to adjust the straps as necessary in order to maintain compression between clinic visits (n=19)
Outcomes	<p>Patients were followed up until healing or 12 weeks and were seen as often as the investigator felt was appropriate. Ulcer area was measured using transparency tracing</p> <p>Mean±sd area healing rate (cm² per day): Group 1. 0.0239±0.0534; Group 2. 0.0433±0.0910, P = 0.27</p> <p>Mean±sd area healing rate (% per day): Group 1. 1.0493±1.5583; Group 2. 2.0357±1.9520, P = 0.56</p> <p>Mean±sd linear healing rate (cm per day)*: Group 1. 0.0060±0.0092; Group 2. 0.0109±0.0125, P = 0.27</p> <p>Mean±sd weeks from enrolment to healing: Group 1. 9.69±3.28; Group 2. 7.98±4.41, P = 0.41</p> <p>Mean±sd total cost per completed patient (US\$, price year not stated, based on clinician time plus materials plus number of visits at \$35 per visit): Group 1. 901.73±576.45; Group 2. 559.41±290.75, P = 0.05</p>
Notes	<p>*This is the linear healing rate of the wound edge toward the wound centre. It is calculated as the change in wound area from baseline to endpoint divided by the average of baseline and endpoint wound perimeter measurements, after the method proposed by Gilman 1990.</p> <p>Completed trial: Group 1. 11 patients; Group 2. 17 patients.</p> <p>Numbers of patients (with reasons) who withdrew before completion: Group 1. 5 patients (1 allergy to Unna's Boot; 1 weeping dermatitis; 1 left town; 1 enrolled with exclusion criterion - immunosuppression; 1 had increasing ulcer size and was referred to surgeon) . Group 2. 2 patients (1 enrolled with exclusion criterion - low ABPI; 1 not healing, referred to surgeon). 3 patients not accounted for in the paper</p> <p>Restricting selection of patients to those with relatively small ulcers is not likely to be representative of the target population seen in clinical practice</p> <p>Ulcers in Group 2. were of shorter baseline duration. No information about skill of care providers</p>

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details provided. "A multicenter, prospective, randomized, parallel-group study was conducted..."
Allocation concealment?	Unclear	No details provided. "A multicenter, prospective, randomized, parallel-group study was conducted..."
Incomplete outcome data addressed? All outcomes	No	38 people randomised; 10 withdrew but unclear if included in analysis; 3 of the withdrawals unaccounted for (unclear

		which group they were from)
Blinded outcome assessment (healing)?	Unclear	“At each ... a tracing of the ulcer outline was made on clear film...” “Data sheets and ulcer tracings were sent to the study coordinator for tabulation and analysis...”
Baseline comparability?	No	Ulcers in Group 2 were of shorter mean duration.

Duby 1993

Methods	RCT (no details on methods). Setting was UK, no other details reported
Participants	<p>67 patients (76 legs) were recruited (source population not described). Inclusion criterion: ABPI \geq 0.9. No other patient selection criteria stated. Number of patients (limbs) male/female: Group 1. 4 (5 limbs) / 16 (20 limbs); Group 2. 7 (7 limbs) / 16 (18 limbs); Group 3. 11 (12 limbs) / 13 (14 limbs) Mean (range) patient age in years: Group 1. 72.6 (47 to 89); Group 2. 70.1 (47 to 85); Group 3. 72.9 (56 to 86) Mean (range) baseline ulcer area in cm²: Group 1. 13.1 (1.1 to 29.4); Group 2. 11.9 (1.0 to 40.3); Group 3. 12.3 (1.5 to 30.1) Mean baseline ulcer duration in months: Group 1. 26.7; Group 2. 20.5; Group 3. 34.5</p>
Interventions	<p>Group 1. Short stretch system comprising: orthopaedic wool; 2 or more layers of short stretch bandage applied in counter rotating directions (Comprilan); and net covering (Tricofix). Bandages were washed and reused. (n=20 patients / 25 limbs) Group 2. Four-layer bandage system comprising : orthopaedic wool; crepe bandage; elastic bandage (Elset); and elastic cohesive bandage (Coban). New bandages were applied at each dressing change. (n=23 patients / 25 limbs) Group 3. Paste-bandage system comprising: zinc and ichthammol paste bandage (Ichthopaste); cotton crepe bandage (Elastocrepe); and elastic tubular bandage (Tubigrip) (n=24 patients / 26 legs) All patients: ulcers were irrigated with saline and a non-adherent dressing applied (Cuticerin). Bandages were changed as required, according to exudate and slippage (mean rate twice weekly for all groups)</p>
Outcomes	<p>Number (%) limbs with complete healing at 12 weeks: Group 1. 10/25 (40%); Group 2. 11/25 (44%); Group 3. 6/26 (23%). The authors reported that the differences for Group 1 versus Group 3 and Group 2 versus Group 3 were significant, but P values were not shown Mean percentage reduction in baseline ulcer area at 12 weeks: Group 1. 60%; Group 2. 76%; Group 3. 43%. The authors reported that the difference between Groups 1 and 2 was not significant but P value not shown</p>
Notes	Higher proportion of males in Group 3: 11/24 compared to 11/43 in other 2 groups combined. Longer baseline ulcer duration in Group 3. Ulcer area was determined weekly using tracings from photographs combined with computerised planimetry. Change in

Duby 1993 (Continued)

	leg volume during the 12 week trial was reported. Data from limbs of same patient are likely to be highly correlated and could bias estimates of treatment effect	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	“The treatments were randomized to each patient in the following manner...” [goes on to merely give numbers receiving each treatment.]
Allocation concealment?	Unclear	No details provided. “The treatments were randomized to each patient in the following manner...” [goes on to merely give numbers receiving each treatment.]
Incomplete outcome data addressed? All outcomes	Yes	Complete healing reported on all 67 people randomised; less clear for continuous outcomes
Blinded outcome assessment (healing)?	Unclear	No details given.
Baseline comparability?	No	Baseline ulcer duration varied across three groups, longer in Group 3

Eriksson 1984

Methods	RCT, open design, outpatient setting, Sweden.
Participants	53 patients were recruited to Part I of the trial (13 male & 40 female; mean age 70.1 years). 44 patients were recruited to Part II (9 patients excluded because of ulcer healing or reasons unrelated to the trial). Inclusion criteria: not stated. Exclusion criteria: overt diabetes mellitus, arterial insufficiency defined as ABPI < 0.75, erysipelas, cellulitis
Interventions	Part I (2 weeks duration): patients were randomised to receive either gauze moistened with normal saline or dextranomer beads (Debrisan). Numbers of patients per group not clear Part II (8 weeks duration): patients were re-randomised to the following groups: 1: Ulcer cleansed with saline followed by application of freeze-dried porcine skin dressing (Skintec). Dressings were changed every other day. No compression was applied (n=11). Patients crossed over to the bandage system received by Group 3 mid study because the porcine skin dressing was no longer available. 2. Ulcer cleansed with saline followed by application of non-adherent aluminium foil dressing (Metallina). Dressings were changed every other day. No compression was applied (n=20).

Eriksson 1984 (Continued)

	3. Zinc oxide paste impregnated inner stocking (ACO) plus outer elastic bandage (Tensoplast) applied after resting with legs elevated for 30 minutes. Changed every 1-2 weeks (n=13)
Outcomes	Part I: no statistically significant differences between groups for changes in ulcer area and volume Part II: Decrease in ulcer area / volume at 8 weeks: Group 1. 65% / 75%; Group 2. 10% / 0%; Group 3. 80% / 90% (NB: values recorded from figure; findings of tests of statistical significance for between-group differences not reported)
Notes	Ulcer area and volume were measured using stereophotogrammetry every 2 weeks. Baseline ulcer area / volume and duration not stated. Six patients in Group 2 had treatment interrupted because of increase of the ulcers and / or signs of clinical infection. Group 3 - no patients discontinued treatment

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"The investigation was designed as a randomized open trial". No further detail
Allocation concealment?	Unclear	"The investigation was designed as a randomized open trial". No further detail
Incomplete outcome data addressed? All outcomes	No	"The treatment with porcine skin had to be stopped in the middle of the study as the dressing was no longer available...Treatment with double layer bandage was then introduced..." Six patients in Group 2 had treatment interrupted because of increase of the ulcers and / or signs of clinical infection; no patients in Group 3 had treatment discontinued - however unclear if these people were analysed
Blinded outcome assessment (healing)?	Unclear	Not stated.
Baseline comparability?	Unclear	No baseline data presented.

Eriksson 1986

Methods	RCT, open design. Setting Sweden, outpatients.
Participants	34 outpatients with chronic venous leg ulcers were recruited (9 males with mean age 66.9 years; and 25 females with mean age 74.3 years). 3 patients in Group 2 were diabetic

Interventions	For all patients the ulcerated limb was immersed for 15 minutes in a bath of tepid potassium permanganate solution, then crusts and debris were removed Group 1: Inner stocking impregnated with zinc oxide paste (ACO) plus an outer elastic bandage (Tensoplast or Porelast Acryl). Bandages were changed every 1-2 weeks (n=17) Group 2: Hydrocolloid dressing (Duoderm) plus elastic bandage (Wero). Dressing renewed 1-2 times per week. Bandage removed at night and reapplied in the morning by the patient (n=17)	
Outcomes	Number (%) patients with complete healing at 12 weeks: Group 1. 7/17 (41%); Group 2. 9/17 (53%). Statistical tests not reported Mean decrease in ulcer area / volume at 12 weeks: Group 1. 75% / 75%; Group 2. 70% / 55% (NB: values recorded from figure; all between-group differences reported as not statistically significant but P values not shown) Number (%) patients who discontinued treatment (with reasons): Group 1. 3/17 (18%) (1 withdrew, 2 had infection of peri-ulcer skin); Group 2. 2/17 (12%) (1 withdrew, 1 had enlargement of study ulcer & development of new ulcer)	
Notes	Ulcer area and volume were measured using stereophotogrammetry every 2 weeks	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"The study was designed as a randomized open trial..."
Allocation concealment?	Unclear	"The study was designed as a randomized open trial..."
Incomplete outcome data addressed? All outcomes	Unclear	For healed outcome only numerators given therefore unclear whether all patients followed up. Numbers for continuous outcomes unclear
Blinded outcome assessment (healing)?	Unclear	Not stated.
Baseline comparability?	Unclear	No baseline data reported.

Methods	RCT (multicentre) with stratification according to study centre and baseline ulcer area ($\leq 10 \text{ cm}^2$ or $> 10 \text{ cm}^2$). Patients were randomised to one of two bandage systems and to one of two primary dressings, using a factorial design. Sample size: the target sample of 240 patients overall could not be recruited. The authors estimated that 159 patients overall provided 81% power to detect 15% difference in healing rates at 5% significance level
Participants	<p>159 patients were recruited from 12 community leg ulcer clinics in the UK (156 patients were evaluated).</p> <p>Inclusion criteria: patient age ≥ 18 years; venous leg ulceration with wound aetiology confirmed using clinical history and ABPI ≥ 0.8; minimum baseline ulcer duration 2 weeks; maximum baseline ulcer duration 52 weeks.</p> <p>Exclusion criteria: pregnancy; causes of ulceration other than venous disease; active cellulitis treated with systemic antibiotics; dry, non-exuding wounds; previous entry to trial.</p> <p>Number of patients male/female: Group 1. 27/47; Group 2. 34/48</p> <p>Mean\pmsd patient age in years: Group 1. 67.5\pm14.3; Group 2. 70.9\pm13.4</p> <p>Proportions of patients with baseline ulcer size $\leq 10 \text{ cm}^2$ / $> 10 \text{ cm}^2$: Group 1. 80%/20%; Group 2. 82%/18%</p> <p>Baseline median (range) baseline ulcer area in cm^2: Group 1. 5.0 (0.3 to 115.8); Group 2. 3.5 (0.5 to 123.1)</p> <p>Median (range) baseline ulcer duration in weeks: Group 1. 8 (2 to 40); Group 2. 8 (2 to 40).</p> <p>Number (%) patients with previous ulceration: Group 1. 29/74 (39%); Group 2. 28/82 (34%)</p> <p>Number (%) patients with DVT: Group 1. 14/74 (19%); Group 2. 8/82 (10%)</p> <p>Number (%) patients chair or bed bound / walking with aid / walking freely: Group 1. 0/74 (0%) / 18/74 (24%) / 56/74 (76%) Group 2. 1/82 (1%) / 14/82 (17%) / 67/82 (82%)</p> <p>Number (%) patients with limb: fully mobile / limited / fixed: Group 1. 54/74 (73%) / 17/74 (23%) / 2/74 (3%) Group 2. 73/82 (89%) / 9/82 (11%) / 0/82 (0%)</p>
Interventions	<p>For all patients, the study limb was washed using emollient dissolved in tap water, the wound was debrided where necessary and a hypoallergenic hydrating cream applied to the surrounding skin. In addition to the bandage comparison, patients were randomised to one of two foam dressings (Allevyn or Mepilex) prior to bandaging. Dressings and bandages were reapplied at least weekly</p> <p>Group 1. Foam dressing as above (52.7% patients received Allevyn) plus four-layer bandage (Flexiban, Setocrepe, Elset, Coban) (n=74)</p> <p>Group 2. Foam dressing as above (51.2% patients received Allevyn) plus short-stretch bandage (Flexiban, Actico) (n=82)</p> <p>Patients with ulcer closure before the end of the trial were provided with class II compression hosiery and continued to be followed up until 24 weeks. Patients who withdrew from randomised treatment were allocated to an alternative treatment and continued to be followed up until wound closure or 24 weeks</p>
Outcomes	Number (%) patients with complete healing at 24 weeks (for those remaining on randomised treatment): Group 1. 51/74 (69%); Group 2. 60/82 (73%) (P value not reported)

	<p>Number (%) patients with complete healing at 24 weeks (intention-to-treat analysis): Group 1. 59/74 (80%); Group 2. 62/82 (76%)</p> <p>Kaplan-Meier analysis: cumulative healing rates at 12 weeks were 56% in both groups; and at 24 weeks Group 1. 85%; Group 2. 83%</p> <p>HR for healing adjusted for study centre, treatment and baseline ulcer area, by intention-to-treat was 1.08 in favour of Group 2 (95% CI 0.63 to 1.85), P = 0.79</p> <p>HR for healing for subgroup of patients requiring aid with walking (Group 1. n=18; Group 2. n=14), by intention-to-treat was 1.35 in favour of Group 2 (95% CI 0.60 to 3.03), P = 0.46</p> <p>Quality of life assessment: Patients completed Nottingham Health Profile at baseline, at healing or withdrawal and at 24 weeks (scores zero to 100, with lower scores indicating better quality of life). Domains include: energy; bodily pain; emotional reactions; sleep; social isolation; and physical mobility. Mean differences in final scores calculated using linear regression with adjustment for baseline scores. 139/156 (89%) patients completed at least one follow-up questionnaire (66 in Group 1 & 73 in Group 2). Overall, statistically significant improvements were observed for all scores at 24 weeks. Improvement was greater for patients with healed limbs (n=114) compared to those who remained unhealed (n=40), the mean difference for the following domains being statistically significant: bodily pain (MD 13.2, 95% CI 3.6 to 22.9, P = 0.008), emotional reactions (MD 10.5, 95% CI 2.8 to 18.1, P = 0.007) and social isolation (MD 8.5, 95% CI 1.2 to 15.9, P = 0.024); a clinically significant difference was seen for sleep (MD 11.2, 95% CI 0.0 to 22.5, P = 0.051). No statistically significant differences were observed between scores for any domain from the two treatment groups</p>	
Notes	<p>In patients with bilateral ulceration, the limb with the largest total ulcerated area was studied</p> <p>3/159 patients were excluded from the analysis (2 ineligible; 1 withdrew after 1 week)</p> <p>Of 156 remaining patients, number (%) withdrawals during trial: Group 1. 16/74 (22%) ; Group 2. 17/82 (21%)</p> <p>Reasons for withdrawal: Group 1. infection 3, peri-ulcer skin maceration 2, other bandage related reason 2, patient request 2, lost to follow-up 6, dressing-related 1; Group 2. infection 1, peri-ulcer skin maceration 2, other bandage related reason 3, patient request 2, lost to follow-up 9</p> <p>Adverse events: Group 1. 23 patients experienced 30 adverse events; Group 2. 22 patients experienced 36 adverse events</p> <p>Number of adverse events related to bandage (none / possible / definite): Group 1. 18/6/6; Group 2. 27/2/7</p> <p>Number of different types of adverse events possibly or definitely device-related: Group 1. tissue damage or new ulcer 2, eczema or reaction to bandage 2, pain 2, maceration 2, other 4; Group 2. tissue damage or new ulcer 3, eczema or reaction to bandage 2, pain 2, maceration 2</p> <p>All bandages were applied according to the manufacturers' instructions</p> <p>Ulcers were measured using transparency tracing combined with computerised planimetry</p>	
Risk of bias		
Item	Authors' judgement	Description

Adequate sequence generation?	Unclear	"Patients were randomized to a bandage system..."
Allocation concealment?	Yes	"Randomization took place ... by means of opening sealed envelopes in sequential order". We were told these envelopes were numbered by the investigators
Incomplete outcome data addressed? All outcomes	Yes	"The analysis based on ITT meant that patients remained in their original randomized groups irrespective of subsequent treatments applied." Three randomised patients were excluded from the analysis "... two due to significant arterial disease... and one who had not given informed consent and who withdrew at 1 week"
Blinded outcome assessment (healing)?	No	Trial authors confirmed that assessment of healing was not blind to treatment
Baseline comparability?	Yes	Groups appear balanced at baseline; randomisation was stratified for ulcer area

Gould 1998

Methods	RCT with blinded outcome assessment (3 separate treatment rooms used for removal of bandages, clinical evaluation of ulcer, and reapplication of bandage). Setting was outpatient leg ulcer clinic in Truro, UK
Participants	39 patients with 46 ulcers (7 had bilateral ulcers) were recruited from local GPs. Inclusion criteria: venous ulcers, ABPI > 0.8, ambulatory. Exclusion criteria: arterial or mixed ulcers, diabetes mellitus, peripheral neuropathy, congestive heart failure, chronic renal or liver disease, infected wounds, ankle circumference < 18 cm or > 25 cm, known sensitivity to paste bandages, ulcer duration < 2 months. Mean (range) patient age: 71.5 years (44 to 87) Mean (range) baseline ulcer area: 7.44 cm ² (0.2 to 60.2) Mean baseline duration of ulcers: 10 months The trial authors reported no statistically significant differences between groups in relation to baseline variables; data were not presented per group
Interventions	Group 1. Three-component compression system comprising: medicated paste bandage, elastic bandage (Setopress), and elasticated viscose stockinette (n=19 patients) Group 2. Three-component compression system comprising: medicated paste bandage, cotton crepe bandage (Elastocrepe), and elasticated viscose stockinette (n=20 patients) All patients: were treated with the elastic bandage (Setopress) for one week prior to start of randomised treatment; received potassium permanganate soaks for 5 minutes prior to application of compression; were provided with class II compression stockings post-

	healing and were followed up by their GP	
Outcomes	Analyses were based on 32 patients with 39 ulcers Number (%) patients with complete healing at 15 weeks: Group 1. 11/19 (58%); Group 2. 7/20 (35%), P = 0.24 Withdrawals: 7/39 (18%) patients withdrew overall (full breakdown per group not reported). 4 withdrew following initial assessment, 1 withdrew after 3 weeks because of ulcer deterioration (Group 2), and 2 were excluded because ineligible (ulcers < 2 months duration at baseline)	
Notes	When there were several ulcers on one leg, the largest wound was included in the trial. In the case of bilateral ulceration, each leg was considered separately and the largest ulcer on each leg was studied; the long-stretch bandage was applied to one leg at random and the short-stretch bandage was applied to the other leg Some healing data will be highly correlated because of patients with two ulcerated limbs; no adjustment made for this in the statistical analysis Ulcer areas were measured using transparency tracing and computerised planimetry. Ulcers were photographed every 2 weeks	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details provided. "The trial was a prospective, randomized, observer-blind, parallel group study..."
Allocation concealment?	Unclear	No details provided. "The trial was a prospective, randomized, observer-blind, parallel group study..."
Incomplete outcome data addressed? All outcomes	No	Thirty nine patients were randomised "...32 patients were available for analysis". Withdrawals not reported by group
Blinded outcome assessment (healing)?	Yes	"Assessments were undertaken weekly at the clinic...Three separate rooms were used respectively for the removal of the bandages, for the clinical evaluation and for the application of new bandages. This ensured tht clinical evaluation was carried out blind to the bandage system used."
Baseline comparability?	Unclear	Described as comparable but data by group not presented.

Hendricks 1985

Methods	RCT (no details about allocation methods). Setting, outpatients, USA
Participants	<p>21 patients were recruited from outpatient clinics.</p> <p>Inclusion criterion: stasis leg ulcers (no definition provided)</p> <p>Exclusion criteria: not stated</p> <p>Number of patients male / female: Group 1. 5 / 5; Group 2. 7 / 4</p> <p>Mean±sd, median (range) patient age in years: Group 1. 59±16, 61 (35 to 86); Group 2. 64±12, 62 (49 to 86)</p> <p>Mean±sd, median (range) baseline total ulcerated area per patient in cm²: Group 1. 28.28±57.99, 2.55 (0.09 to 186.18); Group 2. 45.35±121.78, 4.68 (0.33 to 391.31)</p> <p>Mean±sd, median (range) baseline ulcer duration in months: Group 1. 29.5±35.5, 16.0 (0.5 to 108.0); Group 2. 11.9±17.9, 5.5 (0.5 to 60.0)</p> <p>Number of patients with predisposing factors at baseline (cellulitis / trauma / varicosities / thrombophlebitis / diabetes / anaemia): Group 1. 2 / 7 / 7 / 5 / 3 / 0; Group 2. 5 / 4 / 6 / 4 / 2 / 1</p> <p>Number of patients with unilateral / bilateral ulceration: Group 1. 10 / 0; Group 2. 6 / 5</p> <p>Some patients had multiple ulcers on the same limb.</p>
Interventions	<p>Group 1. Unna's Boot compression system consisting of: zinc oxide and calamine paste impregnated bandage (Dome-Paste); gauze bandage (Kerlix); and elastic bandage. Prior to bandage application, sharp debridement of ulcer was undertaken followed by wound cleansing with 3% hydrogen peroxide and bacitracin / polymyxin ointment (Polysporin) application to the ulcer surface. In cases of ulcer exudate, the wound was dried using a hair-dryer and 1% gentian violet applied. A low-potency corticosteroid cream (Tridesilon 0.05%) was applied to the peri-wound skin. The ulcer was covered with gauze and sometimes foam dressing. Dressings and bandages were changed during clinic visits every 3-9 days, depending on exudate (n=10 patients)</p> <p>Group 2. Open-toe, below-knee, elastic compression stocking (24 mmHg at ankle graduating to 16 mmHg at calf) (Futuro) was applied by the patient each morning and removed at bedtime. Patients were instructed to dry ulcers following bath/shower using gauze dressing prior to cleansing ulcers twice daily using 3% hydrogen peroxide. Then bacitracin / polymyxin ointment (Polysporin) was applied to the ulcer surface and a low-potency corticosteroid cream (Tridesilon 0.05%) applied to the peri-wound skin. A gauze dressing was applied, retained with cloth tape (Dermicel), and sometimes a foam dressing used. Patients attended clinic every 1 or 2 weeks, when sharp debridement was carried out (n=11 patients)</p> <p>All patients: concurrent treatments included: systemic antibiotics as deemed appropriate following ulcer cultures; oral zinc sulphate in cases of zinc deficiency; diuretics as necessary; reducing diet if overweight</p> <p>If patients were not deemed to be making progress at the end of each month in terms of decreasing ulcer size, and also other outcomes relating to changing limb volume, they were re-assigned to the alternate study group</p>
Outcomes	<p>Outcomes as reported by trial authors</p> <p>Complete healing at 78 weeks: Group 1. 7/10 (70%) patients healed. 3 patients switched to the alternative treatment - 2 healed</p> <p>Group 2. 10/14 (71%) patients healed (3 of these had been transferred from Group 1). 6 patients healed just with the stockings (2 bilateral, 2 healed on 1 leg only). 4 patients received the Unna's Boot system</p>

	<p>P = 0.94 for difference between groups</p> <p>Average healing time in weeks: Group 1. 7.3; Group 2. 18.4 (11.8 when one outlier excluded, who took 78 weeks to heal)</p> <p>Withdrawals: Group 1. none reported; Group 2 1 patient withdrew (reason not given)</p> <p>Outcomes recalculated by review author (analysed by intention-to-treat)</p> <p>Number (%) patients with complete healing at 78 weeks: Group 1. 9/10 (90%); Group 2. 9/11 (82%)</p> <p>Cumulative proportions healed at 78 weeks estimated from Kaplan-Meier survival analysis: Group 1. 90%; Group 2. 73%</p> <p>Median (95% CI) time to healing in weeks: Group 1. 7.0 (0.80 to 13.2); Group 2. 18.0 (5.05 to 30.95), P = 0.39 (log rank test)</p>	
Notes	<p>The descriptive statistics on patient age, baseline ulcer area and baseline ulcer duration were calculated by the review author from raw data reported in the paper. Patients in Group 1 had smaller ulcers at baseline, but on average the wounds were of longer duration</p> <p>The compression stockings were fitted according to the manufacturer’s instructions</p> <p>One patient in Group 2 used acetic acid instead of hydrogen peroxide for ulcer cleansing because of wound colonisation with <i>Pseudomonas aeruginosa</i></p> <p>Ulcers were photographed at baseline, then every 2 weeks.</p> <p>Some patients switched back and forth several times between treatments</p> <p>Other reported outcomes included change in leg volume and calf circumference</p>	
<i>Risk of bias</i>		
Item	Authors’ judgement	Description
Adequate sequence generation?	Unclear	“The 21 patients were randomly assigned to two groups...”
Allocation concealment?	Unclear	“The 21 patients were randomly assigned to two groups...”
Incomplete outcome data addressed? All outcomes	Yes	21 participants were randomised and end-point data is presented for 20 participants (1 withdrawal from Group 2)
Blinded outcome assessment (healing)?	Unclear	“Pictures of the ulcers were taken initially and every 2 weeks”
Baseline comparability?	No	Imbalances for baseline ulcer area (larger in Group 2) and duration (older in Group 1)

Methods	RCT (multicentre, pragmatic). Randomisation was stratified by study centre, previous ulceration (yes/no), ulcer area (\leq or $> 10 \text{ cm}^2$) and ulcer duration (\leq or > 6 months). The randomisation code was developed using computer-generated permuted blocks (randomly sized 4 or 6). Patients and nurses were aware of allocated treatment after assignment. Sample size estimation: 200 patients per arm would provide 80% power to detect 15% difference in healing rates at 12 weeks at 5% significance level. Patients were followed up for a minimum of 12 months
Participants	387 patients were recruited from 9 community (leg ulcer services, district nursing or general practice) and outpatient (vascular surgery) centres in the UK. Inclusion criteria: Patients with venous leg ulcer $\geq 1 \text{ cm}$ diameter. Exclusion criteria: Age < 18 years; ABPI < 0.8 ; diabetes mellitus; previous unsuccessful use of a trial bandage. Number of patients male/female: Group 1. 79/116; Group 2. 80/112 Mean \pm sd (range) age in years: Group 1. 71.9 \pm 12.3 (25 to 97); Group 2. 71.3 \pm 14.1 (23 to 96) Number (%) patients fully mobile / needing assistance / immobile: Group 1. 123 (63%) / 72 (37%) / 0 (0%); Group 2. 115 (60%) / 70 (37%) / 3 (2%) Number (%) patients with full ankle mobility / impairment / fixed: Group 1. 131 (67%) / 59 (30%) / 3 (2%); Group 2. 128 (67%) / 58 (30%) / 2 (1%) Median (range) number of ulcer episodes since first ulcer: Group 1. 2 (0 to 50); Group 2. 2 (0 to 64) Mean \pm sd (range) ankle circumference in cm: Group 1. 23.9 \pm 2.9 (16.2 to 34.0); Group 2. 23.9 \pm 2.9 (16.0 to 32.3) Median (range) ulcer duration in months: Group 1. 3 (0.5 to 456); Group 2. 3 (0.5 to 768) Median (range) ulcer area in cm^2 : Group 1. 3.81 (0.19 to 254.58); Group 2. 3.82 (0.35 to 143.93)
Interventions	All patients: ulcers were cleansed using tap water or saline and covered with simple low-adherent dressing. Dressings and bandages were renewed by the usual nursing staff at least weekly Group 1. Four-layer bandage: orthopaedic wool padding, crepe retention bandage, class 3A compression bandage and cohesive compression bandage, all applied with 50% overlap. The original four-layer bandage system and two proprietary kits (Profore and System 4) were randomly allocated (n=195) Group 2. Short-stretch bandage: orthopaedic wool padding covered with 1 or 2 100% cotton short-stretch compression bandages (Comprilan or Rosidal K), applied using spiral, figure-of-8 or modified Putter techniques (n=192)
Outcomes	Number (%) patients with complete healing at 4 months: Group 1. 107/195 (55%); Group 2. 86/192 (45%) (P value not reported - these data were shown as part of the discussion section for comparison with other trials) Number (%) patients with complete healing at one year: Group 1. 152/195 (78%); Group 2. 138/192 (72%) (P value not reported - these data were shown as part of the discussion section for comparison with other trials) Kaplan-Meier estimate of median (95% CI) time to healing in days: Group 1. 92 (71 to 113); Group 2. 126 (95 to 157), log rank comparison P = 0.117 Cox regression model was used to assess impact of treatment centre, ulcer area, ulcer

	<p>duration, ulcer episode, age weight, mobility, ankle mobility and ABPI on time to healing. Following adjustment for treatment centre, number of previous episodes, weight, baseline ulcer area, ulcer duration and ankle mobility, there was a statistically significant increase in the probability of healing in Group 1: HR 0.72 (95% CI 0.57 to 0.91)</p> <p>Kaplan-Meier estimate of cumulative proportion of legs healed at 12 weeks: Group 1. 46.3%; Group 2. 36.7%. Difference 9.6% (95% CI 0 to 20), P = 0.1</p> <p>Kaplan-Meier estimate of cumulative proportion of legs healed at 24 weeks: Group 1. 67.5%; Group 2. 55.4%. Difference 12.1% (95% CI 2 to 22), P = 0.02</p> <p>Number (%) withdrawals: Group 1. 46/195 (24%); Group 2. 66/192 (34%)</p> <p>Number (%) patients with non-bandage related adverse events: Group 1. 33/195 (17%) ; Group 2. 39/192 (20%)</p> <p>Number (%) patients with adverse events possibly related to compression treatment: Group 1. 76/195 (39%); Group 2. 91/192 (47%)</p> <p>Cost-effectiveness and cost-utility analyses: perspective was UK NHS and Personal Social Service; time horizon was 1 year after recruitment; price year 2001; health benefit measured as differences in ulcer-free days (Kaplan-Meier estimate) and quality-adjusted life years (QALYs) estimated from patients' responses to the EuroQol-5D questionnaire. To account for censoring, QALYs were adjusted by the Kaplan-Meier survival estimate over the 1-year time horizon. Mean difference in healing time for ulcers was 10.9 (95% CI -6.8 to 29.1) days in favour of Group 1. MD between treatment groups in QALYs was -0.02 (95% CI -0.08 to 0.04). The MD in total cost between compression systems was £227.32 (95% CI 16.53 to 448.30) per patient per year in favour of Group 1. Sensitivity analyses showed cost-effectiveness estimate to be robust to variation in number of bandages used and unit costs of compression systems. The four-layer bandage emerged as the dominant strategy</p>	
Notes	<p>If patients had multiple ulcers, the limb with the largest eligible ulcer was studied. Healing was defined as complete epithelial cover in the absence of a scab. At healing, the ulcer was photographed and healing was confirmed at the trial office by an investigator blind to treatment allocation. Training in the application of both types of bandages was provided during trial set-up</p> <p>This trial included an assessment of health-related quality of life. Since there was a large amount of missing data for this outcome, a descriptive analysis of findings was reported. The instruments used for data collection were the SF-12 and the Hyland Leg and Foot Ulcer Questionnaire. For the SF-12, scores between treatment groups appeared similar at baseline and over time for physical and mental components. For the Hyland Leg and Foot Ulcer Questionnaire, the scale was scored using two factors: practical and emotional. Baseline and follow-up scores were similar between groups for both factors</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	“The randomisation code was developed using computer generated permuted blocks, which were randomly of size four or six...The allocation sequence was generated by the trial statistician...”

Allocation concealment?	Yes	"After the baseline clinical assessment...the nurse recruiting the patient telephoned the randomisation service..."
Incomplete outcome data addressed? All outcomes	Yes	"Withdrawals from the trial and from allocated treatment were included in the analysis by intention-to-treat (ITT)."
Blinded outcome assessment (healing)?	Yes	<p>"Neither the patients nor the nurses administering the bandages and giving the associated care could be blinded ...The nurse providing the regular leg ulcer care was responsible for documenting the assessments of ulcer progress every 4 weeks, including tracing the ulcer outline. These outcome assessors were therefore not blinded. The ulcer tracing was sent to the Trial Coordination Office where the ulcer area was determined by computerised planimetry by a researcher masked to bandage allocation."</p> <p>"At the point of healing the nurse responsible for the patient's care of the leg ulcer took a Polaroid photograph of the healed ulcer and sent this to the Trial Coordination Office. An investigator unaware of the bandage allocation confirmed ulcer healing. This partially masked outcome assessment as the clinician only took a photograph when he/she had already decided the ulcer was healed."</p>
Baseline comparability?	Yes	Randomisation was stratified by ulcer area, ulcer duration, ulcer episode and clinical centre and resulted in good balance across groups. The primary analysis was also adjusted for important prognostic factors

Methods	<p>RCT (multicentre) with allocation by remote telephone service using a previously prepared centre-stratified randomisation list</p> <p>The aim of the trial was to assess non-inferiority between two compression systems. Sample size: the authors stated that non-inferiority was evaluated by comparing the 90% confidence interval for the between-group difference in complete healing with the non-inferiority limit of 15%, assuming 65% healing rate, 80% power and 5% significance level. The required number of patients was not stated</p>
Participants	<p>178 patients were recruited from 4 study centres in France, Germany, Austria & Switzerland</p> <p>Inclusion criteria: ambulatory ≥ 1 hour/day; patient age 18 to 80 years; venous leg ulceration confirmed using Doppler ultrasound; ulcer < 3 months baseline duration and maximum diameter ≤ 5 cm; ABPI > 0.9.</p> <p>Exclusion criteria: ulcers of diabetic, arterial or mixed aetiology; infected ulcers; co morbidities (decompensated heart failure, cancer, chronic or autoimmune infection, insulin-dependent diabetes, diabetic neuropathy); restricted ankle movement.</p> <p>Number of patients male/female: Group 1. 37/51; Group 2. 35/55</p> <p>Mean\pmsd (range) patient age in years: Group 1. 64.9\pm12.6 (33 to 82); Group 2. 65.1\pm11.7 (24 to 80)</p> <p>Number (%) patients with recurrent ulceration: Group 1. 68/88 (77%); Group 2. 69/90 (77%)</p> <p>Number (%) patients with history of deep vein thrombosis: Group 1. 30/88 (34%); Group 2. 29/90 (32%)</p> <p>Mean\pmsd (range) baseline ulcer surface area in mm²: Group 1. 240.3\pm229.7 (27 to 1356); Group 2. 239.6\pm230.1 (23 to 1042)</p> <p>Mean\pmsd (range) baseline ulcer duration in weeks: Group 1. 5.8\pm3.5 (1 to 12); Group 2. 6.0\pm3.3 (1 to 12)</p>
Interventions	<p>For all patients, the following were disallowed during the trial: use of antibiotics, immunosuppressants, cytotoxic agents and venoactive drugs; new prescriptions or changes in dosage of all types of anti-inflammatory drugs; sclerotherapy, venous surgery and skin grafts. Patients were seen weekly and were asked to wear the compression device continuously between clinic visits. All patients had manual debridement, ulcer cleansing with normal saline and a non-medicated, non-adherent gauze primary dressing</p> <ol style="list-style-type: none"> 1. Tubular compression device. The device was knitted, knee length, heel-less, open-toed, exerted graduated pressure, highest at ankle (30 to 40 mmHg), corresponding to class III compression stockings (n=88) 2. Short-stretch bandage (Rosidal K) (n=90).
Outcomes	<p>Number (%) patients with complete healing: Group 1. 51/88 (58.0%); Group 2. 51/90 (56.7%). Between-group difference in proportions with complete healing -1.3% (90% CI -13.5% to 10.9%)</p> <p>Mean\pmsd, median (range) time to healing in days: Group 1. (n=51) 43.0\pm18.3, 42 (13 to 84); Group 2. (n=51) 43.6\pm18.3, 42 (13 to 85). Between-group difference for median P = 0.80</p> <p>The Kaplan-Meier estimate showed no between-group difference in probability of healing (P = 0.41)</p> <p>Number (%) unhealed patients with reduction in ulcer area: Group 1. 25/37 (67.6%); Group 2. 23/39 (59.0%)</p>

	<p>Cox regression indicated that baseline ulcer area had a significant effect on time to healing (P = 0.002), but baseline ulcer duration and patient age were not significant predictors (P = 0.35 and P = 0.82 respectively)</p> <p>Compliance with bandaging regimen (calculated as number of days compression device worn as a percentage of the number of days participation in the study): Group 1. 96.8%; Group 2. 96.4% (P = 0.42)</p> <p>Tolerability: Group 1. 12 patients complained of pain in lower limb or sensation of tightness on the day after the first application of compression, or 1-2 weeks later. This was resolved in all cases by using larger sized devices. Group 2. no such problems</p> <p>Health-related quality of life assessed using the Nottingham Health Profile showed no difference between treatment groups (information taken from conference abstract therefore only brief details available)</p>	
Notes	<p>188 patients were randomised, this comprising the intention-to-treat population but data were presented on a total per protocol sample of 178. Reasons for exclusion: patient did not consent to use bandages 1; lost to follow up 1; compression treatment used for < 1 week 7; diabetes 1 (breakdown per group not reported)</p> <p>The authors reported that results for the intention-to-treat population were comparable with those for the per protocol population, but the statistics were not reported</p> <p>Compression was applied by the investigator (described as 'experienced') or medical staff ('experienced and well trained') according to manufacturers' instructions. In the discussion section, the authors reiterated that all investigators were specialists, reducing problems with bandage application such as insufficient pressure or non-graduated pressure. Patients and family members were asked not to change the compression device</p> <p>Wounds were measured weekly using transparency tracing combined with computerised planimetry</p>	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"Once a patient was eligible, the investigator received the corresponding treatment number (by telephone from an external randomisation centre) in accordance with a previously prepared centre-stratified randomisation list."
Allocation concealment?	Yes	"Once a patient was eligible, the investigator received the corresponding treatment number (by telephone from an external randomisation centre) in accordance with a previously prepared centre-stratified randomisation list."
Incomplete outcome data addressed? All outcomes	No	Not an ITT analysis. 188 participants were randomised and as this was deemed by the trialists a "non inferiority trial" they undertook a per protocol analysis on only 178

		participants
Blinded outcome assessment (healing)?	Unclear	“Change in ulcer size was evaluated by physicians drawing an outline of the study ulcer on tracing paper. These tracings were then used to calculate the area and diameter of the ulcers.”
Baseline comparability?	Unclear	Insufficient information to judge since whilst mean ulcer area and duration were similar across treatment groups these data will be highly skewed and medians would have been more informative

Jünger 2004b

Methods	<p>RCT (multicentre) with allocation achieved using blocks of 4 patients compiled by a contract research organisation prior to patient recruitment. Non-inferiority trial (non-inferiority margin set at 15% of healing rate)</p> <p>No a priori power calculation was presented. An interim analysis of the first 120 patients completing therapy was planned a priori. It was planned to use the findings of this to estimate the final sample size or to terminate the study prematurely. Since the between-group difference in frequency of complete healing exceeded 15%, the study was stopped after the interim analysis</p> <p>Assessment of healing was conducted by investigators blind to treatment allocation</p>
Participants	<p>134 patients were randomised at 16 study centres (German medical practices specialising in phlebology and German and Dutch phlebology outpatient clinics).</p> <p>Inclusion criteria: venous ulcer, WIDMER stage III, CEAP 6; breadth 1 to 10 cm; baseline ulcer duration < 12 months; reflux of extrafacial cutaneous saphenous veins or deep conducting veins or perforating veins confirmed by Doppler or Duplex sonography; ABPI > 0.9; patient age 18 to 80 years.</p> <p>Exclusion criteria: ambulatory < 1 hour per day; ulcer clinically infected; ulcers of diabetic, arterial or combined aetiology; insulin-dependent diabetes mellitus; diabetic polyneuropathy; deep vein thrombosis in last 3 months; uncontrolled hypertension; advanced coronary disease; primary chronic polyarthritis; ankle dorsal flexion < 5°; vascular surgery or sclerotherapy within last 3 months; concomitant venous medication, immunosuppressants or cytostatics; BMI > 35 kg/m²; general risk factors; non-compliance.</p> <p>All patients were Caucasian.</p> <p>Number of patients male/female: Group 1. 21/40; Group 2. 26/34</p> <p>Mean±sd patient age in years: Group 1. 63±11; Group 2. 63±13</p> <p>Mean±sd BMI in kg/m²: Group 1. 28±4; Group 2. 28±5</p> <p>Mean±sd, median baseline ulcer surface area in mm²: Group 1. 562±788, 274; Group 2. 595±899, 370</p> <p>Mean±sd baseline ulcer duration in days: Group 1. 116±100; Group 2. 156±120</p> <p>Number (%) patients with diabetes: Group 1. 7/61 (11%); Group 2. 7/60 (12%)</p> <p>Number (%) patients who had compression prior to study: Group 1. 54/61 (89%); Group 2. 54/60 (90%)</p>

Interventions	<p>All patients were given instructions and written information on how to apply their respective compression system. Compression therapy was to be applied for at least 8 hours per day. Patients could reapply compression between clinic visits, or could request professional assistance</p> <p>Group 1. U-Stocking (Venotrain ulcertec), consisting of outer and inner stockings, with size specified individually for each patient (3 ready-made widths available, each in 2 lengths) (n=66)</p> <p>Mean±sd ankle pressure of U-Stocking measured while supine was 42.7±13.0 mmHg</p> <p>Group 2. Compression bandages (2 short stretch bandages each of 10 cm width and 5 m length, wrapped around the leg in opposite directions from the metatarsophalangeal joint to the head of the fibula) (n=68)</p> <p>Ankle pressure not reported for compression bandages.</p>
Outcomes	<p>Number (%) patients with complete healing at 12 weeks: Group 1. 29/61 (47.5%); Group 2. 19/60 (31.7%) (95% CI for between-group differences weighted by centre 4. 3% to 28.5%, one-sided P = 0.013)</p> <p>Mean±sd, median (range) days to healing: Group 1. 46±20, 47 (10-83); Group 2. 46±22, 52 (6-80), P = 0.82 (Mann-Whitney U-test)</p> <p>Kaplan-Meier survival analysis indicated a trend in favour of Group 1. (P = 0.057, log rank test). Cumulative proportions of patients healed at 12 weeks as read from survival plot: Group 1. 51%; Group 2. 30%</p> <p>Mean±sd, median (range) % change in ulcer surface area at 12 weeks: Group 1. (n=61) -74.8±42.4, -98.4 (-100 to 83); Group 2. (n=58) -51.4±86.7, -82.9 (-100 to 396.2), P = 0.068 (Mann-Whitney U-test)</p> <p>Mean±sd, median duration of compression therapy (hours per day) assessed during the trial Group 1. 12.7±2.9, 12.2; Group 2. 16.9±5.7, 15.9 (P = 0.0002)</p> <p>Number (%) patients reporting difficulty in application of compression device (mild / moderate / great):</p> <p>Group 1. (n=54) 11 (20%) / 4 (7%) / 2 (4%); Group 2. (n=53) 12 (23%) / 6 (11%) / 0 (0%) (P = 0.9, Chi squared test)</p> <p>Number of adverse events: Group 1. 29 adverse events in 20/65 (31%) patients; Group 2. 42 adverse events in 26/67 (39%) patients</p> <p>Number of serious adverse events: Group 1. 2 serious adverse events, both resulting in discontinuation of study treatment (ulcer bleeding/pain, 1, gastrointestinal bleeding 1) ; Group 2. 4 serious adverse events (ulcer bleeding 1, lymph secretion from ulcer 1, fractured neck of femur - discontinued treatment 1, thrombophlebitis - discontinued treatment 1)</p> <p>Number of non-serious adverse events: Group 1. 2 non-serious adverse events (increased ulcer pain 1, increase in calf circumference & open sites around ulcer - treatment discontinued 1); Group 2. 4 non-serious adverse events (ulcer increased in size 1, ankle flexibility restricted by pain 1, intolerance to compression material leading to discontinuation of treatment 1, phlegmon on lower leg - treatment discontinued 1)</p> <p>Patient questionnaire on comfort of compression showed significantly more patients reporting no problems in Group 1 for: constriction (P = 0.003); restricted freedom of movement (P = 0.0009); sweating under the dressing (P = 0.04); & itching of skin on leg (P = 0.006). There were no significant between-group differences for tightness, leg pain, burning in leg, heat sensation in leg & prickling of leg</p> <p>Mean±sd, median (25% and 75% quartiles) minutes taken for nurse to apply compression</p>

	<p>sion: Group 1. 5.4±5.4, 3 (2 and 5); Group 2. 8.5±6.5, 6 (5 and 10), P < 0.001</p> <p>Number (%) patients receiving professional support for bandage application: Group 1. 6/65 (9.2%); Group 2. 15/67 (22.4%), P = 0.065</p> <p>Cost analysis was based on cost of procedures and associated resources, including: application of stockings or bandages; primary dressings (moist or gauze); debridement (enzymatic or surgical); skin care with zinc paste; skin treatment with topical corticosteroids; physiotherapy; and lymphatic drainage. Labour costs were included; overhead costs were excluded. The number and type of procedures were patient-reported. Estimated cost per % reduction in wound area (euros, price year 2003): Group 1. 2.57; Group 2. 4.58</p>	
Notes	<p>In patients with mulitple ulcers, the largest wound was studied. Ulcers were larger and more chronic at baseline in Group 2. The main analysis should be regarded as the Kaplan-Meier survival analysis: the between-group difference in time to healing was tested using the Mann-Whitney U-test but the log rank test would have been preferable</p> <p>Ulcer surface areas were estimated using a digital image of the wound perimeter traced onto foil combined with computerised planimetry. The calculation was performed at a central research office by a technician who was blind to treatment allocation. Ulcers were photographed</p> <p>Withdrawals / exclusions from analysis: following randomisation 1 patient per group was excluded (Group 1. additional thigh compression needed prior to start of study treatment; Group 2. refused treatment prior to start of therapy). The safety analysis was based on: Group 1. n=65; Group 2. n=67. Of these patients, the following withdrew early and had no efficacy data: Group 1. n=4 (serious adverse event 2, ineligible 2); Group 2. n=7 (serious adverse event 2, ineligible 2, lost to follow up 3). The intention-to-treat population available for the primary efficacy analyses was based on: Group 1. n=61; Group 2. n=60. Of these patients, the following withdrew after at least one post-baseline assessment: Group 1. n=6 (withdrawal of consent 4, poor compliance 2); Group 2. n=6 (withdrawal of consent 2, poor compliance 2, adverse events 2)</p> <p>The authors stated the following: the bandaging method used for Group 2 was standardised in all study centres; all persons involved in providing nursing care were given training in applying compression</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	“Randomization used blocks of 4 patients and was performed at the statistical department of a contract research organisation... prior to patient enrollment”
Allocation concealment?	Yes	“Numbered containers were supplied to the study sites; patients were assigned by the investigators to one of the two treatments by opening a code envelope with available treatment numbers in ascending order.”

Incomplete outcome data addressed? All outcomes	No	134 patients were randomised and 121 were analysed. Six people withdrew from each group
Blinded outcome assessment (healing)?	Yes	The calculations of ulcer surface area were performed at a central research office by a technician who was blind to treatment allocation
Baseline comparability?	No	Possible imbalances for ulcer area (median ulcer was larger in Group 2 and mean duration was also longer in Group 2)

Kikta 1988

Methods	RCT (no further details of methods of allocation). Setting, outpatients, USA
Participants	<p>84 patients with 87 leg ulcers caused by chronic venous insufficiency were recruited from hospital vascular surgery clinics.</p> <p>Exclusion criteria: arterial insufficiency (ABPI < 0.7); uncontrolled diabetes mellitus; use of cancer chemotherapeutic agents or systemic steroids; recent venous surgery; infected ulcers; inability to comply with treatment or follow-up.</p> <p>Mean±sem baseline ulcer area in cm²: Group 1. 9.0±2.2; Group 2. 8.6±2.1</p> <p>Mean±sem baseline ulcer duration in weeks: Group 1. 51±17; Group 2. 45±12</p> <p>The authors reported that groups were comparable for other baseline variables including: patient age; sex; race; previous ulcer treatment; prerandomisation use of antibiotics; origin of chronic venous insufficiency; previous venous, arterial or orthopaedic surgery; prior use of elastic stockings; ischaemic heart disease; congestive heart failure; obesity; hypertension; diabetes mellitus; pulmonary, renal and hepatic diseases; use of oral contraceptives or tobacco; alcoholism; elevated levels of serum haemoglobin, glucose, albumin and creatinine; ankle-brachial pressure index; and whether ulcer was new or recurrent. Data were not presented for these variables. The source population was described as 'inner city, lower socioeconomic class'</p>
Interventions	<p>All patients received instructions regarding leg elevation, restriction of standing activities, care of 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 & left to air dry</p> <p>Group 1. Unna's boot (further details of components not provided) (n=42 ulcers)</p> <p>Group 2. Duoderm hydrocolloid dressing (no compression applied) (n=45 ulcers)</p>
Outcomes	<p>Analysis was based on 66 patients with 69 ulcers: Group 1. n=30 ulcers; Group 2. n=39 ulcers</p> <p>Number (%) of ulcers completely healed at 6 months: Group 1. 21/30 (70%); Group 2. 15/39 (38%) (P = 0.01, Chi Squared test)</p> <p>Lifetable analysis of mean±sem proportion of ulcers healed at 15 weeks: Group 1. 64%±9%; Group 2. 35%±8% (P = 0.01, log rank test)</p> <p>Mean±sem time to healing in weeks: Group 1. 8.4±1.8; Group 2. 7.0±1.5 (P = 0.8,</p>

	<p>Student's t test)</p> <p>Findings from logistic regression suggested that the following were significant predictors of healing: dressing type ($P = 0.002$); and baseline ulcer area ($P = 0.04$). Other covariates that were tested but did not emerge as significant predictors included: baseline ulcer duration, patient age, sex, race, obesity and diabetes</p> <p>Number (%) ulcers withdrawn from study (all withdrew within 2 weeks of randomisation - reasons not provided): Group 1. 12/42 (29%); Group 2. 6/45 (13%) ($P = 0.11$, Fishers' exact test)</p> <p>Number (%) of ulcers with adverse events resulting in discontinuation of treatment: Group 1. 0/30 (0%); Group 2. 10/39 (26%) (8 developed reddish-green exudate, 2 had associated cellulitis requiring hospital admission). $P = 0.004$ for difference between groups (Fisher's exact test)</p> <p>Mean±sem pain score evaluated by patients post-healing using linear scale 1-10 (meaning of values not explained): Group 1. 2.4 ± 0.4; Group 2. 1.2 ± 0.1 ($P = 0.007$, Student's t test)</p> <p>Mean±sem cost of treatment per week in US\$ (price year 1986) based on cost of all dressing materials divided by time to healing (healed ulcers) or duration of therapy (non-healed ulcers). Clinic visit costs and staff costs were excluded: Group 1. 11.76 ± 0.59; Group 2. 14.24 ± 1.63 ($P = 0.16$, Student's t test)</p>
Notes	Ulcer area was measured using tracing and computerised planimetry. Dressings were applied according to manufacturers' instructions

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Patients with leg ulcers... were randomized to receive..."
Allocation concealment?	Unclear	"Patients with leg ulcers... were randomized to receive..."
Incomplete outcome data addressed? All outcomes	No	84 people were randomised however only 66 people were analysed
Blinded outcome assessment (healing)?	Unclear	"Ulcer size was measured by tracing the ulcer outline and then measuring the area with a computerised digital planimeter."
Baseline comparability?	Unclear	Appear similar for baseline area and duration (however only means presented). The authors reported that groups were comparable for other baseline variables including: patient age; sex; race; previous ulcer treatment; prerandomisation use of antibiotics; origin of chronic venous insufficiency; previous venous, arterial or orthopaedic surgery; prior use of elastic stock-

		ings; ischaemic hear disease; congestive heart failure; obesity; hypertension; diabetes mellitus; pulmonary, renal and hepatic diseases; use of oral contraceptives or tobacco; alcoholism; elevated levels of serum haemoglobin, glucose, albumin and creatinine; ankle-brachial pressure index; and whether ulcer was new or recurrent. Data were not presented for these variables
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Knight 1996

Methods	RCT (no further details of methods). Setting was a wound care center in the USA
Participants	10 patients randomly chosen from those attending a wound care centre. Inclusion criteria: venous insufficiency (not defined); leg ulcer of venous aetiology. Exclusion criteria: refused consent. No information was provided about baseline characteristics.
Interventions	Group 1. Four-layer bandage 4 layer (Profore) (n=5 patients) Group 2. Unna's boot (described as a paste impregnated gauze compression dressing) (n=5 patients) All patients received a foam dressing (Allevyn) as the primary dressing. Dressings and bandages were changed weekly
Outcomes	. 9/21; Group 2. 11/19. Previous ulcer recurrence: Group 1. 74%; Group 2. 73%. Mean±sd baseline ulcer area (cm ²): Group 1. 6.38±1.2; Group 2. 6.19±0.8. Mean±sd baseline ulcer duration (weeks): Group 1. 16.6±5.8; Group 2. 16.9±6.2. Inclusion criterion: venous leg ulceration on gaiter area (diagnosed clinicall
Notes	Few details of this trial were available. Data have been extracted from a conference abstract and a brief, unpublished report provided by the trial authors. Ulcer surface area was assessed weekly using transparency tracing and computerised planimetry. Patients were followed up for six weeks. Venous filling index measured by air plethysmography was reported at baseline, day 1 and day 7. This study is described as ongoing, but no follow-up reports have been identified

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"...subjects for the study are randomly assigned..."
Allocation concealment?	Unclear	No details provided. "...subjects for the study are randomly assigned..."

Knight 1996 (Continued)

Incomplete outcome data addressed? All outcomes	Unclear	10 patients recruited; data on 10 participants. NB this trial was ongoing at time of trial report but no further data received
Blinded outcome assessment (healing)?	Unclear	Wounds were measured by transparency tracing combined with computerised planimetry but unclear how these images were assessed and whether observers were blinded
Baseline comparability?	Unclear	No baseline data presented.

Koksal 2003

Methods	RCT (method of randomisation not stated). Setting University Hospital Clinic in Turkey
Participants	60 outpatients were recruited. Average (range) age in years: Group 1. 51 (24 to 70); Group 2. 49 (20 to 72). Sex male/female: Group 1. 9/21; Group 2. 11/19. Previous ulcer recurrence: Group 1. 74%; Group 2. 73%. Mean±sd baseline ulcer area (cm ²): Group 1. 6.38±1.2; Group 2. 6.19±0.8. Mean±sd baseline ulcer duration (weeks): Group 1. 16.6±5.8; Group 2. 16.9±6.2. Inclusion criterion: venous leg ulceration on gaiter area (diagnosed clinically) with area 5 to 8 cm ² . Exclusion criteria: ABPI < 0.8; clinical infection requiring treatment; diabetes; causes of leg ulceration other than venous
Interventions	Concurrent treatments: all ulcers were cleansed with normal saline and debrided (no further details of agents used) when necessary 1. Unna's Boot containing calamine, zinc oxide, glycerine, sorbitol, gelatine & magnesium aluminium silicate (n=30) 2. Hydrocolloid dressing (Comfeel) plus class II elastic compression stocking providing 30 to 40 Hgmm (n=30) Dressings were changed every 3 to 7 days.
Outcomes	Ulcer area measured using transparency tracing and planimetry (instrument not stated) . Areas calculated by an investigator blind to treatment allocation Patients with complete healing at 4 months: Group 1. 20/27 (74%); Group 2. 21/26 (81%), P > 0.05 Mean±sd healing rate (cm ² per week): Group 1. 1.28±0.72; Group 2. 1.16±0.38, P > 0.05 Mean±sd weeks to healing: Group 1. 6.85±3.60; Group 2. 6.65±3.31, P > 0.05 Mean±sd pain score during application (measured with visual analogue scale zero to 10, where zero represents no pain & 10 worst imaginable pain): Group 1. 3.69±1.35; Group 2. 1.88±1.48, P < 0.0001 Mean±sd pain score at home (measured as above): Group 1. 3.27±1.08; Group 2. 1.88±1.11, P < 0.0001

Koksal 2003 (Continued)

Notes	<p>It is unclear whether patients in Group 2 removed stockings when going to bed. Regarding care provider skill, the paper reports that 'two dedicated and trained outpatient nurses applied both treatment modalities'</p> <p>Withdrawals: Group 1: 3 (2 patients had infected ulcers & 1 patient was hospitalised); Group 2: 4 (1 patient had infection; 1 had severe reaction to dressing; 1 did not attend clinic; 1 lost to follow up)</p> <p>No patient experienced a serious adverse event during the trial. One treatment-related adverse event was reported in Group 2</p>
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Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"The patients were randomly assigned into two groups"
Allocation concealment?	Unclear	"The patients were randomly assigned into two groups"
Incomplete outcome data addressed? All outcomes	No	60 patients were recruited and for complete healing analysis was based on 53 participants. For continuous outcomes, denominator unclear. Three patients withdrew from Group 1 and 4 from Group 2
Blinded outcome assessment (healing)?	Yes	Ulcer tracings and planimetry were performed by a technician who was unaware of the treatment allocation
Baseline comparability?	Unclear	Mean ulcer area and duration were similar however medians were not presented and data likely to be skewed

Kralj 1996

Methods	RCT (open design). Setting included both in-patients and out-patients in Slovenia
Participants	<p>40 patients were recruited.</p> <p>Inclusion criteria: stasis leg ulcer, age < 86, complete mobility, written, informed consent.</p> <p>Exclusion criteria: ABPI < 0.8, systemic connective tissue disease, serological positive rheumatoid arthritis, severe concurrent diseases.</p> <p>Number of patients male/female: Group 1. 6/10; Group 2. 8/10</p> <p>Mean (range) patient age in years: Group 1. 65 (40 to 86); Group 2. 61 (36 to 85)</p> <p>Mean (range) baseline ulcer area in cm²: Group 1. 18.6 (1 to 57); Group 2. 17.2 (1 to 47)</p> <p>Mean (range) duration of ulcers in months: Group 1. 7.9 (1 to 24); Group 2. 6.9 (1 to 36)</p>

Interventions	Group 1. 4 layer (Profore): wool , crepe, Litepress, Co-Plus (n=20 patients) Group 2. hydrocolloid dressing (Tegasorb) and single layer inelastic bandage (Porelast) (n=20 patients) For all patients, bandages were changed at least weekly.	
Outcomes	Number (%) patients with complete healing during 6 month trial (NB patients started treatment at different points within this 6-month period): Group 1. 7/20 (35%); Group 2. 8/20 (40%) Mean (range) days to healing: Group 1. 57.6 (7 to 106); Group 2. 84.9 (28 to 180) Number (%) patients withdrawing from trial (reasons): Group 1. 4/20 (20%) (1 admitted to hospital with heart condition, 1 did not have transport to clinic, 2 unknown reason) ; Group 2. 2/20 (10%) (1 cerebrovascular apoplexy, 1 unknown reason)	
Notes	The maximum length and maximum width of the ulcer was measured at each bandage change. Ulcer surface area was calculated as follows: $a^3 \times b \times \pi / 4$ (where a=maximum length (cm) and b=maximum width (cm)). If patients had multiple ulcers, the total ulcerated area was studied. Study described as ongoing	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Communication with trialists confirmed that randomisation was by sealed envelope but not clear if opaque or numbered. Method of sequence generation unclear
Allocation concealment?	Unclear	Communication with trialists confirmed that randomisation was by sealed envelope but not clear if opaque or numbered
Incomplete outcome data addressed? All outcomes	No	40 patients recruited; 4 people withdrew from Group 1 and 2 from Group 2. These people were not included in the analysis
Blinded outcome assessment (healing)?	Unclear	“Wounds were assessed by authors...” (personal correspondence)
Baseline comparability?	Unclear	Mean ulcer areas and durations similar but not very informative since data skewed

Methods	RCT with randomisation by computer-generated tables and stratification by baseline ulcer area. The strata were (cm squared): small (0.25 to 2.5); medium (> 2.5 to 25); large (>25 to 100). For stratification purposes, ulcer area was measured using diameter product (multiplication of maximum length and width)
Participants	112 patients referred to a hospital leg ulcer outpatient clinic in the UK were recruited. Number of patients with small / medium / large ulcers at baseline: Group 1. 18 / 23 / 16; Group 2. 17 / 23 / 15. Exclusion criteria: ABPI < 0.8; diabetes; rheumatoid arthritis; systemic lupus erythematosus; positive sickle cell test; HIV; ulcer size < 0.25 cm ² or > 100 cm ² ; known sensitivity to Viscopaste; receiving drugs that might affect ulcer healing; non-venous diagnosis of ulcer on clinical examination; no venous abnormality detected using haemodynamic assessment, even if clinical examination indicated venous aetiology
Interventions	Concurrent treatment for both groups: ulcer and surrounding skin was cleansed with saline-soaked cotton wool balls. Standardised figure-of-eight technique used for bandaging 1. Viscopaste bandage plus Tensopress (elastic bandage) plus Tensoshape (graduated cotton-elastic tubular retaining bandage) (n=57) 2. Viscopaste bandage plus Elastocrepe (inelastic bandage) plus Tensoshape (description as above) (n=55) All dressings were undisturbed until the next clinic visit; frequency of clinic visits not stated
Outcomes	Number of patients with complete healing (assessed by photograph) at 26 weeks: Group 1. 33/57 (58%); Group 2. 34/55 (62%), P = 0.623 (P value generated from Kaplan-Meier estimates & log rank test) Patients with large ulcers were significantly less likely to heal within 26 weeks than those with small or medium-sized ulcers ($\chi^2=18.05$, P < 0.001), and this was independent of the treatment effect Further analysis at 40 weeks showed that 1 extra patient per group had healed - this did not affect statistical significance of the between-group difference Mean [range] (95% CI) weeks to healing: Group 1. 10 [2 to 23] (8 to 12); Group 2. 11 [3 to 25] (9 to 13), not significant Median weeks to healing: Group 1. 9; Group 2. 9.5, not significant
Notes	Unclear whether photographic confirmation of healing was done by assessor blind to treatment allocation Care providers were 'seven experienced ulcer clinic nurses'. Number of patients excluded post-randomisation because ineligible: Group 1. 4; Group 2. 5 Numbers of patients who withdrew from treatment during trial (with reasons): Group 1. 8 (1 had bandage skin damage (pretibial skin necrosis), 1 refused treatment, 3 were lost to follow-up, 3 had incomplete data record); Group 2. 8 (1 had paste allergy; 2 were non-compliant; 3 were lost to follow-up; 2 had incomplete data record) Costs per bandage: Group 1. £4.38; Group 2. £2.54 (price year not stated) Mean initial ankle pressures using the Borgnis medical stocking test apparatus: Group 1. 45 mmHg; Group 2. 24 mmHg

<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"Computer generated tables were used to randomise patients"
Allocation concealment?	Unclear	No further details provided.
Incomplete outcome data addressed? All outcomes	Yes	112 people were randomised and 112 analysed for complete healing however unclear other outcomes
Blinded outcome assessment (healing)?	Unclear	No detail provided.
Baseline comparability?	Unclear	Randomisation was stratified by ulcer area at baseline however neither mean nor median ulcer area by group presented

Meyer 2003

Methods	RCT with randomisation by computer-generated tables and stratification by baseline ulcer area. The strata were (cm squared): small (0.25 to 2.5); medium (> 2.5 to 25); large (> 25 to 100). For stratification purposes, ulcer area was measured using diameter product (multiplication of maximum length and width). For patients with bilateral ulcers, the combined area of the ulcers on both legs was used for stratification. Using an a priori power calculation, it was estimated that the study had 50% power to detect a difference of 20% in frequency of complete healing at the 95% significance level
Participants	133 patients referred to a hospital leg ulcer outpatient clinic in the UK were recruited; sex male/female: Group 1. 34/30 Group 2. 41/28. Median age in years: Group 1. 68 Group 2. 64. Mean duration of ulcer in months: Group 1. 19.8 Group 2. 14.8. Number of patients with small / medium / large ulcers at baseline: Group 1. 25 / 18 / 21 Group 2. 21 / 21 / 27 Exclusion criteria: ABPI < 0.9; diabetes; rheumatoid arthritis; systemic lupus erythematosus; positive sickle cell test; HIV; ulcer size < 0.25 cm ² or > 100 cm ² ; known sensitivity to paste; ulcer not of venous aetiology; failure to comply with exit investigations
Interventions	Concurrent treatment for both groups: ulcer and surrounding skin was cleansed with saline-soaked cotton wool balls. Standardised figure-of-eight technique used for bandaging 1. 3-layer bandage consisting of: Steripaste bandage plus Setopress bandage plus Tubgrip bandage (n=64) 2. 4-layer bandage consisting of: Velband orthopaedic wool plus crepe bandage plus Elset compression bandage plus Coban bandage (n=69) All dressings were undisturbed until the next clinic visit; frequency of clinic visits was initially weekly, this being extended to fortnightly in patients deemed to be making good

	progress in terms of healing	
Outcomes	<p>Patients were followed up to healing or until 52 weeks</p> <p>Number of patients with complete healing (assessed by photograph) at 52 weeks: Group 1. 51/64 (80%); Group 2. 45/69 (65%), P = 0.031</p> <p>Median (95% CI) weeks to healing: Group 1. 12 (10 to 15); Group 2. 16 (13 to 21), P = 0.04</p> <p>Kaplan-Meier survival estimates showed that the difference in probability of healing between the two bandages did not become apparent until 20 weeks after randomisation, P = 0.036 (log rank test). The authors reported that this estimate remained robust when the analysis was repeated selecting only patients with venous ulceration confirmed with haemodynamic assessment at completion or withdrawal, but full details not shown in the paper</p> <p>The authors stated that ulcer duration did not influence healing, but patients with large ulcers were significantly less likely to heal than those with small or medium ulcers, this effect being independent of treatment (full details of these analyses not shown)</p> <p>Scores for bandage comfort, pain on bandaging and ease of putting on shoes over bandages (all assessed using an un validated scale of 1 - 4 at each visit) increased over the study period, indicating improvement for both groups, but no significant differences were detected between groups</p> <p>Group 1 contained significantly more patients with post-thrombotic calf veins; this was assessed at completion or withdrawal using ascending phlebography (full details of analysis not shown)</p>	
Notes	<p>Numbers of patients who withdrew from treatment during trial (with reasons): Group 1. 10 (4 due to adverse events, 2 were non-compliant, 3 lost to follow-up, 1 refused treatment); Group 2. 11 (2 due to adverse events, 5 were non-compliant, 3 lost to follow-up, 1 refused treatment)</p> <p>Unclear whether photographic confirmation of healing was done by assessor blind to treatment allocation</p> <p>Care providers were described as 'seven experienced ulcer clinic nurses' and as 'dedicated nursing staff who are fully trained in four-layer bandaging'</p> <p>Statistical calculations were performed by two statisticians who were independent of one another and of the study investigators</p>	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer generated tables were used to randomise patients.
Allocation concealment?	Yes	No further detail provided.
Incomplete outcome data addressed? All outcomes	Yes	133 people were randomised and complete healing data provided on 133 participants. Unclear for other outcomes. Ten people withdrew from Group 1 and 11 from Group 2

Blinded outcome assessment (healing)?	Unclear	Unclear whether photographic confirmation of healing was done by assessor blind to treatment allocation
Baseline comparability?	Unclear	Randomisation was stratified by ulcer area at baseline however neither mean nor median ulcer area by group presented

Milic 2007

Methods	RCT. Randomisation was computer generated. Some details of sample size calculation provided (80% power, significance level 5%) but intended clinical difference to be detected not clear
Participants	<p>150 patients were recruited. Number male/female: Group 1. 39/36 Group 2. 34/41. Median (range) patient age in years: Group 1. 55 (33 to 80); Group 2. 57 (34 to 81). Median (range) number of previous episodes of ulceration: Group 1. 5 (2 to 10); Group 2. 5 (1 to 11).</p> <p>Median (range) baseline ulcer surface area (cm²): Group 1. 72 (24 to 210); Group 2. 64 (20 to 195).</p> <p>Median (range) baseline ulcer duration in years: Group 1. 7 (0.6 to 28); Group 2. 6 (0.6 to 21).</p> <p>Number (%) patients with previous deep vein thrombosis: Group 1. 25/72 (35%); Group 2. 20/66 (30%).</p> <p>Number (%) patients who had previously undergone stripping of great saphenous vein: Group 1. 14/72 (19%); Group 2. 12/66 (18%).</p> <p>Number (%) patients who had previously undergone superficial endoscopic perforator vein surgery: Group 1. 5/72 (7%); Group 2. 5/66 (8%).</p> <p>The authors reported that groups were similar at baseline for CEAP classification.</p> <p>None of the patients had previously received compression.</p> <p>Inclusion criteria: patient age ≥ 18 years; venous leg ulceration diagnosed using ABPI assessment and colour duplex ultrasonography; baseline ulcer surface area > 20 cm²; baseline ulcer duration > 6 months.</p> <p>Exclusion criteria: ABPI < 0.8; causes of ulceration other than venous; heart failure (ejection fraction < 35); pregnancy; cancer; diabetes</p>
Interventions	<p>All patients were treated on an ambulatory basis. All had mechanical debridement using sterile gauze. Dressings were changed every 1 to 7 days, depending on exudate. Extensive exudation was treated with crystal acidum boricum, applied to the wound following debridement. In cases of no exudate, a dry dressing was applied. Bandage systems were worn day and night. No antibiotics were used. All patients received aspirin (100 mg, presume this is daily dose)</p> <ol style="list-style-type: none"> 1. Cotton gauze without tension (50% overlap) plus cotton crepe bandage plus knee-length tubular compression device (Tubulcus) providing 35 to 40 mm Hg at ankle plus medium-stretch elastic compression bandage (Niva). After healing, patients continued to wear Tubulcus (n=75) 2. Cotton gauze without tension (50% overlap) plus cotton crepe bandage plus two medium stretch elastic compression bandages (Niva). After healing, patients wore class

	II compression hoisery providing 20 to 25 mm Hg (Rudo) (n=75) Mean of 3 values (range) interface pressure in mm Hg, measured using Trickovic sensor placed 8 cm above medial malleolus with patient in supine position: Group 1. 50 (46 to 56); Group 2. 44 (37 to 49)	
Outcomes	Kaplan-Meier estimate of cumulative proportion of patients with complete healing of study limb at 500 days: Group 1. 93%; Group 2. 51%, P < 0.001 Kaplan-Meier estimate of median (range) days to healing: Group 1. 133 (28 to 464); Group 2. 211 (61 to 438) Cox regression did not show a relationship between time to healing and any baseline variable Recurrence rate during 1-year follow-up: Group 1. 16/67 (24%); Group 2. 18/34 (53%) , P < 0.05 Number (%) patients healed following recurrence, after additional compression therapy using the same regimen: Group 1. 16/16 (100%); Group 2. 16/18 (89%) Number (%) with adverse events: Skin excoriation on front of ankle or just below knee: Group 1. 12/72 (17%); Group 2. not reported Slippage of device at knee, causing pressure/pain: Group 1. 34/72 (47%); Group 2. not reported Patients complaining of pain at start of treatment: Group 1. 8/72 (11%); Group 2. 19/66 (29%)	
Notes	Median participant ages per arm indicate relatively young patients in this trial. Withdrawals: Group 1. 3 patients (2 lost to follow up, 1 had a stroke); Group 2. 9 patients (1 died in road-traffic accident, 8 requested to change treatment groups). Patients were reviewed every 2 months during the one-year follow up period	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	“Randomization was computer generated”
Allocation concealment?	Unclear	No further details provided.
Incomplete outcome data addressed? All outcomes	No	Withdrawals: Group 1. 3 patients (2 lost to follow up, 1 had a stroke); Group 2. 9 patients (1 died in road-traffic accident, 8 requested to change treatment groups)
Blinded outcome assessment (healing)?	Unclear	No details given.
Baseline comparability?	No	Larger baseline median ulcer area and longer median duration of ulceration in Group 1

Moffatt 1999

Methods	RCT with allocation by sequential numbers on a randomisation list, stratified by study centre and baseline total ulcerated area on reference limb (\leq or >10 cm ²). The authors estimated that the study had 80% power that the 95% confidence interval for the between-group difference in healing rates would not exceed a difference of 15%, assuming: equally effective treatments; an overall healing rate of 80% difference in healing rates; and 5% significance level
Participants	<p>232 patients newly presenting to community leg ulcer services in UK were recruited (2 study centres).</p> <p>Inclusion criteria: patient aged at least 18; not pregnant; venous ulceration.</p> <p>Exclusion criteria: ABPI < 0.8; non-venous ulceration; patients who had entered the trial previously.</p> <p>Number of patients male/female: Group 1. 53/62; Group 2. 53/64.</p> <p>Mean\pmsd patient age in years: Group 1. 67.8\pm13.5; Group 2. 67.1\pm15.2.</p> <p>Median (range) baseline ulcer duration in weeks: Group 1. 8 (0 to 2080); Group 2. 7 (0 to 728).</p> <p>Proportion of patients with baseline ulcer area < 10 cm²: Group 1. 82%; Group 2. 84%.</p> <p>Proportion of patients able to walk freely: Group 1. 74%; Group 2. 79%.</p> <p>Proportions of patients with mobile/fixed limb: Group 1. 83%/17% Group 2. 92%/8%</p>
Interventions	<p>All patients received a low-adherent primary dressing (Tricotex). All bandages were changed at least weekly</p> <p>1. Original Charing Cross 4-layer bandage comprising wool, crepe, Elset and Coban. Constituents varied slightly according to ankle circumference (n=115).</p> <p>2. Profore 4-layer bandage comprising wool, crepe, Litepress and Co-Plus. Constituents varied slightly according to ankle circumference (n=117)</p> <p>Following healing, all patients were prescribed compression stockings and returned to regular follow-up clinics</p>
Outcomes	<p>Number (%) patients with complete healing at 12 weeks: Group 1. 69/115 (60.0%); Group 2. 84/117 (71.8%). Difference 11.8% (95% CI -0.3% to 23.9%)</p> <p>Number (%) patients with complete healing at 24 weeks: Group 1. 84/115 (73%); Group 2. 89/117 (76%). Difference 3.0% (95% CI -8.2% to 14.2%)</p> <p>Kaplan-Meier estimate of healing at 24 weeks: Group 1. 82%; Group 2. 84%</p> <p>HR for healing showed a non-significant trend in favour of Group 2: 1.18 (95% CI 0.87 to 1.59), P = 0.28 (stated as adjusted for baseline variables but unclear exactly which ones)</p> <p>Quality of life was assessed using Nottingham Health Profile at baseline, 12 & 24 weeks (scores zero to 100, with lower scores indicating better quality of life). Domains include: energy; bodily pain; emotional reactions; sleep; social isolation; and physical mobility. Mean differences in final scores calculated using ANOVA with adjustment for baseline scores. 208/232 (90%) patients completed at least one follow-up questionnaire (99 in Group 1 & 109 in Group 2). There were no statistically significant between-group differences for any domain</p>
Notes	<p>In patients with bilateral ulceration, the limb with the larger area of ulceration was studied</p> <p>Number (%) withdrawals: Group 1. 18 (16%); Group 2. 17 (15%)</p> <p>Reasons for withdrawal: Group 1. non-attendance for treatment 9; bandage discomfort</p>

	<p>6; change in treatment by other clinician 1; adverse event 2 (exacerbation of arthritis 1; below-knee skin irritation 1)</p> <p>Group 2. non-attendance for treatment 3; bandage discomfort 9; change in treatment by other clinician 2; death 1; adverse event 2 (profuse bleeding from ulcer 1; pressure damage 1)</p> <p>Adverse events: Group 1. 14 adverse events in total (infection 4, skin irritation 4, excess exudate 2, new ulcer 1, skin irritation & pain 1, other 2); Group 2. 13 adverse events in total (infection 2, skin irritation 3, pain 1, skin irritation & pain 2, skin irritation & new ulcer 1, infection & pain 1, other 3)</p> <p>Methods of wound measurement / assessment not stated.</p>
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Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"Randomisation took place... by means of sequential numbers on a randomisation list which was stratified for ulcer size..."
Allocation concealment?	Unclear	No further details provided.
Incomplete outcome data addressed? All outcomes	Yes	233 people were recruited; 232 had at least one follow up visit; 18 people from Group 1 and 17 from Group 2 withdrew. Analysis by intention to treat
Blinded outcome assessment (healing)?	Unclear	No detail given.
Baseline comparability?	Unclear	Median baseline ulcer duration slightly longer in Group 1.

Moffatt 2003a

Methods	<p>RCT (multicentre), with computer-generated randomisation schedules provided to study centres as sequential number lists . Randomisation stratified by study centre and baseline ulcer area (\leq or >10 cm²). Sample size: the original target of 120 patients was not recruited. It was estimated that 54 patients per arm provided 74% power to detect 25% difference in healing rates at 5% significance level</p>
Participants	<p>112 patients newly presenting to community leg ulcer clinics were recruited from 5 UK study centres.</p> <p>109 patients comprised the intention-to-treat population (defined as those attending ≥ 1 follow-up visit).</p> <p>Inclusion criteria: signs and symptoms of chronic venous ulceration; ABPI ≥ 0.8; patient age ≥ 18 years; ankle circumference > 18 cm; baseline ulcer duration ≥ 2 weeks.</p> <p>Exclusion criteria: pregnancy; causes of ulceration other than venous disease; active cellulitis treated with systemic antibiotics; previously entered trial.</p> <p>Number of patients male/female: Group 1. 24/33; Group 2. 23/29.</p>

	<p>Mean±sd patient age in years: Group 1. 70.2±14.4; Group 2. 71.8±11.3.</p> <p>Number of patients with baseline ulcer area ≤10 cm²/ >10 cm²: Group 1. 48/9; Group 2. 45/7.</p> <p>Median (range) baseline ulcer duration in weeks: Group 1. 6 (2 to 104); Group 2. 6 (2 to 1040).</p> <p>Number (%) patients with previous ulceration: Group 1. 24/57 (42%); Group 2. 24/52 (46%).</p> <p>Number (%) patients with history of deep vein thrombosis: Group 1. 4/57 (7%); Group 2. 4/52 (8%).</p> <p>Number (%) patients with diabetes: Group 1. 1/57 (2%); Group 2. 4/52 (8%).</p> <p>Number (%) patients with rheumatoid arthritis: Group 1. 5/57 (9%); Group 2. 3/52 (6%).</p> <p>Number of patients walking with aid / walking freely: Group 1. 17/40; Group 2. 7/45.</p> <p>Number of patients with limb fully mobile / limited / fixed: Group 1. 45/12/0; Group 2. 43/7/2.</p> <p>Number of patients using drugs that could affect healing: Group 1. 1 (steroids); Group 2. 0</p>
Interventions	<p>All patients: the study limb was washed using emollient dissolved in tap water, the wound was debrided and a simple hypoallergenic hydrating cream applied to the surrounding skin. A simple non-adherent dressing was applied to the ulcer, followed by the randomised bandage system. Dressings and bandages were changed at least weekly</p> <p>Group 1. Four-layer bandage (Profore) (n=57)</p> <p>Group 2. Two-layer bandage (Surepress) (n=52)</p> <p>All bandages were applied according to manufacturers' instructions</p> <p>Patients who withdrew from randomised treatment were allocated to an alternative treatment and continued to be followed up for 24 weeks. After healing, patients were prescribed compression stocking and returned to usual follow-up clinics</p>
Outcomes	<p>Number (%) patients with complete healing at 12 weeks: Group 1. 40/57 (70%); Group 2. 30/52 (58%). The trial authors reported the following measure of effect for this outcome: odds ratio 4.23 (95% CI 1.29 to 13.86), P = 0.02. Correspondence with trial authors confirmed that this estimate was adjusted for the following baseline variables: sex, ulcer area, ulcer duration, ankle circumference, whether patient taking medication, previous ulceration and limb ABPI</p> <p>*Number (%) patients with complete healing when randomised treatment discontinued: Group 1. 47/57 (82%); Group 2. 24/52 (46%). Difference 36% (95% CI 18% to 55%), P < 0.001</p> <p>*Number (%) patients with complete healing at the end of the study period, including withdrawals from randomised treatment, some of whom switched treatment groups: Group 1. 50/57 (88%); Group 2. 40/52 (77%) (P value not reported)</p> <p>Cox regression: HR for time to healing over 24 weeks 1.18 (95% CI 0.69 to 2.02), P = 0.55 (Correspondence with trial authors confirmed that this estimate was adjusted for the following baseline variables: sex, ulcer area, ulcer duration, ankle circumference, whether patient taking medication, previous ulceration and limb ABPI)</p> <p>Number of adverse events: Group 1. 7 patients, 8 adverse events; Group 2. 19 patients, 21 adverse events. Number of adverse events described as severe: Group 1. 2; Group 2. 2</p> <p>Frequency & description of device-related adverse events: Group 1. 6 patients with 7</p>

	<p>events (irritation 2, pain/discomfort 1, slippage 1, tissue breakdown 1, excessive pressure 2); Group 2. 17 patients with 27 events (irritation 4, pain/discomfort 7, slippage 9, tissue breakdown 3, excessive pressure 4)</p> <p>Number (%) of withdrawals: Group 1. 7/57 (12%); Group 2. 28/52 (54%)</p> <p>Mean days to withdrawal: Group 1. 32; Group 2. 21</p> <p>Number (%) withdrawals with complete healing: Group 1. 3/7 (43%); Group 2. 16/28 (57%) (P value not reported but stated between-group difference not statistically significant)</p> <p>Mean number of dressing changes per week: Group 1. 1.1; Group 2. 1.5 (P = 0.0002)</p> <p>Mean weekly cost of treatment per patient (based on clinic costs including dressings & other materials, home care costs including nurse time, dressings & other materials, taking into account frequency of dressing changes per week, price year 2000 using average NHS costs): Group 1. £79.91; Group 2. £83.56</p> <p>Mean cost per patient over 24 weeks (based on estimated mean cost per week and assuming 82.5% rate of wound closure at 24 weeks for both groups, and mean time to healing of 8.2 weeks for both groups): Group 1. £876; Group 2. £916</p> <p>Assessment of health-related quality of life (information taken from conference abstract) : patients completed SF-36 at baseline, 24 weeks and at healing / withdrawal. Analysis adjusted for baseline scores; number of patients included in analysis not stated. There were no significant differences between the two bandage systems</p>	
Notes	<p>Patients with bilateral ulceration were randomised to one treatment only. The limb with the largest total area of ulceration was studied. Healing was defined as full epithelialisation</p> <p>Possible imbalance of baseline ulcer duration (range larger in Group 2, median similar for both groups)</p> <p>*Details of analyses of complete healing were confirmed through correspondence with the author</p> <p>The authors surmised that the lower costs in Group 1 were explained by less frequent dressing changes when compared with Group 2</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	“Randomisation took place ... by means of sequential numbers on a randomisation list that was stratified for ulcer size...”
Allocation concealment?	No	Author communication: “There appears to be no allocation concealment. I certainly can’t find evidence that randomisation envelopes were used”
Incomplete outcome data addressed? All outcomes	Yes	112 people were recruited; analysis by intention to treat (“...meant that patients remained in their original randomised groups irrespective of subsequent treatments applied...”), however only 109 people analysed

Moffatt 2003a (Continued)

Blinded outcome assessment (healing)?	Unclear	No detail provided.
Baseline comparability?	Unclear	Median ulcer duration similar across groups although maximum value greater in group receiving two-component compression. Impossible to judge for ulcer area as neither mean nor median supplied

Moody 1999

Methods	RCT (method of allocation not stated beyond 'randomised'). Study was conducted in the UK, other details of setting not reported
Participants	<p>52 patients were recruited</p> <p>Inclusion criteria: patient age ≥ 18 years; mobile; venous leg ulcer >2 cm at its widest perpendicular diameter; ABPI ≥ 0.8.</p> <p>Number of patients male/female: Group 1. 7/19 Group 2. 7/19</p> <p>Average (range) patient age in years: Group 1. 73 (51 to 85); Group 2. 70 (45 to 88)</p> <p>Mean baseline ulcer duration in months: Group 1. 55; Group 2. 46 (no variance data presented)</p>
Interventions	<p>Where possible, patients had study limb immersed in warm water with added emollient, then dried. The ulcer was irrigated with a saline spray and a primary dressing applied (Solvaline N for wounds with little exudate and Silicone NA Ultra for moderate to high levels of exudate). Dressings and bandages were changed according to need, taking in to account exudate, bandage slippage and patient preference. Dressings/bandages were re-applied either at the clinic or at the patient's home</p> <p>1. Undercast padding (Cellona) plus short-stretch compression bandage (Rosidal K) (n=26)</p> <p>2. Undercast padding (SurePress padding) plus long-stretch compression bandage (Sure-Press bandage) (n=26)</p> <p>Both bandages were applied using a simple spiral technique.</p>
Outcomes	<p>Outcomes were assessed at 12 weeks. Patients were seen weekly by a research nurse. Wounds were photographed at regular intervals</p> <p>Number (%) patients with complete healing at 12 weeks: Group 1. 8/26 (31%) Group 2. 8/26 (31%)</p> <p>Average (presumably mean, but not stated) weeks to healing: Group 1. 9.91 Group 2. 9.3 (no variance data presented)</p> <p>Average (presumably mean, but not stated) percentage reduction in ulcer area at 12 weeks (measured by a single assessor using computerised analysis of weight of cut-out acetate tracing of wound perimeter): Group 1. 73% Group 2. 52% (no variance data presented)</p> <p>Number (%) patients with increase in ulcer size during study: Group 1. 4/26 (15%) Group 2. 6/26 (23%)</p> <p>Number (%) patients with clinical infection developing during study period: Group 1. 3/26 (12%); Group 2. 4/26 (15%)</p>

Moody 1999 (Continued)

Notes	<p>One ulcer per patient was included in the study.</p> <p>Changes in sub-bandage pressure were undertaken over a 7 days period, evaluated with an Oxford pressure monitor. These measurements appear to have been performed on healthy volunteers</p> <p>Training in application of both types of bandages was offered to study care providers. Bandages were applied according to manufacturers' instructions. The authors reported that, by the end of the study, around 7 patients per group (or their relatives) could correctly apply the bandages</p> <p>1 patient had an acute eczema episode during the study and 1 had a chest infection (group allocation not stated)</p> <p>3 patients in Group 1 experienced initial bandage slippage due to reduction of limb oedema, necessitating re-application of the bandage within 6 hours. 1 patient was withdrawn because of difficulties in performing adequately frequent bandage re-application</p> <p>No information was provided on baseline ulcer area. Patients in Group 1 had ulcers of longer baseline duration, on average</p> <p>Few details were provided on data analysis methods.</p> <p>Changes in limb oedema were reported in the paper.</p> <p>Unable to gain further information from trial author.</p>
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Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details provided beyond describing the trial as "randomized"
Allocation concealment?	Unclear	No details provided.
Incomplete outcome data addressed? All outcomes	Unclear	Report states the number of people healed in each group but not clear what denominator was at end of follow up
Blinded outcome assessment (healing)?	Unclear	No details provided.
Baseline comparability?	Unclear	Little information. Mean ulcer duration appears longer in Group 1 but no variance data presented nor data on other variables

Morrell 1998

Methods	<p>RCT (multicentre, pragmatic). Patients were allocated to treatment groups according to a random assignment schedule prepared in advance of recruitment. Randomisation was separate for each study site. Outcome assessment was non-blind. Sample size: the authors estimated that 206 patients were required to provide 80% power to detect an increase in healing from 50% to 70%, at 5% significance level</p>
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Participants	<p>233 patients were recruited from 8 community based research clinics in four health trusts in Trent, UK.</p> <p>Inclusion criteria: venous leg ulcer of at least 3 months duration at study entry; ability to travel to clinic.</p> <p>Exclusion criteria: ABPI < 0.8.</p> <p>Number of patients male/female: Group 1. 43/77; Group 2. 35/78</p> <p>Mean±sd patient age in years: Group 1. 73.8±10.9; Group 2. 73.2±11.6</p> <p>Mean±sd baseline ulcer surface area in cm²: Group 1. 16.2±28.9; Group 2. 16.9±40.8</p> <p>Mean±sd baseline ulcer duration in months: Group 1. 27.5±53.8; Group 2. 29.7±82.3</p> <p>Mean± sd body mass index (kg/m²): Group 1. 27.0±6.7; Group 2. 27.1±6.0</p> <p>Number (%) patients requiring aid with walking: Group 1. 66/120 (55%); Group 2. 57/113 (50%)</p> <p>Number (%) patients with history of deep vein thrombosis: Group 1. 28/120 (23%); Group 2. 25/113 (22%)</p> <p>Number (%) patients with diabetes mellitus: Group 1. 8/120 (7%); Group 2. 10/113 (9%)</p> <p>Patients were assessed for health status at baseline using SF-36, EuroQol, the McGill short form pain questionnaire and the Frenchay activities index. Groups were comparable at baseline for all domains</p>
Interventions	<p>Group 1. Weekly treatment with four-layer bandage in a leg ulcer clinic. The Charing Cross technique was used comprising non-adherent primary dressing, absorbent orthopaedic wadding, crepe bandage, elastic compression bandage, cohesive compression bandage. Clinic co-ordinators all completed a course on leg ulcer management (ENB N18) as well as additional training in applying four-layer bandages. Each clinic employed support nurses trained in the application of four-layer compression bandages. After healing, patients received class II compression stockings and were reviewed at the clinic every 3 months. Transport was provided free of charge to patients (n=120)</p> <p>Group 2. Usual care at home by district nursing service. Frequency of visits varied and could be several per week. A variety of wound cleansers, primary dressings, topical agents, securing agents and bandages were used. The bandages included compression, tubigrip and light support bandages, all of which could be used alone or with other devices. Access to four-layer bandages was minimal (n=113)</p>
Outcomes	<p>Number (%) patients with complete healing at 12 months: Group 1. 78/120 (65%); Group 2. 62/113 (55%)</p> <p>Kaplan-Meier estimates of cumulative % healed at 12 weeks: Group 1. 34%; Group 2. 24% (difference 10%, 95% CI -2% to 22%)</p> <p>Kaplan-Meier estimate of median weeks to healing within 12 month follow-up period: Group 1. 20; Group 2. 43 (P = 0.03, log rank test)</p> <p>Cox regression: following adjustment for prognostic factors (patient age, baseline ulcer area, baseline ulcer duration, history of deep vein thrombosis) the estimated hazard ratio was 1.65 (95% CI 1.15 to 2.35, P value not reported) (in favour of Group 1)</p> <p>Number (%) patients with recurrence following initial healing during trial: Group 1. 27/78 (35%); Group 2. 14/62 (23%)</p> <p>The between-group difference in time to recurrence was not statistically significant (P = 0.38, log rank test)</p> <p>Mean ulcer-free weeks during 12 month follow-up: Group 1. 20.1; Group 2. 14.2 (difference 5.9, 95% CI 1.2 to 10.5)</p>

	No significant differences were found between the groups in change in health status Mean±sd total NHS costs per patient per year (baseline analysis, £ sterling, price year 1995): Group 1. £877.60±674.30; Group 2. £863.09±865.32 (P = 0.90). The baseline analysis was based on cost of treatment (staff time, materials, transport, overheads) and cost of other health services (GP and hospital). Sensitivity analyses assessed effects of changing treatment costs and overheads in Group 2, and changes in clinic attendance costs in Group 1. The authors reported that changes in assumptions did not significantly alter the magnitude of estimated costs (central estimates shown, no data on variance or statistical tests of between-group differences)	
Notes	Withdrawals: Group 1. 17 (died 9, moved away 2, hospital admission 3, dropped out with no further information available 3); Group 2. 23 (died 7, referred elsewhere 3, moved away 6, hospital admission 3, nursing home admission 3, dropped out with no further information available 1) Complete healing was defined as re-epithelialisation of all the patient’s areas of ulceration. Wound surface area was measured every 4 weeks using tracing from photographs combined with computerised planimetry. Fine indelible pens were used to obtain tracings. Assessors were trained in an attempt to standardise measurement techniques and minimise inter-rater error	
<i>Risk of bias</i>		
Item	Authors’ judgement	Description
Adequate sequence generation?	Yes	“A random assignment schedule and serially numbered, sealed, opaque allocation envelopes were prepared in advance for each of the 8 clinic sites.”
Allocation concealment?	Yes	“Serially numbered, sealed opaque allocation envelopes were prepared in advance for each of the 8 study sites”
Incomplete outcome data addressed? All outcomes	Yes	“All the data analysis was by intention to treat”. Survival analysis
Blinded outcome assessment (healing)?	No	“The nurse recorded the date of healing, defined as the data of epithelialisation of all ulcers...”
Baseline comparability?	Unclear	Only means presented; these appear similar but data likely to be highly skewed

Methods	RCT with 2X2X2 factorial design evaluating: drugs - pentoxifylline versus placebo; dressings - knitted viscose versus hydrocolloid; and compression bandages - four-layer versus single-layer. Randomisation was stratified by study centre and ulcer type (simple venous / non-simple) using permuted blocks of 8. Outcome assessment was non-blind. Sample size: assuming 40% healing rate at 24 weeks using 4-layer bandage or knitted viscose dressing, it was estimated that 200 patients would provide 80% power to detect 20% difference in healing rates at 24 weeks at 5% significance level (2 tailed)
Participants	<p>245 patients with venous leg ulcers treated in the community or as outpatients from 2 centres in Falkirk and Edinburgh (UK) were recruited. All study centres had widespread use of high compression prior to the trial.</p> <p>Inclusion criteria: patient age > 18 years; clinical signs of venous disease; venous disease confirmed with hand-held Doppler; venous leg ulcer \geq 1 cm length and \geq 8 weeks duration.</p> <p>Exclusion criteria: severe concurrent disease; life expectancy <6 months; immunosuppressed; immobile; ABPI < 0.8; diabetes mellitus; taking warfarin, steroids, oxpentifylline, oxerutins or naftidrofuryl; infected or gangrenous ulcers; females who were pregnant, lactating or premenopausal not using contraception; sensitivity to methulxanthines or caffeine.</p> <p>Number of patients male / female: Group 1. 39/89; Group 2. 41/76</p> <p>Mean\pmsd, median (range) patient age in years: Group 1. 71.5\pm10.3, 73 (46 to 93); Group 2. 68.3\pm12.2, 68 (34 to 91)</p> <p>Mean\pmsd, median (range) baseline ulcer area in mm²: Group 1. 1025\pm2637, 385 (54 to 26,311); Group 2. 661\pm879, 393 (50 to 5560)</p> <p>Mean\pmsd, median (range) baseline ulcer duration in months: Group 1. 11.1\pm17.3, 5.0 (2 to 96); Group 2. 15.1\pm35.2, 5.0 (2 to 240)</p> <p>Number (%) patients walking without aid: Group 1. 49/128 (38%); Group 2. 36/117 (31%)</p> <p>Number (%) patients with simple / non-simple venous disease (non-simple defined as seropositive rheumatoid arthritis or venous pathology not confirmed with hand-held Doppler): Group 1. 103 (80%) / 25 (20%); Group 2. 97 (83%) / 20 (17%)</p> <p>Number (%) patients randomised to pentoxifylline / placebo: Group 1. 64/128 (50%) / 64/128 (50%); Group 2. 57/117 (49%) / 60/117 (51%)</p> <p>Number (%) patients randomised to knitted viscose dressing / hydrocolloid dressing: Group 1. 62/128 (48%) / 66/128 (52%); Group 2. 65/117 (56%) / 52/117 (44%)</p>
Interventions	<p>All patients had ulcers cleansed with tap water and surrounding skin moisturised with arachis or olive oil. Dressings & bandages were renewed at least weekly</p> <p>Group 1. Single layer bandage (hydrocolloid-lined, woven, elastomeric, adhesive bandage applied in a figure-of-8 technique from toe to knee) (n=128).</p> <p>Group 2. Four-layer bandage (Charing Cross technique comprising wool, crepe, Elset, Coban) (n=117)</p> <p>Also randomised comparison of dressings (knitted viscose dressing or hydrocolloid) and drug treatment (oxpentifylline versus placebo)</p>
Outcomes	<p>Analyses based on 245 patients with both simple and non-simple venous ulceration:</p> <p>Number (%) patients with complete healing at 24 weeks: Group 1. 63/128 (49%); Group 2. 78/117 (67%), P = 0.009</p> <p>Median days to healing (Kaplan-Meier estimate): Group 1. 168; Group 2. 78 (P value not reported)</p>

	<p>Cox proportional hazards models: an initial model including terms for drug, dressing and bandage and all possible interactions (but no terms for baseline characteristics) did not detect any statistically significant interaction between the different treatments ($P > 0.14$); a subsequent model adjusted for drug, dressing, bandage, study centre, ulcer aetiology (simple or non-simple), baseline ulcer area, baseline ulcer duration, and history of ulceration (years since first ulcer), HR 2.0 (95% CI 1.4 to 2.9), $P < 0.0005$, in favour of Group 2. The following were significant independent predictors drug ($P = 0.046$), baseline area ($P < 0.0005$), ulcer duration ($P = 0.017$) and ulcer history ($P = 0.01$)</p> <p>Withdrawals (bandages and dressings considered together): overall, 68/245 (28%) withdrew from original bandage or dressing or both. No.(%) patients changed bandage due to adverse event: Group 1. 36/128 (28%); Group 2. 17/117 (15%). Estimates from logistic regression indicated a statistically significant interaction between dressing and bandage in terms of predicting withdrawal ($P < 0.001$)</p> <p>Analyses based on 200 patients with simple venous ulceration:</p> <p>Number (%) patients with complete healing at 24 weeks: Group 1. 50/103 (49%); Group 2. 67/97 (69%)</p> <p>Quality of life assessment: patients underwent Nottingham Health Profile assessment at baseline and 24 weeks (scores zero to 100 with lower scores indicating better quality of life) . Domains: energy; pain; emotional reactions; sleep; social isolation; & physical mobility. Mean between-group differences in final scores were adjusted for baseline scores; analysis was by intention-to-treat. Patients in Group 2 (n=95 available) had significantly greater improvement (adjusted mean difference, 95% CI) in the following when compared with Group 1 (n=98 available): energy 7.9 (0.2 to 15.6), $P = 0.04$; and physical mobility 4.5 (0.0 to 9.0), $P = 0.046$. Mean differences for the other domains were not statistically significant between the 2 bandage groups</p> <p>Withdrawals: overall 65/200 (32.5%). Number (%) patients who withdrew first from bandage system with or without simultaneous withdrawal from the randomised drug and dressing treatment: Group 1. 21/103 (20%); Group 2. 5/97 (5%)</p>	
Notes	<p>Treatment delivered by experienced leg ulcer nurses for all patients.</p> <p>Healing was defined as complete epithelial cover in the absence of scab for all ulcers on study limb.</p> <p>Ulcer area was measured by transparency tracing and blind scanning</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details given.
Allocation concealment?	Yes	“Sealed, sequentially numbered opaque envelopes were used to allocate participants to placebo or pentoxifylline, knitted viscose or hydrocolloid dressings, and four-layer or adhesive single-layer bandages”
Incomplete outcome data addressed? All outcomes	Yes	“Primary analysis was by intention to treat”. Survival analysis

Blinded outcome assessment (healing)?	No	"Nurses completed a dressing log at each leg ulcer dressing visit which recorded whether or not an ulcer was healed."
Baseline comparability?	Yes	Medians provided for ulcer area and duration and these appear fairly well balanced plus analysis was adjusted (Cox regression)

O'Brien 2003

Methods	RCT (pragmatic). Randomisation was achieved by computer generated list. It was estimated a priori that the study had 80% power of detecting a 20% between-group difference in healing rates at 12 weeks, at 5% significance level. The authors also considered the sample size appropriate to detect differences in quality of life (but statistics for this not provided)
Participants	<p>200 patients were recruited from the community, Ireland. Sex male / female: Group 1. 35/65; Group 2. 33/67.</p> <p>Mean±sd patient age in years: Group 1. 71.7±9.8; Group 2. 71.4±11.5.</p> <p>Median (interquartile range) baseline ulcer area (cm²): Group 1. 3.5 (1.3 to 8.1); Group 2. 2.7 (1.6 to 6.2).</p> <p>Median (interquartile range) ulcer duration at baseline (weeks): Group 1. 9 (4 to 27); Group 2. 11 (5 to 28).</p> <p>Number of patients with history of DVT in affected leg: Group 1. 15/100 (15%); Group 2. 9/100 (9%).</p> <p>Number of patients with diabetes: Group 1. 3/100 (3%); Group 2. 5/100 (5%).</p> <p>Number of patients with rheumatoid arthritis: Group 1. 1/100 (1%); Group 2. 2/100 (2%).</p> <p>Baseline quality of life scores for CIVIQ & SF-36 reported in secondary paper; groups appeared to be comparable on most domains (Clarke-Moloney 2005).</p> <p>Inclusion criteria: venous leg ulceration identified clinically; ABPI > 0.9; not treated with 4-layer bandage.</p> <p>In patients with bilateral leg ulcers, the leg with the larger surface area of ulceration was included in the analysis</p>
Interventions	<p>All treatments were provided in a community setting.</p> <p>1. 4-layer bandage application was standardised and comprised: a sterile wound contact layer; a padding bandage; a light conformable bandage; a light compression bandage; and a flexible cohesive bandage. The combined system provided compression of 40 mmHg at the ankle (measurement method not explained). 12 patients were non-compliant due to intolerance of bandage. 11 patients had high absorbency dressings and 8 patients had desloughing agents (n=100)</p> <p>2. Usual care - treatment was not standardised but was determined by the public health nurse or GP. Treatment included an assortment of topical applications such as hydrocolloids, alginates, paraffin and iodine dressings. Various absorbency dressings, low-pressure bandages and elasticated support were also used. 1 patient had laser therapy; 5 patients had compression at some stage during the trial (n=100)</p>

Outcomes	<p>All patients were followed up for 12 weeks.</p> <p>Patients in Group1 were 1.8 (95% CI 1.2 to 2.9) times more likely to heal by 12 weeks than those in Group 2</p> <p>Proportions healed at 12 weeks (from Kaplan-Meier analysis): Group 1. 54%; Group 2. 34% (P < 0.001)</p> <p>Time to healing significantly better in Group 1 (P = 0.006, log rank test)</p> <p>Healing rates remained significantly different after controlling for age, baseline ulcer area, baseline ulcer duration, DVT, diabetes and rheumatoid arthritis in Cox regression (P = 0.015)</p> <p>The mean difference (95% CI) in reduction in ulcer size between the two groups was not significantly different: -1.1 (-2.9 to 0.7)</p> <p>Costs per leg healed were based on dressing use, nursing time (for dressings, administration & travel) and nurses' mileage expenses. Median (interquartile range) overall cost per leg healed in Euros (presume price year same as trial accrual period, i.e. 1999 - 2000) : Group 1. 209.7 (137.5 to 269.4); Group 2. 234.6 (168.2 to 345.1), P = 0.04</p> <p>Health related quality of life was assessed during treatment (at 6 weeks) in unhealed patients: Group 1. 79/85 (93%); Group 2. 91/95 (96%). Overall, Group 1 achieved better quality of life benefits compared with Group 2, particularly in the areas of physical activity and social functioning</p> <p>Disease specific instrument (CIVIQ - 20 items covering 4 domains: psychosocial, physical functioning, social functioning and pain; lower scores reflect better quality of life) . Between-group difference at 6 weeks was significant for physical functioning (P = 0.006), social functioning (P = 0.001) & global score (P = 0.006), all differences in favour of Group 1. Full statistics on scores in paper (Clarke-Moloney 2005)</p> <p>Generic instrument (SF-36 - 36 items covering 8 domains: physical functioning, role limitation due to physical health, bodily pain, general health, vitality, social functioning, role limitation due to emotional problems, and mental health; higher scores reflect better quality of life). Between-group difference at 6 weeks was significant for physical functioning (P = 0.001), role limitation - physical (P = 0.006) & mental health (P = 0.03), all differences in favour of Group 1. Full statistics on scores in paper (Clarke-Moloney 2005)</p>	
Notes	<p>The authors state that the ulcerated area was measured and photographed by a research officer but the wound measurement instrument was not described</p> <p>All leg ulcer dressings were done by the usual community nurse. Before the start of the study, all public health nurses in the region underwent formal training in the application of 4-layer bandaging; this was achieved by workshops and individual instruction</p> <p>Patient follow up during trial: Group 1. 1 died, 2 lost to follow up; 98 full or partial data gathered; Group 2. 0 died, 0 lost to follow up, 100 full or partial data gathered</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"A random intervention and control list was generated for 200 patients by computer..."

Allocation concealment?	Yes	"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"
Incomplete outcome data addressed? All outcomes	Yes	"Intention to treat analysis was carried out."
Blinded outcome assessment (healing)?	Unclear	"When complete healing occurred in the 12 week interval, a photograph of the site was taken to provide an objective review of outcome..." It is not clear if any assessment of photographs was masked
Baseline comparability?	No	Median ulcer area larger in Group 1.

Partsch 2001

Methods	RCT (multicentre) with stratification by study centre and total ulcerated area of study limb (\leq or $> 10 \text{ cm}^2$). Sample size: it was estimated that 112 patients would provide 77% power to detect a 25% difference in the proportion of patients healed at 16 weeks at 5% significance level (2 sided test)
Participants	<p>116 patients were recruited from 7 outpatient clinics (2 in Austria, 5 in Netherlands). Trial report based on 112 patients.</p> <p>Inclusion criteria: patient age > 18 years; new episode of venous leg ulceration; ulcer aetiology confirmed by Doppler or clinical history. Patients with infected ulcers were eligible if the trial interventions were considered appropriate.</p> <p>Exclusion criteria: ABPI < 0.8; ulcer of diabetic, rheumatoid or malignant aetiology.</p> <p>Number of patients male/female: Group 1. 20/33; Group 2. 22/37</p> <p>Median (range) patient age in years: Group 1. 68 (34 to 85); Group 2. 71 (32 to 87)</p> <p>Number (%) patients bed or chair bound / walking with aid / walking freely: Group 1. 1 (2%) / 3 (6%) / 49 (92%); Group 2. 2 (3%) / 4 (7%) / 53 (90%).</p> <p>Number (%) patients with history of hypertension / diabetes / DVT: Group 1. 13 (25%) / 1 (2%) / 14 (26%); Group 2. 12 (20%) / 4 (7%) / 12 (20%)</p> <p>Mean baseline ankle circumference in cm: Group 1. 23.4; Group 2. 23.3</p> <p>Median (range) baseline ulcer duration in weeks: Group 1. 5 (1 to 1040); Group 2. 4 (1 to 780)</p> <p>Median (range) baseline ulcer area cm^2: Group 1. 1.5 (0.4 to 72.7); Group 2. 1.9 (0.4 to 70.1)</p>
Interventions	All patients: ulcers were cleansed with water or saline and covered with a simple non-adherent dressing. Ulcers in the hollow behind the malleolus were additionally covered with a foam pad to increase local pressure. Bandaging took place weekly unless more frequent dressing changes were required (median interval between visits was 7 days for

	both groups). Patients were encouraged to walk as much as possible Group 1. Four-layer bandage (Profore) (n=53) Group 2. Short-stretch bandage comprising orthopaedic padding plus 2 short stretch bandages (Rosidal K) applied using the Putter technique (n=59)	
Outcomes	<p>Number (%) patients healed at 16 weeks: Group 1. 33/53 (62%); Group 2. 43/59 (73%) . Difference in proportion healed 11% (95% CI -28 to 7%)</p> <p>Kaplan-Meier estimates: cumulative proportions healed at 16 weeks Group 1. 78% Group 2. 85%; median (95% CI) days to healing Group 1. 57 (47 to 85) Group 2. 63 (43 to 70)</p> <p>Cox regression: an initial model containing terms for treatment and study centre showed a centre effect, with 4/7 centres having a higher healing rate than the other 3 (P = 0.003). When the models were re-fitted including terms for initial area & duration of ulcer, there was no evidence of a centre effect (P = 0.79). The final model included terms for treatment, study centre, baseline ulcer area, baseline ulcer duration and the SF-36 dimension 'mental health. HR 1.19 (95% CI 0.73 to 1.91), P = 0.49 (represents non-significant trend towards higher healing rate for Group 2)</p> <p>Withdrawals for patients not included in analysis, breakdown per group not reported: 3 patients had no post-treatment follow-up data; 1 patient had basal cell carcinoma</p> <p>Number of withdrawals during trial for patients included in analysis: Group 1. 12 (patient's request 7, lost to follow-up 3, adverse event 1, other 1); Group 2. 7 (patient's request 2, lost to follow-up 2, lack of response 1, adverse event 1, other 1). Further details of adverse events not reported</p>	
Notes	<p>Patients with bilateral ulceration were randomised to one treatment only, the study limb being the one with the largest area of total ulceration. Ulcers were measured using tracing and computerised planimetry</p> <p>The authors stated that whilst staff at all participating centres were trained in the application of four-layer bandaging prior to the study, they all had many years of experience of applying the short-stretch bandage</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"Randomisation was carried out separately for each centre and further stratified according to ..." ulcer area. No further detail given
Allocation concealment?	Unclear	"Randomisation was carried out separately for each centre and further stratified according to ..." ulcer area. The trial authors informed us that sealed envelopes were used
Incomplete outcome data addressed? All outcomes	Yes	116 people were recruited and 112 people were analysed. Of the 4 people excluded from the analysis, 3 did not provide any follow up data and one was recruited in

		error
Blinded outcome assessment (healing)?	No	Author correspondence.
Baseline comparability?	Yes	Median ulcer area and duration fairly well balanced. Analysis by Cox model

Polignano 2004a

Methods	RCT (multicentre), computerised randomisation list generated remotely, block randomisation used. The intended sample of 100 patients was not recruited because of changing practice in the study clinics and so the study was underpowered to detect between-group differences in healing outcomes
Participants	<p>68 patients (each with one wound) were recruited from 4 study centres in Italy. Both inpatients & outpatients recruited. All patients were ambulant.</p> <p>Number of patients male/female: Group 1. 16/23; Group 2. 10/19.</p> <p>Mean±sd, median (range) patient age in years: Group 1. 68.4±13.9, 72.0 (23.0 to 89.0); Group 2. 68.6±9.6, 69.0 (43.0 to 87.0).</p> <p>Mean±sd, median (range) baseline ulcer area (length x width) in cm²: Group 1. 10.1±11.4, 5.5 (0.8 to 52.5); Group 2. 9.3±12.8, 3.6 (0.3 to 47.5).</p> <p>Number (%) patients with baseline ulcer duration <7 days/ 7 days-1 month / 1-6 month / 6-12 months:</p> <p>Group 1. 3 (8%) /16 (41%) /5 (13%) /15 (38%); Group 2. 2 (7%) /16 (55%) /5 (17%) /6 (21%)</p> <p>Inclusion criteria: patient age ≥ 18 years; venous ulceration confirmed by Doppler.</p> <p>Exclusion criteria: pregnancy; ABPI < 0.8; rheumatoid vasculitis; diabetic foot ulceration; malignant ulceration; clinically infected ulcer; excessive exudate; ulcer area > 10 cm².</p>
Interventions	<p>Bandages were changed at least weekly in both groups.</p> <p>Group 1. Four-layer bandage (Profore) (n=39)</p> <p>Group 2. Unna's Boot comprising zinc oxide paste bandage (Viscopaste) plus elastic cohesive bandage (Tensoplast) (n=29)</p>
Outcomes	<p>Patients were followed up until healing or 24 weeks. Ulcer area was measured every 4 weeks</p> <p>Number (%) patients with complete healing at 24 weeks: Group 1. 29/39 (74%); Group 2. 19/29 (66%), P = 0.42. Estimate of difference between proportions healed 0.09 (95% CI -0.13 to 0.31)</p> <p>Estimate from Cox proportional hazards model including terms for bandage type, baseline ulcer area and baseline ulcer duration: HR 1.62 (95% CI 0.87 to 3.02), P = 0.13. Baseline ulcer area had a significant effect on healing with larger ulcers taking longer to heal (P = 0.01) but ulcer duration did not have a significant effect (P = 0.12)</p> <p>Kaplan-Meier estimate of median days to healing: Group 1. 53 (95% CI 35 to 84). Group 2. 56 (95% CI 49 to 84)</p> <p>Mean±sd, median (range) percentage reduction in ulcer area (estimated by ([Initial ulcer area - final area]/initial area) x 100) at 24 weeks: Group 1. 79.1±65.7, 100.0 (-283.3 to 100.0); Group 2. 24.6±165.5, 100.0 (-489.3 to 100.0), P = 0.30</p>

	Mean±sd, median (range) percentage reduction in ulcer area per day (estimated by dividing percentage reduction by number of days in trial): Group 1. 2.3±3.7, 1.9 (-13.5 to 14.3); Group 2. 0.0±6.3, 1.3 (-22.2 to 7.7), P value not reported The between-group difference for change in pain score from baseline to final assessment (assessed with visual analogue scale) was not significant (P = 0.32) Number (%) of patients experiencing no change in pain / decrease in pain / increase in pain: Group 1. (n=34) 12 (35%) / 21 (62%) / 1 (3%) Group 2. (n=24) 3 (13%) / 19 (79%) / 2 (8%)	
Notes	A nurse applied the bandages in accordance with manufacturers' instructions Withdrawals: 3 patients per group discontinued treatment due to an unassociated medical condition. One patient per group discontinued because of an adverse event (intolerance to treatment and pain) The numbers allocated to each group do not appear to be well balanced (57% in group 1). The trial author explained that this was because difficulties with recruitment (see methods, above) Components of Unna's Boot and details of randomisation / allocation concealment were confirmed by the trial authors	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Author provided clarification: "... the allocation was done by a remote computer. The list of randomisation the computer provided was sealed in an envelope and opened when a patient was recruited..."
Allocation concealment?	Yes	Author provided clarification: "... the allocation was done by a remote computer. The list of randomisation the computer provided was sealed in an envelope and opened when a patient was recruited..."
Incomplete outcome data addressed? All outcomes	Yes	Analysis for healing by intention to treat though others e.g., pain, only on a subset of participants. Difficult to judge completeness of continuous outcome data 68 people recruited and healing data reported on all 68.
Blinded outcome assessment (healing)?	Unclear	No details provided.
Baseline comparability?	No	Ulcers slightly larger in Group 1 at baseline; duration of ulcer data only presented categorically however appears that more people with longer duration ulcers in Group 1

Methods	RCT (multicentre) pilot study.
Participants	<p>56 patients with venous leg ulcers were recruited from 3 study centres in Italy</p> <p>Inclusion criteria: venous leg ulcer with surface area > 2cm² but < 10 cm in any dimension; ABPI > 0.8; ankle circumference 18 cm to 30.5 cm.</p> <p>Exclusion criteria: 'champagne-bottle' shaped legs; severe arthritis; history of poor concordance with therapy; hypersensitivity to any study material; immobility; systemic antibiotic use; infected or mixed aetiology ulcers; recent history of participants in other clinical investigations.</p> <p>Number of patients male/female: Group 1. 8/21 Group 2. 13/14</p> <p>Mean±sd (range) patient age in years: Group 1. 70.8±10.5 (42 to 89); Group 2. 67.3±13.6 (38 to 92).</p> <p>Mean±sd (range) body weight in kg: Group 1. 75.2±13.8 (55 to 120); Group 2. 78.3±15.9 (53 to 110).</p> <p>Mean±sd (range) height in cm: Group 1. 167±9 (155 to 190); Group 2. 168±11 (146 to 188).</p> <p>Mean±sd (range) ABPI: Group 1. 1.0±0.1 (0.80 to 1.10); Group 2. 1.0±0.1 (0.9 to 1.20).</p> <p>Number (%) patients with major clinical condition present: Group 1. 16/29 (55%); Group 2. 5/27 (19%)</p> <p>Number (%) patients with history of allergy: Group 1. 1/29 (3%); Group 2. 2/27 (7%)</p> <p>Number (%) patients with abnormalities present at clinical examination: Group 1. 9/29 (31%); Group 2. 3/27 (11%)</p> <p>Mean±sd (range) baseline ulcer surface area in cm²: Group 1. 9.7±9.4 (0.4 to 40.0); Group 2. 9.3±8.1 (0.49 to 30.8).</p> <p>Mean±sd (range) baseline maximum ulcer diameter in cm: Group 1. 4.6±2.9 (1.0 to 11.8); Group 2. 4.4±2.5 (1.2 to 12.5).</p> <p>Number (%) patients with baseline ulcer duration ≤ 6 months / > 6 months: Group 1. 10/29 (34%) / 19/29 (66%); Group 2. 11/27 (41%) / 16/27 (59%).</p> <p>Number (%) patients with baseline exudate level assessed as none / mild / moderate / heavy:</p> <p>Group 1. 7/29 (24%) / 12/29 (41%) / 9/29 (31%) / 1/29 (3%)</p> <p>Group 2. 8/27 (30%) / 9/27 (33%) / 7/27 (26%) / 3/27 (11%)</p>
Interventions	<p>Patients in both groups received wound cleansing as needed and application of gauze</p> <p>1. Short-stretch bandage (Comprilan) (n=29)</p> <p>2. SurePress Comfort (consists of 2 knee-high nylon & spandex stockings which are latex free; a medium compression overstocking and light compression understocking designed to provide a high compression system overall). Can be applied by the patient. (n=27)</p>
Outcomes	<p>The study duration was 12 weeks with assessments at baseline then 4-weekly thereafter. Wounds were measured at each visit using direct transparency tracing and photography</p> <p>Efficacy analysis was based on all 56 patients. Safety analysis was based on 53 patients (Group 1. 28, Group 2. 25), patients being excluded because they failed to attend the first interview</p> <p>Number (%) patients with complete healing during 12 week study period: Group 1. 5/29 (17%, 95% CI 4 to 45%); Group 2. 12/27 (44%, 95% CI 21 to 71%), P = 0.027</p> <p>Mean±sd (95% CI) days to healing: Group 1. 101±7 (87 to 114); Group 2. 72±5 (62 to 82), P = 0.027 (log rank test)</p>

	<p>Mean±sd (range) local ulcer pain intensity under compression assessed at the start of treatment using 100 mm visual analogue scale: Group 1. 29.5±34.0 (0.0 to 100.0); Group 2. 33.4±31.8 (0.0 to 100.0)</p> <p>Local ulcer pain decreased significantly more in Group 2 (70% decrease) versus Group 1 (less than 20% decrease) (P = 0.017, unpaired t-test)</p> <p>Number of patients with onset of new venous ulcers during the study period: Group 1. 2; Group 2. 3</p> <p>Comfort while wearing compression (assessed with 4-point verbal rating scale at weeks 2-4): Group 2 had superior comfort during entire study period compared with Group 1 (P = 0.038, full statistics not reported in paper)</p> <p>Self-rated patient concordance with using compression (assessed using questions rated on a 3-point scale at weeks 2-4): no significant difference between groups, most patients reported good concordance</p> <p>Percentage of patients reporting good concordance (range over assessment week period) : Group 1. 80.8% to 92.9%; Group 2. 92.3 to 100.0%</p>	
Notes	<p>Number (%) of patients withdrawing from study overall with numbers per reason (adverse event / inefficacy / consent withdrawn / lost to follow-up): Group 1. 11/29 (38%) 5 / 4 / 1 / 1; Group 2. 4/27 (15%) 0 / 1 / 1 / 2</p> <p>One adverse event in Group 1 was considered to be potentially related to compression therapy (bullous dermatitis)</p> <p>When patients withdrew from either group because of inefficacy, this was due to development of a new ulcer. In such cases, an alterative compression system was used</p> <p>The proportions of patients with a major clinical condition or abnormalities present at the baseline clinical examination were higher in Group 1. As no further details were provided about these variables, it is difficult to judge whether they could have influenced healing</p>	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	“This study was a multicentre (3) open label comparative randomized parallel group pilot trial”. No further detail given
Allocation concealment?	Unclear	No further details provided.
Incomplete outcome data addressed? All outcomes	Yes	“Data were analysed according to the intention to treat principle and included all patients recruited into the study. The last observation carried forward method was also used... Efficacy analysis was based on the ITT data set of 56 patients...3 patients (2 in the test group and 1 in the reference group) failed to report for the first interview so were excluded from the safety data set. The safety data set thus included 53 patients, 25 in the test group and 28 in the reference group.”

Blinded outcome assessment (healing)?	Unclear	No details provided. "Acetate tracings and photographs of the ulcer were taken at each visit to evaluate the proportion of the wound that was healing."
Baseline comparability?	Unclear	Mean ulcer area looks similar but no median data provided. Impossible to judge comparability of ulcer duration as only presented as categorical data

Rubin 1990

Methods	RCT (multicentre), outpatient setting, USA.
Participants	36 consecutive ambulatory patients with lower-extremity chronic venous stasis ulceration were recruited from hospital clinics. Exclusion criteria: history of non-compliance; ABPI < 0.8; history of risk factors such as collagen vascular disease, uncontrolled diabetes, ongoing dermatological disorders; and chronic corticosteroid therapy. Mean (range) baseline ulcer area in cm ² : Group 1. 76.0 (0.02 to 600.0); Group 2. 32.2 (6.0 to 270.0)
Interventions	All patients were instructed regarding the need for leg elevation, signs and symptoms of wound complications and the need for concordance with follow-up. All dressings were changed weekly or twice weekly by the hospital-based nursing staff, in accordance with prescription. All wounds were cleansed with 20% poloxamer 188 solution (Shur-Cleans) . Reapplication of the elastic bandage was performed as necessary between dressing changes, either at home or at the clinic Group 1. Unna's boot (gauze bandage impregnated with glycerin, zinc oxide and calamine lotion) plus elastic bandage applied from toes to knee (n=19 patients) Group 2. Polyurethane foam dressing (Synthaderm) plus elastic bandage applied from toes to knee (n=17 patients)
Outcomes	Number (%) of patients with complete healing at 12 months: Group 1. 18/19 (95%); Group 2. 7/17 (41%) (P < 0.005, Chi squared test) Mean healing rate in cm ² per day: Group 1. 0.5; Group 2. 0.07 (P = 0.004, Student's t test) Number (%) patient withdrawals from treatment during 12 month trial: Group 1. 0/19 (0%); Group 2. 9/17 (53%) (all Group 2 withdrawals were because of malodorous drainage resulting from autolytic debridement) 6 of the 9 patients who withdrew in Group 2 experienced enlargement of the ulcer during the trial
Notes	Wounds measured by the same investigator at each dressing change using tracing and planimetry (exact methods not specified) The elastic bandages used in all patients appear to have been used as a retaining wrap; comments in the discussion section suggest that these bandages did not provide compression

Risk of bias

Rubin 1990 (Continued)

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details provided. Merely describes the trial as "randomized"
Allocation concealment?	Yes	"Each patient was randomised by the study co-ordinator to either a polyurethane foam dressing or Unna's boot dressing treatment protocol. The study co-ordinator did not see the randomization card and was therefore blinded as to the treatment cohort"
Incomplete outcome data addressed? All outcomes	Unclear	All randomised patients contributed healing data however less clear for continuous outcomes whether all participants were included. Nine people classed as withdrawals in Group 2 whilst none in Group 1. It is somewhat unclear whether withdrawal meant withdrawal from trial treatment but trial outcomes were observed or merely that patients were withdrawn from follow up but included in the denominator as unhealed
Blinded outcome assessment (healing)?	Unclear	No details provided.
Baseline comparability?	No	Mean area only presented however mean area much larger in Group 1

Scriven 1998

Methods	RCT (block method with stratification by ulcer area $\leq 10\text{cm}^2$ / $>10\text{cm}^2$). Patients with bilateral ulceration had each limb randomised separately. Setting was leg ulcer clinic, UK
Participants	<p>53 ambulant patients with 64 ulcerated limbs were recruited from a venous ulcer assessment clinic.</p> <p>Inclusion criteria: active lower limb ulceration; venous aetiology defined as venous reflux > 0.5 seconds duration and ABPI > 0.8.</p> <p>Exclusion criteria: not stated.</p> <p>Number of patients male / female (breakdown per group not reported): 20 / 33</p> <p>Median (range) patient age in years: Group 1. 70 (45 to 91); Group 2. 73 (36 to 93)</p> <p>Median [mean] (range) baseline ulcer area in cm^2: Group 1. 13.3 [49.6] (2 to 378); Group 2. 8.3 [19.1] (2 to 104)</p> <p>Number (%) limbs with baseline ulcer area $> 10\text{cm}^2$: Group 1. 21/32 (66%); Group 2. 14/32 (44%)</p> <p>Median (range) baseline ulcer duration in months: Group 1. 13 (1 to 480); Group 2. 21 (3 to 360)</p>

Interventions	<p>Group 1. Four-layer bandage system comprising: orthopaedic wool (Velband); crepe bandage; elastic bandage (Elset); and elastic cohesive bandage (Coban). Bandages were replaced at each dressing change (n=32 limbs)</p> <p>Group 2. Short stretch system comprising: orthopaedic wool (Velband); short stretch bandage applied with 50% stretch and 50% overlap between turns (Rosidal K); and elastic cohesive bandage applied without stretch (Coban). Bandages were washed and reused and replaced after 20 washes (n=32 limbs)</p> <p>All patients: compression therapy was applied for 12 weeks. Bandage application was standardised and carried out by nursing staff who were trained and experienced in compression bandaging. The primary dressing was a simple non-adherent dressing covered with gauze. Bandages were changed once a week unless strike through of exudate. After withdrawal (either due to ulcer deterioration during the trial or failure to heal at 12 weeks), patients could opt to receive the alternative bandage. Post-healing, class II compression stockings were provided</p>	
Outcomes	<p>Kaplan-Meier estimate of limbs with complete healing at one year: Group 1. 55%; Group 2. 57% (P = 1.0, log rank test)</p> <p>Number of adverse events (description): Group 1. 1 (minor haemorrhagic blistering of toes distal to bandage); Group 2. 4 (2 pressure-induced iatrogenic ulceration, 2 maceration)</p> <p>Number (%) limbs withdrawn (reasons): Group 1. 1/32 (3%) (patient did not attend follow-up clinics); Group 2. 2/32 (6%) (1 died, 1 did not attend follow-up clinics)</p> <p>Unit cost and estimated cost of treatment over 6 months, based on costs of bandage systems only (£ sterling, price year not stated): Group 1. £15.10 and £392.60; Group 2. £7.10 and £184.56</p>	
Notes	<p>Ulcer area was measured every two weeks using transparency tracing and computerised planimetry. Ulcer healing was defined as full re-epithelialisation. Limb volume was assessed during the trial. Ankle sub-bandage pressure was assessed using the Oxford Pressure Monitor. Addition of the unstretched cohesive bandage to the short-stretch bandage system (Group 2) resulted in a pressure increase of 11.5 mmHg</p> <p>The trial authors' analysis was conducted on an intention-to-treat basis (the 3 withdrawals were included). Data from both study arms were merged and subject to Chi-squared analysis to examine association between healing and the following: baseline ulcer area > 10cm²; ulcer duration > 6 months; previous deep vein thrombosis; and presence of deep venous reflux. No statistically significant associations were detected</p> <p>The baseline ulcer area was larger in Group 1</p> <p>Limbs are not independent with respect to healing and this may have influenced the results</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Limb randomisation was achieved using sealed envelopes naming the type of bandage to be applied determined by a block randomisation method

Allocation concealment?	Yes	Limb randomisation was achieved using sealed envelopes naming the type of bandage to be applied determined by a block randomisation method
Incomplete outcome data addressed? All outcomes	Yes	"During the study period one patient died after two attendances and two patients repeatedly failed to attend... these two patients represented two ulcerated limbs randomised to 4 layer bandage one limb and short stretch bandage one limb. They were subsequently considered as treatment failures and are thus included in the analysis of results on an intention to treat basis."
Blinded outcome assessment (healing)?	No	No details in study report however trial authors confirmed that outcome assessment was not blinded
Baseline comparability?	No	Larger median ulcer area in Group 1 however median ulcer duration longer in Group 2

Taylor 1998

Methods	RCT with randomisation performed by minimization of prognostic factors (age, sex, body mass index, mobility, range of ankle movement, ulcer area, ulcer duration and living alone). Setting was community, Salford, UK
Participants	36 consecutive patients referred to UK leg ulcer clinic from GP Inclusion criteria: venous ulceration; ABPI > 0.8 Number of patients male/female: Group 1. 7/9; Group 2. 4/10 Median (range) patient age in years: Group 1. 73 (28 to 85); Group 2. 77 (60 to 84). Number of patients with full/limited mobility: Group 1. 10/6; Group 2. 7/7. Median (range) degrees of ankle movement: Group 1. 40 (20 to 65); Group 2. 40 (26 to 60). Median (range) baseline ulcer area in cm ² : Group 1. 5.4 (0.4 to 74.8); Group 2. 4.2 (0.6 to 76.0). Number of patients with ulcer duration < 6months / > 6months: Group 1. 7/9; Group 2. 9/5
Interventions	Group 1. Four-layer bandage based on Charing Cross system. Patients were treated by either a specialist nurse or a district nurse, both of whom were experienced in leg ulcer management and the application of compression bandages. Patients with painful or sloughy ulcers initially received hydrocolloid as the primary dressing (Granuflex or Comfeel) and had twice weekly dressing changes. Otherwise a non-adherent dressing was used and bandages were changed weekly either at the patient's home or at the community leg ulcer clinic (n=18 patients)

	<p>Group 2. Contined with usual treatment by GP and district nurse. Patients were treated 2 to 3 times weekly at their homes by their usual district nurse. A wide variety of preparations were used including different cleansing agents, dressings, topical applications, skin treatments and bandages (some of which could have provided compression). Application of high-compression bandaging was not permitted (n=18 patients)</p> <p>All patients: those who healed within the trial period received class II compression stocking and were followed up in the leg ulcer review clinics</p>	
Outcomes	<p>Number (%) of patients with complete healing at 12 weeks (assuming losses did not heal, calculated by review author):</p> <p>Group 1.12/18 (66.7%); Group 2. 3/18 (16.6%)</p> <p>Number (%) of patients with complete healing at 12 weeks (study completers, as reported in paper):</p> <p>Group 1. 12/16 (75%); Group 2. 3/14 (21%), P = 0.003 for difference between groups</p> <p>Median time to healing: Group 1. 55 days; Group 2. 84 days</p> <p>Comparison of healing distributions using the Lee-Desu statistic suggested that patients in Group 1 healed faster than those in Group 2 (overall comparison statistic 8.603, P = 0.0034)</p> <p>Number (%) patients who withdrew from trial (reasons): Group 1. 2/18 (11%) (1 died, 1 had scabies); Group 2. 4/18 (22%) (1 died, 1 healed before treatment, 1 treated with four-layer bandage, 1 developed cellulitis)</p> <p>Cost analyses took account of consumables, district nurse time (including travel) and mileage costs. Estimates are presented in £ sterling (price year not stated):</p> <p>Median (range) weekly treatment costs: Group 1. 17.26 (13.45 to 20.16); Group 2. 21.07 (8.71 - 42.47) (P = 0.042)</p> <p>Mean (95% CI) between-group difference in weekly treatment costs: 6.45 (1.22 to 11.68), P = 0.042</p> <p>Median (range) whole trial costs: Group 1. 116.87 (52.63 to 261.74); Group 2. 240.28 (74.65 to 588.05), P = 0.016</p> <p>Mean (95% CI) between-group difference in whole trial costs: 113.51 (29.71 to 197.31), P = 0.016</p>	
Notes	<p>In patients with multiple ulcers, the total ulcerated area was studied. Ulcer area was measured weekly using transparency tracing and computerised planimetry</p>	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	“Eighteen patients were randomly allocated to each treatment group using the method of minimisation of prognostic factors...”
Allocation concealment?	Yes	We have assumed that the minimisation programme resulted in allocation concealment

Taylor 1998 (Continued)

Incomplete outcome data addressed? All outcomes	No	Authors did not undertake an ITT analysis; 2 people withdrew from Group 1 and 4 from Group 2 including one person who was not included in the analysis because they received the Group 1 treatment
Blinded outcome assessment (healing)?	Unclear	"Weekly each patient had the perimeter of their ulcer traced onto an acetate and the area measured using a computerised planimeter..."
Baseline comparability?	No	Ulcers in Group 1 had larger baseline area and were also of longer duration

Travers 1992

Methods	RCT (details of methods not provided). Setting: leg ulcer clinic, Nottingham, UK
Participants	27 patients attending leg ulcer clinic were recruited. Inclusion criterion: venous ulcers (ABPI > 0.9) Exclusion criteria: not stated. Mean±sd patient age in years: Group 1. 54±3; Group 2. 59±4 Mean±sd baseline ulcer area in mm ² : Group 1. 3097±1818; Group 2. 2304±1221 Mean±sd baseline ulcer duration in months: Group 1. 23±7; Group 2. 35±13
Interventions	All patients: ulcers cleansed with sterile normal saline and hydrocolloid primary dressing applied. Bandages were changed 1-2 times per week Group 1. Single-component system consisting of elastic cohesive bandage (Panelast Acryl) applied from foot to below-knee with 50% overlap (n=15 patients) Group 2. Three-component system applied from foot to below-knee consisting of: zinc oxide and calamine paste bandage (Calaband); non-adhesive elastic bandage (Tensopress) applied with 50% overlap and 50% stretch; and elasticated tubular bandage (Tensogrip) (n=12 patients)
Outcomes	Mean±se % change relative to baseline ulcer area at 7 weeks (values taken from figure) : Group 1. -90±3; Group 2. -83±5 (authors report no statistically significant difference between groups using Student's t test but P value not shown) All patients completed the trial.
Notes	Ulcer area was measured weekly using transparency tracing and computerised planimetry. The variability statistics used in the trial report were not specified. They are presumed by the review author to be standard deviation for baseline variables and standard error (shown on figure) for the outcome Sub-bandage ankle pressure was measured with the patient in a supine position using the Oxford Pressure Monitor. Average pressure at the start of treatment: Group 1. 50 mmHg; Group 2. 44 mmHg (between-group difference reported as not significant by authors but P value not shown). Average pressure after one week of treatment: Group 1. 23 mmHg; Group 2. 35 mmHg (P < 0.01). This suggested better maintenance of

	compression by the three-component system The authors state that costs of the bandages were equivalent but no data were shown	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"...randomly allocated" - no further detail provided.
Allocation concealment?	Unclear	No further details provided.
Incomplete outcome data addressed? All outcomes	Yes	All 27 patients recruited "completed the trial".
Blinded outcome assessment (healing)?	Unclear	No detail provided.
Baseline comparability?	Unclear	Greater mean area at baseline in Group 1 and longer mean duration in Group 2 however mean data not useful as highly skewed

Ukat 2003

Methods	RCT (2 centres). Randomisation was simple and unstratified. Sample size: it was estimated that the study had 80% power to detect 25% difference in healing rates at 12 weeks, at 5% significance level
Participants	89 patients were recruited from 2 study centres in Germany, 1 inpatient and 1 outpatient. Inclusion criterion: venous leg ulceration. Exclusion criteria: ABPI < 0.8; rheumatoid vasculitis; ulceration of diabetic or malignant aetiology; use of corticosteroids; clinically infected ulcer; circumferential ulcer. Around 60% patients were female. Mean patient age in years: Group 1. 67; Group 2. 70 Mean body mass index (kg/m ²): Group 1. 27; Group 2. 28 Number (%) of ulcers with baseline duration > 6 months: Group 1. 23/44 (52%); Group 2. 25/45 (56%) Mean±sd, median (range) baseline ulcer area in cm ² : Group 1. 17.7±34.1, 6.5 (1.0 to 220.5); Group 2. 12.2±14.8, 6.6 (1.8 to 70.7)
Interventions	All patients: ulcers were cleaned with Ringer-Lactate Solution and covered with a polyurethane foam film dressing (Allevyn Hydrocellular) Group 1. Four-layer bandage (Profore), reapplied weekly or more often if required (n=44) Group 2. Short-stretch bandage comprising 2 bandages 10 cm wide. Bandages were reapplied daily by patient, family member or nurse (n=45) When healed, the patients were prescribed class II compression stockings and returned to the regular follow-up clinics

Outcomes	<p>Number (%) patients healed at 12 weeks: Group 1. 13/44 (30%); Group 2. 10/45 (22%)</p> <p>Kaplan-Meier estimate indicated that patients in Group 1 healed significantly faster compared with Group 2 (P = 0.03)</p> <p>Cox regression: hazard ratio 2.9 (95% CI 1.1 to 7.5) in favour of 4LB during the 12 week study period (with adjustment for bandage type, study centre, per-wound skin condition, baseline ulcer area, baseline ulcer duration, and including an interaction term for study centre and bandage type); no statistically significant interaction between treatment and study centre (P = 0.713); healing was significantly slower for wounds of longer baseline duration (P = 0.01) and those with peri-wound skin affected by oedema, dermatosclerosis or erythema (P = 0.03)</p> <p>Median (mean) reduction in ulcer area between baseline and 12 weeks: Group 1. 77% (58%); Group 2. 56% (46%)</p> <p>Number of patients rating bandage comfort as 'excellent' out of a total of 38 patients completing this assessment (numbers assessed per group not reported): Group 1. 15; Group 2. 4</p> <p>Comparison of costs was based on cost per bandage, cost of other disposables (e.g. primary dressings, wadding), and assumption of 30 minutes of nursing per bandage change at 14 Euros per hour</p> <p>Cost per patient (euros): Group 1. 587; Group 2. 1,345.</p> <p>Cost per ulcer healed (euros): Group 1. 1, 845; Group 2. 5, 502</p> <p>Number (%) withdrawals because of patient's request or loss to follow-up: Group 1. 7/44 (16%); Group 2. 7/45 (16%)</p> <p>Withdrawals due to adverse events: Group 1. 1 withdrawal because of heart and lung problems; Group 2. 1 withdrawal because of pain</p>	
Notes	<p>Patients with bilateral ulceration were randomised to receive one treatment only. The limb with the largest total area of ulceration was studied. Wound surface area was measured using tracing and computerised planimetry, and ulcers were photographed at every clinic visit</p>	
Risk of bias		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	"This was a prospective randomized controlled comparative study..."
Allocation concealment?	Yes	"Randomisation was performed by opening sealed envelopes containing information about the proposed treatment"
Incomplete outcome data addressed? All outcomes	Unclear	<p>"Patients were analysed according to the treatment received..."</p> <p>"Dropouts were included in the analysis..." (7 from each Group) however it is not clear <i>how</i> they were included (may have been last observation carried forward as the authors say "dropouts were included in the analy-</p>

		sis as they formed part of the full analysis patient population that is all patients who had a venous leg ulcer, an initial baseline assessment and at least one follow up assessment...)"
Blinded outcome assessment (healing)?	No	"The clinician took photographs of the ulcers at every follow up visit..." but no mention of assessment of photographs by anyone else
Baseline comparability?	Unclear	Median ulcer areas similar between groups; ulcer duration difficult to assess from information provided

Vowden 2000

Methods	RCT. Setting was vascular leg ulcer clinic, UK.
Participants	<p>149 patients were recruited</p> <p>Inclusion criteria: venous leg ulceration; ankle circumference < 25 cm; ABPI \geq 0.8.</p> <p>Number of male/female patients: Group 1. 29/21; Group 2. 27/23; Group 3. 23/26</p> <p>Mean (range) patient age in years: Group 1. 66.4 (39 to 88); Group 2. 67.1 (24 to 88); Group 3. 68.9 (29 to 86)</p> <p>Mean (range) baseline ulcer area in cm²: Group 1. 4.9 (0.5 to 16.5); Group 2. 6.76 (0.5 to 51); Group 3. 5.8 (1 to 28)</p> <p>Mean (range) baseline ulcer duration in weeks: Group 1. 142 (1 to 1040); Group 2. 177 (1 to 2500); Group 3. 112 (1 to 1400)</p> <p>Number (%) patients with recurrent ulceration at baseline: Group 1. 35/50 (70%); Group 2. 33/50 (66%); Group 3. 33/49 (67%)</p> <p>Number (%) patients with good / moderate / poor baseline ankle mobility:</p> <p>Group 1. 22/50 (44%) / 16/50 (32%) / 12/50 (24%)</p> <p>Group 2. 15/50 (30%) / 18/50 (36%) / 17/50 (34%)</p> <p>Group 3. 20/49 (41%) / 16/49 (33%) / 13/49 (27%)</p> <p>Number (%) patients with good / moderate / poor baseline general mobility:</p> <p>Group 1. 24/50 (48%) / 17/50 (34%) / 9/50 (18%)</p> <p>Group 2. 19/50 (38%) / 20/50 (40%) / 11/50 (22%)</p> <p>Group 3. 19/49 (39%) / 15/49 (31%) / 15/49 (31%)</p> <p>Number (%) patients with history of deep vein thrombosis: Group 1. 20/50 (40%); Group 2. 20/50 (40%); Group 3. 7/49 (14%)</p> <p>Number (%) patients with popliteal reflux time > 0 \leq 1.5 seconds / > 1.5 seconds assessed by duplex ultrasound:</p> <p>Group 1. 10/42 (24%) / 13/42 (31%)</p> <p>Group 2. 11/44 (25%) / 8/44 (18%)</p> <p>Group 3. 10/37 (27%) / 16/37 (43%)</p>
Interventions	<p>All patients received disease-specific information and education (no further details on this) and all received treatment on a weekly basis</p> <p>1. Original Charing Cross four-layer bandage system consisting of orthopaedic wool</p>

	<p>(Soffban, Smith & Nephew), crepe bandage (Smith & Nephew), elastic bandage (Elset, Seton Scholl) and elastic cohesive bandage (Coban, 3M) (n=50)</p> <p>2. Modified Charing Cross four-layer bandage system consisting of orthopaedic wool (Soffban, Smith & Nephew), elastic bandage (K-Lite, Parema), elastic bandage (K-Plus, Parema) and adhesive elastic bandage (Coban, Smith & Nephew) (n=50)</p> <p>3. A four-layer bandage kit (Robinson Ultra Four) consisting of wound dressing, Sohfast, K-Lite, K-plus and Cohfast (n=49)</p> <p>At the end of the 20-week study period, patients who had healed received compression hosiery and those who had withdrawn or remained unhealed were treated with the original Charing Cross system</p>	
Outcomes	<p>Patients with complete healing at 12 weeks: Group 1. 60%; Group 2. 76%; Group 3. 60% (Chi squared analysis for comparison between the 3 groups, P = 0.16)</p> <p>Patients with complete healing at 20 weeks: Group 1. 87%; Group 2. 84%; Group 3. 83% (Chi squared analysis for comparison between the 3 groups, P = 0.56)</p>	
Notes	<p>Estimated cost per bandage system (presume price year 1999-2000): Group 1. £5.82; Group 2. £4.10; Group 3. £5.83</p> <p>There was baseline imbalance for ulcer duration, ulcer area, history of deep vein thrombosis & popliteal reflux</p> <p>Few details were provided about wound measurement except to say that ulcers were photographed and mapped</p> <p>3 patients withdrew because of non-compliance (breakdown per group not reported)</p> <p>5 patients were withdrawn because of medical reasons: falling ABPI, skin malignancy on another leg site, medical admission for respiratory disease, cellulitis & death unrelated to treatment (breakdown per group not reported)</p> <p>Number of patients withdrawn because of potential bandage-related complications, namely persistent skin reddening and discomfort / superficial skin damage: Group 1. 0/0; Group 2. 2/1; Group 3. 1/1. These 5 patients continued with compression bandaging after withdrawal, using an extra padded Charing Cross system and all healed within 4 weeks of withdrawal</p> <p>Assessment of patients’ opinion of the bandages assessed by direct questioning during the weekly bandage changes, indicated that participants were equally tolerant of all 3 compression systems</p> <p>Assessment of staff preference before, during and after the study showed an initial greater preference for the original Charing Cross system, but there was no bandage preference by the end of the 20-week study. This assessment was based on consideration of handling, ease of application, bandage performance over the preceding 7 days & ease of removal</p> <p>In the concluding comments, the authors mentioned that care had been provided by expert bandagers</p>	
<i>Risk of bias</i>		
Item	Authors’ judgement	Description
Adequate sequence generation?	Unclear	No details provided; merely described as a “randomized, controlled study”

Vowden 2000 (Continued)

Allocation concealment?	Yes	Information from trial author: "randomisation was by sealed envelopes"
Incomplete outcome data addressed? All outcomes	No	<p>149 people recruited however outcomes not presented with denominators so impossible to judge extent of follow up</p> <p>3 patients withdrew because of non-compliance (breakdown per group not reported)</p> <p>5 patients were withdrawn because of medical reasons: falling ABPI, skin malignancy on another leg site, medical admission for respiratory disease, cellulitis & death unrelated to treatment (breakdown per group not reported)</p> <p>Number of patients withdrawn because of potential bandage-related complications, namely persistent skin reddening and discomfort / superficial skin damage: Group 1. 0/0; Group 2. 2/1; Group 3. 1/1. These 5 patients continued with compression bandaging after withdrawal, using an extra padded Charing Cross system and all healed within 4 weeks of withdrawal</p> <p>Contact with the trial authors confirmed that the analysis had been conducted on a per protocol basis; information on denominators not available</p>
Blinded outcome assessment (healing)?	Unclear	No details provided.
Baseline comparability?	No	Smaller mean ulcer area in Group 1; shorter mean duration in Group 3

Wilkinson 1997

Methods	RCT (limbs were allocated to study groups using a remote randomisation service with numbers generated by random number tables, using blocks of four and stratification according to baseline ulcer area: $< 9.9 \text{ cm}^2$ and $\geq 10 \text{ cm}^2$). Community setting in South Buckinghamshire, UK.
Participants	<p>29 patients with 35 ulcerated legs were recruited through district and practice nurses.</p> <p>Inclusion criteria; uncomplicated venous leg ulcer (confirmed by dermatologist) being treated by district or practice nurse.</p> <p>Exclusion criteria: peripheral vascular disease, cellulitis, ABPI < 0.8, contact allergy to latex, ulcer on foot or toes, rheumatoid arthritis, collagen vascular disease, ankle circumference < 18 or $> 25 \text{ cm}$.</p> <p>Number of limbs with baseline ulcer area $< 9.9 \text{ cm}^2$ / $\geq 10 \text{ cm}^2$: Group 1. 12/5; Group</p>

	2. 12/6 Number of limbs belonging to male/female patients: Group 1. 8/9; Group 2. 5/13 Mean (range) patient age in years for baseline ulcer area < 9.9cm ² / ≥ 10 cm ² : Group 1. 77 (62 to 86) / 72 (49 to 92); Group 2. 75 (53 to 86) / 76 (49 to 85) Mean (range) baseline ulcer area in cm ² : Group 1. 11.2 (0.25 to 49.6); Group 2. 8.6 (0.25 to 45.0) Mean (range) baseline ulcer duration in months for baseline ulcer area < 9.9cm ² / ≥ 10 cm ² : Group 1. 14.2 (1 to 48) / 36.8 (6 to 60); Group 2. 18.3 (1 to 48) / 28.2 (5 to 60)	
Interventions	Group 1. Charing Cross four-layer bandage (Profore) comprising: knitted viscose primary dressing (Tricotex), orthopaedic wool (Soffban), crepe bandage, elastic bandage (Litepress), and cohesive elastic bandage (Coplus) (n=17 legs) Group 2. Alternative four-layer bandage comprising: knitted viscose primary dressing (Tricotex), elasticated viscose stockinette (Tubifast), lint applied in separate strips horizontally around the leg, elastic bandage (Setopress), and elasticated viscose stockinette (Tubifast) (n=18 legs) All patients: wound cleansing solutions and emollients were standardised; bandages were changed weekly; patients were supplied with class II compression stockings post-healing	
Outcomes	Number (%) limbs with complete healing at 12 weeks: Group 1. 8/17 (47%); Group 2. 8/18 (44%) (P = 0.51, Chi-squared test for between-group difference in proportions healed, not healed and withdrawn) OR (95% CI) estimated by trial authors for healing in Group 1 compared with Group 2: 1.11 (0.24 to 5.19) Mean percentage reduction in ulcer area during trial, based on unhealed limbs completing the trial: Group 1. (n=5) 39%; Group 2. (n=8) 34% (P = 0.89, t-test for between-group difference) Number (%) limbs withdrawn from treatment (reasons): Group 1. 4/17 (24%) (1 developed cellulitis, 1 bandage uncomfortable/slipped, 1 allergic to bandage, 1 bandage too painful); Group 2. 2/18 (11%) (1 leg painful & possibly infected, 1 bandage too painful)	
Notes	In limbs with more than one ulcer, the largest wound was included in the trial. Ulcer area was estimated by diameter product (maximum length x maximum width of ulcer) every 4 weeks. The trial authors stated that measurements of sub-bandage pressure were not made. Ulcer healing was defined as a 'continuous layer of epithelial cells across the ulcer surface'. Outcome assessment was non-blind. Nurses were taught to apply the bandages by the research nurse	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Yes	"...patients' ulcerated legs allocated to one of two groups using numbers generated by random number tables..."

Allocation concealment?	Yes	"...randomisation was based on random numbers and was calculated in blocks of four... the nurses ringing for randomisation were unaware of the block randomisation. .."
Incomplete outcome data addressed? All outcomes	Unclear	Recruited 29 patients with 35 limbs and "all 35 limbs included in the healing analysis". Four limbs were withdrawn from Group 1 and two from Group 2 therefore not clear <i>how</i> withdrawals included in the analysis (whether assumed unhealed or whether ascertained healing status)
Blinded outcome assessment (healing)?	No	"Not observer blind"
Baseline comparability?	No	Mean ulcer area greater in Group 1; mean duration data impossible to interpret

In previous versions of this review the study by [Scriven 1998](#) was cited as London et al (1996).

In the previous version of this review Meyer (2000) was referred to (under the section ongoing studies) as Burnand.

In the previous version of this review [Moffatt 1999](#) was cited as McCollum et al (1997). The latter is now a secondary reference of [Moffatt 1999](#).

In the previous version of this review [Nelson 2007a](#) was cited as [Nelson 1995](#). The latter is now a secondary reference of [Nelson 2007a](#).

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Baccaglini 1998	Not randomised.
Blair 1988	Primarily a dressings trial; comparison between bandages not randomised
Cameron 1996	Historical control, therefore not randomised.
Cherry 1990	Healing not measured as an outcome.
Horakova 1994	Not randomised.
Jünger 2006	Patients did not have ulceration; primary outcome was skin condition
Kucharzewski 2003	Not randomised.
Marston 1999	Not randomised.

(Continued)

Nissinen-Paatsamala 1995	Not randomised.
Northeast 1990	Treatment effect confounded by use of steroids in one treatment group but not the other
Olofsson 1996	Treatment groups differed systematically other than in terms of compression systems used (one group treated by a surgeon and the other by dermatologists). In addition, several different types of compression were used within each group, meaning that the relative effectiveness of each system would be difficult to estimate
Russo 1999	Have abstract only; randomisation not mentioned.
Sabolinski 1995	Both groups have compression, comparison is of dressings.
Scriven 2000	Case series primarily assessing sub-bandage pressures.
Sikes 1985	Not randomised.
Sironi 1994	Comparison of different protocols of delivering dressings and topical agents; patients in both study groups received the same type of compression
Smith Strom 2006	Dressings trial; all patients receive same type of compression
Torra i Bou 2003	Not randomised (uncontrolled before-after study).
Vowden 2001	Non-comparative study.
Walker 1996	Have abstract only.
Zamboni 2004	Comparison is venous reflux surgery versus compression but both study groups receive the same type of compression system

Characteristics of studies awaiting assessment [ordered by study ID]

Alvarez 2005

Methods	RCT
Participants	80 patients with venous leg ulcers
Interventions	4LB versus Unna's Boot
Outcomes	Time to healing; frequency of complete healing.
Notes	Abstract only - have requested full report.

Harley 2004

Methods	RCT
Participants	30 patients with chronic venous ulcers
Interventions	4LB versus compression with two components
Outcomes	Complete healing, adverse events.
Notes	Awaiting full report.

Jawien 2008

Methods	RCT
Participants	112 patients with 121 venous ulcers
Interventions	4LB versus compression with two components
Outcomes	No data
Notes	Abstract only, identified at late stage during handsearching. Yet to request full report

Moffatt 2003b

Methods	RCT
Participants	300 patients with venous leg ulcers
Interventions	4LB versus compression with 2 components (Proguide, Smith & Nephew)
Outcomes	No data
Notes	Abstract only - have requested full report.

Moffatt 2008

Methods	RCT (cross-over)
Participants	81 participants with venous leg ulcers
Interventions	4LB versus compression with two components
Outcomes	Bandage slippage, percentage change in wound surface area, health-related quality of life
Notes	Awaiting full report.

Taradaj 2007

Methods	RCT
Participants	73 patients with venous leg ulcers
Interventions	At least some patients appear to receive compression. Exact nature of comparisons and interventions to be confirmed
Outcomes	Change in wound surface area.
Notes	Report is in Polish - further details on interventions requested from translator

Zuccarelli 1997

Methods	RCT
Participants	48 patients with venous leg ulcers
Interventions	Two types of compression bandages but properties of devices unclear. Distinction between bandage types being confirmed
Outcomes	Change in wound surface area; adverse events.
Notes	Report is in French - further details on interventions requested from translator

DATA AND ANALYSES

Comparison 1. Compression vs no compression (primary dressing only)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Ulcers completely healed at 6 months	1	87	Risk Ratio (M-H, Fixed, 95% CI)	1.50 [0.90, 2.50]

Comparison 2. Compression vs no compression (non-compressive bandage)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 1 year	1	36	Risk Ratio (M-H, Fixed, 95% CI)	2.30 [1.29, 4.10]

Comparison 3. Compression vs no compression (usual treatment)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 3 months	1	36	Risk Ratio (M-H, Fixed, 95% CI)	4.0 [1.35, 11.82]
2 Patients with complete healing at 1 year	1	233	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.96, 1.47]
3 Patients with recurrence during 1 year follow-up	1	140	Risk Ratio (M-H, Fixed, 95% CI)	1.53 [0.88, 2.66]

Comparison 4. Single-component compression (inelastic) vs multi-component compression

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 6 months	1	40	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.51, 2.55]

Comparison 5. Single-component compression (elastic) vs compression based on paste bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 3 months	3		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
2 Percentage change during trial relative to baseline ulcer area	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3 Healing rate (cm squared per week adjusted for baseline ulcer perimeter)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Comparison 6. Single-component compression (elastic) vs four-layer bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing during trial period	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Comparison 7. Two-component (outer elastic) vs two-component (outer inelastic)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 1 month	1	43	Risk Ratio (M-H, Fixed, 95% CI)	3.48 [0.42, 28.63]
2 Patients with complete healing at 3-6 months	2	95	Risk Ratio (M-H, Fixed, 95% CI)	1.23 [0.67, 2.25]
3 Patients with complete healing at 1 year	1	43	Risk Ratio (M-H, Fixed, 95% CI)	3.48 [1.14, 10.60]

Comparison 8. Two-components versus four-components

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 3 months	1	109	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.62, 1.10]

2 Patients with complete healing at 6 months up to point of withdrawal from randomised treatment	1	109	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.41, 0.77]
3 Patients with complete healing at 6 months including withdrawals from randomised treatment	1	109	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.73, 1.05]

Comparison 9. 3 components including elastic bandage vs 3 components including inelastic bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients/limbs with complete healing during trial	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Complete healing at 3-4 months	2	171	Risk Ratio (M-H, Fixed, 95% CI)	1.83 [1.26, 2.67]
1.2 Complete healing at 6 months	1	112	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.69, 1.27]

Comparison 10. Charing Cross 4LB vs Other 4LB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients/limbs with complete healing during trial	2		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
1.1 Complete healing at 3 months	2		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
1.2 Complete healing at 6 months	1		Risk Ratio (M-H, Fixed, 95% CI)	Not estimable

Comparison 11. 3 components including paste bandage vs 3 components including inelastic bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Limbs with complete healing at 3 months	1	51	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [0.74, 4.06]

Comparison 12. 4LB vs multi-layer SSB

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing during trial period	5		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Patients with complete healing at 3-4 months	4	638	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.96, 1.31]
1.2 Patients with complete healing at 6 months (intention to treat)	1	156	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.89, 1.25]
1.3 Patients with complete healing at 6 months (those on randomised treatment)	1	156	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.77, 1.15]
1.4 Patients with complete healing at 1 year	1	387	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.97, 1.22]
2 Patients with complete healing at 3-4 months (random effects)	4	638	Risk Ratio (M-H, Random, 95% CI)	1.07 [0.85, 1.36]
3 Hazard ratio estimates for time to healing	4		Hazard Ratio (95% CI)	Subtotals only
3.1 4 trials	4	744	Hazard Ratio (95% CI)	0.80 [0.66, 0.97]
3.2 Omitting Partsch 2001	3	632	Hazard Ratio (95% CI)	0.74 [0.60, 0.91]
3.3 Omitting Ukat 2003	3	655	Hazard Ratio (95% CI)	0.83 [0.68, 1.00]
3.4 Omitting Franks 2004	3	588	Hazard Ratio (95% CI)	0.76 [0.62, 0.94]
3.5 Omitting Iglesias 2004	3	357	Hazard Ratio (95% CI)	0.99 [0.70, 1.38]
3.6 UK trials only	2	543	Hazard Ratio (95% CI)	0.77 [0.62, 0.95]
3.7 Continental European trials only	2	201	Hazard Ratio (95% CI)	0.93 [0.61, 1.43]

Comparison 13. 4LB versus compression system with paste bandage as the base

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients/limbs with complete healing during trial	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Patients/limbs with complete healing at 3 months	2	71	Risk Ratio (M-H, Fixed, 95% CI)	1.34 [0.78, 2.28]
1.2 Patients with complete healing at 6 months	1	68	Risk Ratio (M-H, Fixed, 95% CI)	1.13 [0.82, 1.57]
1.3 Patients with complete healing at 1 year	1	133	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.66, 1.01]
2 Patients/limbs with complete healing at 3 months (random effects)	2	71	Risk Ratio (M-H, Random, 95% CI)	1.23 [0.54, 2.82]
3 Percentage reduction of baseline ulcer area at 6 months	1	68	Mean Difference (IV, Fixed, 95% CI)	54.50 [-9.17, 118.17]

4 Healing rate (pooled)	2	78	Std. Mean Difference (IV, Fixed, 95% CI)	0.52 [0.06, 0.97]
5 Healing rate (Knight)	1	10	Mean Difference (IV, Fixed, 95% CI)	0.8 [-0.11, 1.71]

Comparison 14. Adjustable inelastic compression boot vs other compression system

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Limbs with complete healing at 3 months	1	24	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.32, 3.10]
2 Healing rate	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 cm squared per week	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.2 cm squared per day	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.3 percentage per day	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable
2.4 cm per day (linear rate)	1		Mean Difference (IV, Fixed, 95% CI)	Not estimable

Comparison 15. Single-layer compression stocking vs paste bandage system

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete healing in trial period (varying lengths)	2		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Patients with complete healing at 4 months	1	60	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.74, 1.48]
1.2 Patients with complete healing at 18 months	1	21	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.64, 1.29]
2 Healing rate (cm squared per week)	1	60	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.41, 0.17]

Comparison 16. Two-layer stocking versus short-stretch bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 3 months	2	177	Risk Ratio (M-H, Fixed, 95% CI)	1.72 [1.14, 2.58]
2 Patients with complete healing at 3 months (random effects)	2	177	Risk Ratio (M-H, Random, 95% CI)	1.70 [1.08, 2.67]
3 Percentage reduction of baseline ulcer area at 3 months	1	119	Mean Difference (IV, Fixed, 95% CI)	23.4 [-1.32, 48.12]

Comparison 17. Tubular compression vs short-stretch bandage

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Patients with complete healing at 3 months	1	178	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.76, 1.26]

Comparison 18. Elastic high compression vs inelastic compression (multi-layer) (RR and 95% Confidence Interval)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete healing in trial period (varying lengths)	2	172	Risk Ratio (M-H, Fixed, 95% CI)	1.81 [1.24, 2.64]

Comparison 19. Multi-layer high compression systems vs single layer systems (RR and 95% Confidence Interval)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete healing in trial period (varying lengths)	4	280	Risk Ratio (M-H, Fixed, 95% CI)	1.41 [1.12, 1.77]

Comparison 20. Multi-layer high compression vs inelastic compression (RR and 95% Confidence Interval)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Complete healing in trial period (varying lengths)	4	164	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.78, 1.55]