

Venous leg ulcers

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ABSTRACT

INTRODUCTION: Leg ulcers usually occur secondary to venous reflux or obstruction, but 20% of people with leg ulcers have arterial disease, with or without venous disorders. Between 1.5 and 3.0 in 1000 people have active leg ulcers. Prevalence increases with age to about 20 in 1000 people aged over 80 years. **METHODS AND OUTCOMES:** We conducted a systematic overview, aiming to answer the following clinical questions: What are the effects of treatments for venous leg ulcers? What are the effects of organisational interventions for venous leg ulcers? What are the effects of advice about self-help interventions in people receiving usual care for venous leg ulcers? What are the effects of interventions to prevent recurrence of venous leg ulcers? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). **RESULTS:** At this update, searching of electronic databases retrieved 116 studies. After deduplication and removal of conference abstracts, 63 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 43 studies and the further review of 20 full publications. Of the 20 full articles evaluated, four systematic reviews were updated and four RCTs were added at this update. We performed a GRADE evaluation for 23 PICO combinations. **CONCLUSIONS:** In this systematic overview, we categorised the efficacy for 13 interventions based on information about the effectiveness and safety of advice to elevate leg, advice to keep leg active, compression stockings for prevention of recurrence, compression bandages and stockings to treat venous leg ulcers, laser treatment (low level), leg ulcer clinics, pentoxifylline, skin grafting, superficial vein surgery for prevention of recurrence, superficial vein surgery to treat venous leg ulcers, therapeutic ultrasound, and topical negative pressure.

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INTERVENTIONS	
TREATMENTS FOR VENOUS LEG ULCERS	ORGANISATIONAL INTERVENTIONS
Beneficial	Unknown effectiveness
Compression bandages and stockings (more effective than no compression)	Leg ulcer clinics
Pentoxifylline (oral)	
	SELF-HELP INTERVENTIONS
Likely to be beneficial	Unknown effectiveness
Compression stockings versus compression bandages (both likely to be beneficial, but insufficient evidence to compare treatments)	Advice to elevate leg
	Advice to keep leg active
Unknown effectiveness	PREVENTING RECURRENCE
Topical negative pressure	Beneficial
Laser treatment (low-level)	Compression (bandages and stockings) to prevent recurrence
Skin grafting	
Superficial vein surgery to treat venous leg ulcers	Likely to be beneficial
	Superficial vein surgery to prevent recurrence
Therapeutic ultrasound	

Key points

- Leg ulcers are usually secondary to venous reflux or obstruction, but 20% of people with leg ulcers have arterial disease, with or without venous disorders.
- The [last version of this overview](#) on treatment and prevention of venous leg ulcers included a range of interventions.
- This updated overview focuses on interventions selected because they are the most likely to be available in current clinical practice.
- We have searched for evidence from RCTs and systematic reviews of RCTs on the effectiveness and safety of these treatments in people with venous leg ulcers — some of whom had concurrent diabetes mellitus or rheumatoid arthritis.

- **Compression (bandages and stockings)** heals more ulcers compared with no compression, but we don't know which **compression technique** is most effective.

Compression is used for people with ulcers caused by venous disease who have an adequate arterial supply to the foot.

The effectiveness of compression bandages depends on the skill of the person applying them.

- **Oral pentoxifylline** increases ulcer healing in people receiving compression.
- We don't know whether **therapeutic ultrasound**, **superficial vein surgery**, **skin grafting**, **leg ulcer clinics**, **laser treatment**, or advice to **elevate legs** or **increase activity** increase healing of ulcers in people treated with compression.
- **Compression bandages and stockings** reduce recurrence of ulcers compared with no compression, and should ideally be worn for life.
- **Superficial vein surgery** may also reduce recurrence.

Clinical context

GENERAL BACKGROUND

Venous leg ulceration occurs secondary to venous reflux or obstruction. It affects up to 3 in 1000 people, and is more common in older people. Venous leg ulceration has a negative impact on quality of life and results in considerable costs to both patients and healthcare providers.

FOCUS OF THE REVIEW

The aim of this overview is to update the research evidence for the management of venous leg ulceration. This update focuses on evidence for interventions that are likely to be available in current clinical practice. Dressings and larvae therapy are excluded from this overview because systematic reviews have not identified any robust evidence of benefit associated with dressings or larvae.

COMMENTS ON EVIDENCE

Overviews of trials in venous ulceration have commented upon the general poor quality and short follow-up, which limit the generalisability of the research.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried out from the date of the last search, June 2011, to March 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 116 studies. After deduplication and removal of conference abstracts, 63 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 43 studies and the further review of 20 full publications. Of the 20 full articles evaluated, four systematic reviews were updated and four RCTs were added at this update.

DEFINITION Definitions of leg ulcers vary, but the following is widely used: an open sore in the skin of the lower leg due to high pressure of the blood in the leg veins. ^[1] Some definitions exclude ulcers confined to the foot, whereas others include ulcers on the whole of the lower limb. This overview deals with ulcers of venous origin in people without concurrent arterial insufficiency.

INCIDENCE/ PREVALENCE Between 1.5 and 3.0/1000 people have active leg ulcers. Prevalence increases with age to about 20/1000 people aged over 80 years. ^[2] Most leg ulcers are secondary to venous disease; other causes include arterial insufficiency, diabetes, and rheumatoid arthritis, or, less commonly, autoimmune disease, cancer, or tropical disease. ^[3] The annual cost to the NHS in the UK has been estimated at £300 million. ^[4] This does not include the loss of productivity due to illness.

AETIOLOGY/ RISK FACTORS Leg ulceration is strongly associated with venous disease. However, about one fifth of people with leg ulceration have arterial disease, either alone or in combination with venous problems, which may require specialist referral. ^[5] Venous ulcers (also known as varicose or stasis ulcers) are caused by venous reflux or obstruction, both of which lead to poor venous return and venous hypertension.

PROGNOSIS People with leg ulcers have a poorer quality of life than age-matched controls because of pain, odour, and reduced mobility. ^[6] In the UK, audits have found wide variation in the types of care (hospital inpatient care, hospital clinics, outpatient clinics, home visits), in the treatments used (topical agents, dressings, bandages, stockings), and in healing rates and recurrence rates. ^[7]

AIMS OF INTERVENTION	To promote healing; to reduce recurrence; to improve quality of life, with minimal adverse effects.
OUTCOMES	Healing rates (ulcer area, number of ulcers healed, number of ulcer-free limbs, time to complete ulcer healing); recurrence rates (number of new ulcer episodes, number of ulcer-free weeks or months, frequency of dressing/bandage changes, number of people who are ulcer free); quality of life ; adverse effects . For the question on prevention of recurrence we have reported recurrence rates, quality of life, and adverse effects only.
METHODS	<p>Search strategy <i>BMJ Clinical Evidence</i> search and appraisal date March 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to March 2014, Embase 1980 to March 2014, The Cochrane Database of Systematic Reviews 2014, issue 3 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. Inclusion criteria Study design criteria for inclusion in this systematic overview were systematic reviews and RCTs published in English, at least single-blinded, and containing 20 or more individuals or limbs (10 in each arm), with no minimum number to be followed up. There was no minimum length of follow-up. We excluded all studies described as 'open', 'open label', or not blinded unless blinding was impossible. <i>BMJ Clinical Evidence</i> does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. Evidence evaluation A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed <i>a priori</i> with our expert contributors. In consultation with the expert contributors, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the overview. In addition, information that did not meet our pre-defined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' section. Adverse effects All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although <i>BMJ Clinical Evidence</i> presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. Comment and Clinical guide sections In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As <i>BMJ Clinical Evidence</i> does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. Structural changes this update At this update, we have removed the following previously reported question: What are the effects of adjuvant treatments for venous leg ulcers? Data and quality To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). <i>BMJ Clinical Evidence</i> does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 34). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).</p>

QUESTION What are the effects of treatments for venous leg ulcers?

OPTION COMPRESSION (BANDAGES AND STOCKINGS) VERSUS NO COMPRESSION

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- Compression (bandages and stockings) heals more ulcers compared with no compression.
- Compression is used for people with ulcers caused by venous disease who have an adequate arterial supply to the foot.

- The effectiveness of compression bandages depends on the skill of the person applying them.

Benefits and harms

Compression (bandages and stockings) versus no compression:

We found one systematic review (search date 2012, 8 RCTs) comparing all forms of compression with no compression, [8] and one subsequent RCT. [9] The RCTs included in the review were heterogeneous, using different forms of compression in different settings and populations. Therefore, the results were not pooled. See Comment for further general information and observational data about harms of compression.

Healing rates

Compression (bandages and stockings) compared with no compression Compression (bandages, stockings, Unna's boot) seems to be more effective than no compression at increasing healing rates (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
[8] Systematic review	66 people (69 ulcers) Data from 1 RCT	Proportion of ulcers healed 21/30 (70%) with compression 15/39 (38%) with no compression	RR 1.82 95% CI 1.15 to 2.89	● ○ ○	compression
[8] Systematic review	36 people Data from 1 RCT	Healing 18/19 (95%) with compression 7/17 (41%) with no compression	RR 2.30 95% CI 1.29 to 4.10	● ● ○	compression
[8] Systematic review	36 people Data from 1 RCT	Healing 12/18 (67%) with compression 4/18 (22%) with no compression	RR 3.00 95% CI 1.19 to 7.56	● ● ○	compression
[8] Systematic review	200 people Data from 1 RCT	Proportion of ulcers healed , over 12 weeks 54% with 4-layer elastomeric high-compression bandaging 34% with no compression Absolute numbers not reported	P <0.001	○ ○ ○	compression
[8] Systematic review	84 people with 87 venous leg ulcers Data from 1 RCT	Proportion of ulcers healed , 6 months 21/42 (50%) with compression 15/45 (33%) with no compression (primary dressing) The RCT was classified as being at high risk of bias	RR 1.50 95% CI 0.90 to 2.50 P = 0.12	↔	Not significant
[9] RCT 3-armed trial	321 people with venous leg ulcers	Proportion of ulcers healed , 12 weeks 71/107 (66%) with compression (short-stretch bandaging) 64/107 (60%) with compression (4-layer bandaging) 30/107 (28%) with no compression	P <0.001 for each type of compression v no compression	○ ○ ○	compression
[9] RCT 3-armed trial	321 people with venous leg ulcers	Proportion of ulcers healed , 6 months 77/107 (72%) with compression (short-stretch bandaging) 72/107 (67%) with compression (4-layer bandaging) 31/107 (29%) with no compression	P <0.001 for each type of compression v no compression	○ ○ ○	compression

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[8] Systematic review	73 people Data from 1 RCT	Mean % reduction in ulcer area (relative to baseline) , 7 weeks 69% with compression 54% with no compression (normal saline dressing plus ultrasound therapy) 63% with no compression (normal saline dressing) All patients also received pharmacotherapy	P >0.05 for difference across all 3 groups Between-group differences not assessed		
[9] RCT 3-armed trial	321 people with venous leg ulcers	Time to ulcer healing 9.8 weeks with compression (short-stretch bandaging) 10.4 weeks with compression (4-layer bandaging) 18.3 weeks with no compression	P <0.001 for each type of compression v no compression	○○○	compression

Recurrence rates

Compression (bandages and stockings) compared with no compression We don't know whether compression used for healing is more effective at reducing post-healing recurrence rates compared with no compression in people with venous leg ulcers at 1 year ([very low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[8] Systematic review	140 people Data from 1 RCT	Recurrence rate , 12 months 27/78 (35%) with compression 14/62 (22%) with no compression 'No compression' included various types of dressings and bandages, including compression, tubigrip, and light support bandages It is unclear how many people in the 'no compression' group received some form of compression	RR 1.53 95% CI 0.88 to 2.66 P = 0.13	↔	Not significant
[8] Systematic review	140 people Data from 1 RCT	Mean ulcer-free weeks , 12 months 20.1 weeks with compression 14.2 weeks with no compression 'No compression' included various types of dressings and bandages, including compression, tubigrip, and light support bandages It is unclear how many people in the 'no compression' group received some form of compression	Difference: 5.9 weeks 95% CI 1.2 weeks to 10.5 weeks	○○○	compression

No data from the following reference on this outcome. [9]

Quality of life

Compression (bandages and stockings) compared with no compression We don't know whether compression is more effective than no compression at improving quality of life in people with venous leg ulcers ([low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Quality of life					
[9] RCT 3-armed trial	321 people with venous leg ulcers	Score on mental component of the SF-12 (baseline scores not reported; higher score favourable) , 12 weeks 47.3 with compression (short-stretch bandaging) 50.0 with compression (4-layer bandaging) 47.2 with no compression	Significance not assessed		
[9] RCT 3-armed trial	321 people with venous leg ulcers	Score on mental component of the SF-12 (baseline scores not reported; higher score favourable) , 24 weeks 55.3 with compression (short-stretch bandaging) 55.2 with compression (4-layer bandaging) 56.5 with no compression	Significance not assessed		
[9] RCT 3-armed trial	321 people with venous leg ulcers	Score on physical component of the SF-12 (baseline scores not reported; higher score favourable) , 12 weeks 47.5 with compression (short-stretch bandaging) 47.7 with compression (4-layer bandaging) 44.1 with no compression	Significance not assessed		
[9] RCT 3-armed trial	321 people with venous leg ulcers	Score on physical component of the SF-12 (baseline scores not reported; higher score favourable) , 24 weeks 53.5 with compression (short-stretch bandaging) 54.0 with compression (4-layer bandaging) 53.1 with no compression	Significance not assessed		
[9] RCT 3-armed trial	321 people with venous leg ulcers	Score on Charing Cross Venous Ulcer Questionnaire (baseline scores not reported; lower score favourable) , 12 weeks 21.6 with compression (short-stretch bandaging) 22.4 with compression (4-layer bandaging) 25.1 with no compression	Significance not assessed		
[9] RCT 3-armed trial	321 people with venous leg ulcers	Score on Charing Cross Venous Ulcer Questionnaire (baseline scores not reported; lower score favourable) , 24 weeks 21.0 with compression (short-stretch bandaging) 20.9 with compression (4-layer bandaging) 25.1 with no compression	Significance not assessed		

No data from the following reference on this outcome. ^[8]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[8] Systematic review	36 people Data from 1 RCT	Withdrawal rate 12 ulcers with compression 6 ulcers with no compression (hydrocolloid dressing) None of the people receiving compression discontinued treatment because of adverse effects; 9 people in the dressings group withdrew due to adverse effects, including cellulitis and wound exudate	Not reported		

No data from the following reference on this outcome. ^[9]

Further information on studies

^[8] Many RCTs used a cut-off of 0.9 for the precise ankle/brachial pressure index below which compression is contraindicated (which is higher than the often-quoted value of 0.8; see Comment).

Comment: High levels of compression applied to limbs with insufficient arterial supply or inexpert application of bandages can lead to tissue damage and, at worst, amputation. ^[10] One observational study (194 people) found that four-layer compression bandaging for several months was associated with toe ulceration in 12 (6%) people. ^[11]

People thought to be suitable for high-compression treatments (bandages, stockings, and compression leggings) are those with clinical signs of venous disease (ulcer in the gaiter region, from the upper margin of the malleolus to the bulge of the gastrocnemius; staining of the skin around an ulcer; or eczema) and adequate arterial supply to the foot as determined by ankle/brachial pressure index. The precise ankle/brachial pressure index, below which compression is contraindicated, is often quoted as 0.8; however, many RCTs included in the review used the higher cut-off of 0.9. ^[8] Effectiveness is likely to be influenced by the ability of those applying the bandage to generate safe levels of compression and by the fitting of appropriately sized compression stockings or leggings. Bandages may be applied by the person with the leg ulcer or by a carer, nurse, or doctor. We found no comparisons of healing rates between specialist and non-specialist application of compression. Training improves bandaging technique among nurses. ^[12] Bandages containing elastomeric fibres can be applied weekly, as they maintain their tension over time. Bandages made of wool, cotton, or both, such as short-stretch bandages, may need to be re-applied more frequently, as they do not maintain their tension.

OPTION COMPRESSION STOCKINGS VERSUS COMPRESSION BANDAGES

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- Although there is evidence that [compression, p 3](#) increases healing rates in people with leg ulcers, we don't know which compression technique is most effective.

- Evidence from several poor-quality trials found quicker healing or higher healing rates associated with stockings than with bandages.

Benefits and harms

Compression stockings or tubular garments versus compression bandages:

We found two systematic reviews (search dates 2012, 11 RCTs; ^[8] and 2008, 8 RCTs ^[13]) and two subsequent RCTs ^[14] ^[15] comparing compression stockings or tubular garments with compression bandages. There was some overlap of RCTs (7 RCTs common to both reviews from a total of 12 identified RCTs) between the two reviews. ^[8] ^[13] The second review ^[13] included a meta-analysis for this comparison, so we have reported the synthesised data here, plus data from RCTs that were not included in the meta-analysis. The two reviews do not report recurrence for this comparison, therefore, data on recurrence are reported from one RCT identified by both reviews. ^[16]

Healing rates

Compression stockings compared with compression bandages Compression stockings may be more effective than high-compression bandaging at increasing healing rates and reducing mean time to healing in people with venous leg ulcers ([very low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
^[13] Systematic review	People with venous leg ulcers 8 RCTs in this analysis 1 RCT included in the pooled data had a crossover design	Complete ulcer healing 222/342 (65%) with compression stockings 161/346 (47%) with compression bandages	OR 0.44 95% CI 0.32 to 0.61 P <0.00001 The review reported significant heterogeneity between trials, P = 0.02		compression stockings
^[13] Systematic review	People with venous leg ulcers 7 RCTs in this analysis	Mean time to healing 11.63 weeks with compression stockings 14.77 weeks with compression bandages 535 people in this analysis	SMD -0.33 95% CI -0.50 to -0.16 P <0.0001 The review reported significant heterogeneity among trials, P = 0.03		compression stockings
^[17] RCT	80 people with venous leg ulcers In review ^[8]	Complete ulcer healing , 2 months 15/40 (38%) with compression stockings plus drug therapy 5/40 (13%) with 2-layer short-stretch bandaging plus drug therapy All participants received drug therapy, including micronised flavonoid fraction (diosmin 450 mg, hesperidin 50 mg), 2 tablets of 500 mg once daily (MPFF, Detralex)	P = 0.01		compression stockings
^[18] RCT	55 people with recurrent, large (mean 13 cm ²), and long-lasting (mean 27 months) venous leg ulcers In review ^[8]	Ulcer healing , 90–180 days 22% with compression stockings 5% with compression bandages Absolute numbers not reported	P = 0.40		Not significant
^[18] RCT	55 people with recurrent, large (mean 13 cm ²), and long-lasting (mean 27 months) venous leg ulcers	Mean time to healing , 180 days 56 days with compression stockings 60 days with compression bandages	P = 0.94		Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
	In review ^[8]				
^[19] RCT 3-armed trial	46 people with venous leg ulcers	<p>Percentage of ulcers healed , 12 weeks</p> <p>53% with compression stockings</p> <p>63% with ProGuide 2-layered bandage system</p> <p>60% with Profore 4-layered bandage system</p> <p>Absolute numbers not reported</p> <p>This RCT may have been under-powered for this comparison</p>	P >0.05	↔	Not significant
^[14] RCT 5-armed trial	147 people with venous leg ulcer	<p>Percentage of ulcers healed , 2 months</p> <p>17/30 (59%) with ulcer stocking</p> <p>17/19 (89%) with multi-layer short-stretch bandage</p> <p>5/30 (17%) with two-layer short-stretch bandages</p> <p>6/30 (20%) with Unna's boots</p> <p>All participants received standard drug therapy before compression commenced, including micronised purified flavonoid fraction 450 mg diosmin, 50 mg hesperidin, 2 tablets of 500 mg (Daflon 500) once daily</p> <p>The remaining arm evaluated intermittent pneumatic compression</p>	<p>Statistically significant differences between two-layer short-stretch bandages v ulcer stocking and v multi-layer short-stretch bandage</p> <p>Statistically significant differences between Unna's boots v ulcer stocking and v multi-layer short-stretch bandage</p> <p>P = 0.03 in all cases and favouring comparator</p> <p>Statistical significance of other between-group differences not assessed</p>		
^[15] RCT	103 people with venous leg ulcers	<p>Percentage of ulcers healed , 24 weeks</p> <p>86% with four-layer bandaging</p> <p>77% with compression stockings</p>	P = 0.24	↔	Not significant

Recurrence rates

Compression stockings compared with compression bandages Compression bandages plus tubulcus may be more effective at reducing recurrence rates than compression bandages alone at 12 months in people with extensive venous leg ulcers (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence rates					
^[16] RCT	138 people with extensive venous leg ulceration (ulceration surface 20–210 cm ² , duration 7 months–28 years) In review ^[8] ^[13]	<p>Recurrence rate , 12 months</p> <p>16/67 (24%) with multi-layer bandaging system plus tubulcus</p> <p>18/34 (53%) with multi-layer bandaging system with elastic bandages only</p> <p>Tubulcus: a heelless open-toed elastic compression device knitted in tubular form</p>	P <0.05	○○○	multi-layer bandaging system plus tubulcus

No data from the following reference on this outcome. ^[14] ^[15]

Quality of life

No data from the following reference on this outcome. ^[8] ^[13] ^[14] ^[15]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[20] RCT	134 people In review ^[13]	Adverse effects with stocking with short-stretch bandages Suspected causal relationship reported between treatments and increased pain from the ulcer (U-Stocking), enlarged ulcer due to poor wrapping of the bandage, restricted flexibility of the ankle due to pain (bandages), and an intolerance reaction to the compression material with suspected delayed allergic reaction	Significance not assessed		
^[21] RCT	188 people In review ^[13]	Pain caused by treatment 14% with stocking 0% with short-stretch bandage 178 people in this analysis Those affected complained of pain, and were subsequently given a larger stocking	Significance not assessed		
^[13] Systematic review	53 people Data from 1 RCT	Mean pain scores at bandaging (pain score range: 0–10; lower score = less pain) 1.88 with compression stockings 3.27 with compression bandages 1 treatment-related adverse effect was reported in the group receiving the stocking; there were no further details relating to the nature of the adverse effect	SMD –1.25 95% CI –1.84 to –0.66		compression stockings
^[13] Systematic review	53 people Data from 1 RCT	Withdrawal rate 4 with compression stocking 3 with compression bandage 1 person in the compression bandage group had a severe reaction to the dressing	P value not reported		
^[13] Systematic review	56 people Data from 1 RCT	Ulcer pain because of treatment with compression stocking with compression bandage Absolute results not reported	P = 0.017		compression stocking
^[13] Systematic review	56 people Data from 1 RCT	Withdrawal rate 38% with compression stocking 15% with compression bandage	P value not reported		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		Absolute numbers not reported 1 withdrawal was deemed potentially related to compression (bullous dermatitis) in compression stocking group			

No data from the following reference on this outcome. ^[8] ^[14] ^[15]

Comment: See Comment in option on Compression bandages and stockings versus no compression, p 3 for information regarding risks of high levels of compression. We are aware of an RCT published subsequent to our search date, which we will evaluate at the next update for inclusion in this overview. ^[22]

Clinical guide

Traditionally, stockings were mainly used for post-healing prevention. This limited evidence suggests that hosiery might form part of the menu of compression therapies for healing.

OPTION TOPICAL NEGATIVE PRESSURE

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- We don't know whether topical negative pressure is beneficial, as we only found one RCT with small numbers that met *BMJ Clinical Evidence* criteria.

Benefits and harms

Topical negative pressure versus usual care:

We found two systematic reviews (search dates 2002, ^[23] and 2004 ^[24]) and one subsequent RCT. ^[25] Both reviews identified one RCT (24 people), which compared topical negative pressure with simple dressings. ^[23] ^[24] The single RCT identified by the reviews was carried out in people with any type of chronic wound, but included some people with venous leg ulcers. However, it may have been too small to detect a clinically important difference in outcomes between topical negative pressure and simple dressings. Therefore, it is not reported further here apart from inclusion in the analysis on adverse effects. The subsequent RCT included 60 people with venous, arteriovenous, or arteriosclerotic leg ulcers. ^[25]

Healing rates

Topical negative pressure compared with usual care Topical negative pressure (vacuum-assisted closure [VAC]) may be more effective than conventional wound care techniques at reducing time to complete healing in people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
^[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration 26 had venous ulcers	Time to complete healing 29 days with topical negative pressure (VAC) 45 days with control (conventional wound care techniques)	P = 0.001	○○○	VAC

Recurrence rates

Topical negative pressure compared with usual care [Topical negative pressure \(VAC\)](#) may be no more effective at reducing median time to recurrence of ulcers or proportion of healed ulcers that recur compared with conventional wound care techniques in people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration ([very low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Median length of time to recurrence 4 months with topical negative pressure (VAC) 2 months with control (conventional wound care techniques)	P = 0.47	↔	Not significant
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Proportion of healed ulcers that recurred , 12 months 52% with topical negative pressure (VAC) 42% with control (conventional wound care techniques) Absolute numbers not reported	P = 0.41	↔	Not significant

Quality of life

No data from the following reference on this outcome. ^[25]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[23] Systematic review	18 people Data from 1 RCT	Adverse effects 3/18 (17%) wounds with topical negative pressure No data with usual care Adverse effects included osteomyelitis, calcaneal features, or both 2 people suffered calcaneal features while ambulating on the topical negative pressure dressing (against medical advice); both people eventually required amputation	Significance not assessed		
[23] Systematic review	24 people Data from 1 RCT	Pain with topical negative pressure with simple foam dressing Pain in some people with topical negative pressure with initial collapse, foam dressing removal, or both	Significance not assessed		

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Erysipelas 1 with topical negative pressure (VAC) 0 with control (conventional wound care techniques)	Reported as not significant P value not reported	↔	Not significant
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Pain 3 with topical negative pressure (VAC) 1 with control (conventional wound care techniques)	P value not reported		
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Wound infection 0 with topical negative pressure (VAC) 1 with control (conventional wound care techniques)	P value not reported		
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Postoperative bleeding at donor site 0 with topical negative pressure (VAC) 2 with control (conventional wound care techniques)	P value not reported		
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Non-healing ulcers 1 with topical negative pressure (VAC) 1 with control (conventional wound care techniques)	P value not reported		
[25] RCT	60 hospitalised people with venous, arteriovenous, or arteriosclerotic ulcers of at least 6 months' duration	Cutaneous damage secondary to treatment 7 with topical negative pressure (VAC) 2 with control (conventional wound care techniques)	P <0.05	○○○	control

Further information on studies

[24] One review reported that one of the 10 RCTs of topical negative therapy under way at that time included venous leg ulcers.

[25] In the RCT, all the included people had chronic ulcers (>6 months' duration) and were hospitalised throughout. This limits the applicability of this evidence, as most ulcers are treated outside hospital. Only 43% had venous ulcers in this study; the remainder were arteriovenous or arteriosclerotic ulcers.

Comment: None.

OPTION PENTOXIFYLLINE (ORAL)

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .

- Oral pentoxifylline seems to increase ulcer healing in people with venous leg ulcers receiving compression.


Benefits and harms

Oral pentoxifylline versus placebo:

We found one systematic review (search date 2012, 12 RCTs).^[26] The systematic review compared pentoxifylline (oxpentifylline), with or without compression, with placebo or with other treatments, in people with venous leg ulcers.^[26]

Healing rates

Oral pentoxifylline compared with placebo Oral pentoxifylline plus compression seems to be more effective than placebo plus compression at increasing the proportion of people with healed venous leg ulcers at 8 to 24 weeks (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
^[26] Systematic review	People with venous leg ulcers, receiving compression 7 RCTs in this analysis	Proportion of people with healed ulcers, over 8–24 weeks 221/348 (64%) with pentoxifylline 126/311 (40%) with placebo	RR 1.51 95% CI 1.3 to 1.76		pentoxifylline


Recurrence rates

No data from the following reference on this outcome.^[26]

Quality of life

No data from the following reference on this outcome.^[26]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[26] Systematic review	People receiving compression Number of trials not reported	Adverse effects 55/297 (18%) with pentoxifylline 33/252 (13%) with placebo Nearly half the adverse effects were gastrointestinal (dyspepsia, vomiting, or diarrhoea)	RR 1.27 95% CI 0.89 to 1.83		Not significant

Further information on studies

^[26] One RCT identified by the review found no significant difference in healing rates at 3 months in people receiving compression between pentoxifylline and defibrotide (11/12 [92%] with pentoxifylline v 9/11 [82%] with defibrotide; RR 1.12, 95% CI 0.81 to 1.55).

Comment: The review provided evidence for there being a benefit for pentoxifylline, both in the presence of compression and also where no compression was used.

Clinical guide

Oral pentoxifylline is not licensed for use in venous disease in all countries. The most commonly reported side effects are gastrointestinal disturbances such as nausea and indigestion, which the affected patients mostly reported as tolerable. However, when making prescribing decisions, the risks of polypharmacy should be considered, as many patients with venous leg ulceration are older adults and may already be taking a variety of drugs for other health conditions.

OPTION LASER TREATMENT (LOW-LEVEL)

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- We don't know whether laser treatment increases healing of ulcers in people treated with compression, compared with sham or control treatment.

Benefits and harms

Low-level laser treatment versus sham treatment or control:

We found two systematic reviews (search date 2001, 4 RCTs; [27] and 1999, 5 RCTs [28]) and four subsequent RCTs (in 5 publications). [29] [30] [31] [32] [33] The second review [28] identified, but did not describe fully, the four RCTs identified by the first review, and did not perform a meta-analysis.

Healing rates

Low-level laser treatment compared with sham or control treatment We don't know whether low-level laser treatment is more effective at increasing ulcer healing rates at 4 weeks to 9 months compared with sham or control treatment (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
[27] Systematic review	People with venous leg ulcers 2 RCTs in this analysis	Healing rates , over 12 weeks 17/44 (39%) with low-level laser treatment 14/44 (32%) with sham treatment	RR 1.21 95% CI 0.73 to 2.03	↔	Not significant
[27] Systematic review 3-armed trial	People with venous leg ulcers Data from 1 RCT	Proportion of ulcers healed , after 9 months' treatment 12/15 (80%) with laser plus infrared light 5/15 (33%) with non-coherent, unpolarised red light 3-armed trial; the remaining arm evaluated low-level laser treatment	RR 2.40 95% CI 1.12 to 5.13	●●○	laser plus infrared light
[29] RCT 3-armed trial	65 people receiving compression and drug treatment	Reduction in area of ulceration 4.25 cm ² (27%) with laser 5.21 cm ² (39%) with sham laser 2.98 cm ² (18%) with no treatment Unclear if the "no additional treatment" was established by randomisation	Reported as not significant P value not reported The RCT may have lacked power to detect clinically important differences	↔	Not significant
[30] [31] RCT 3-armed trial	44 people	Reduction in ulcer size with compression plus low-level laser	The RCT reported within-group rather than between-group differences Reported as not significant	↔	Not significant

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		with compression plus placebo laser with compression alone Absolute results not reported	The RCT may have lacked power to detect clinically important differences		
[32] RCT 4-armed trial	83 people	Complete healing 3/21 (14%) with low-level laser therapy plus conservative treatment 3/20 (15%) with conservative treatment alone The remaining arms assessed surgery (22 people) and surgery plus laser (20 people)	P value not reported Reported as not significant	↔	Not significant
[33] RCT	34 people with venous leg ulcers	Complete healing , 9 weeks 3/18 (17%) with low-level laser therapy 4/16 (25%) with hydrocellular dressing	P = 0.62	↔	Not significant

Recurrence rates

No data from the following reference on this outcome. [\[27\]](#) [\[28\]](#) [\[29\]](#) [\[30\]](#) [\[31\]](#) [\[32\]](#) [\[33\]](#)

Quality of life

No data from the following reference on this outcome. [\[27\]](#) [\[28\]](#) [\[29\]](#) [\[30\]](#) [\[31\]](#) [\[32\]](#) [\[33\]](#)

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[30] [31] RCT 3-armed trial	44 people	Proportion of people with increase in ulcer area 28% with compression plus low-level laser 11% with compression plus placebo laser Absolute numbers not reported The remaining arm included compression alone	Significance not assessed		

No data from the following reference on this outcome. [\[27\]](#) [\[28\]](#) [\[29\]](#) [\[32\]](#) [\[33\]](#)

Further information on studies

- [27] [29] [29] [30] [31] [32] [33] The laser power, wavelength, frequency, duration, and follow-up of treatment were different for all of the trials.
- [28] The review did not assess complete ulcer healing.

Comment: Eye protection is required when using some types of laser, as the high-energy beam may damage the retina.

OPTION SKIN GRAFTING

- For GRADE evaluation of interventions for Venous leg ulcers, [see table, p 34](#) .
- There is insufficient evidence to assess the effects of skin grafting for people with venous leg ulcers. We only found one RCT meeting *BMJ Clinical Evidence* inclusion criteria.

Benefits and harms

Skin grafts versus usual care or versus each other:

We found one systematic review (search date 2012, 17 RCTs, 1034 people) [34] of skin grafts (autografts, allografts, xerografts, or growth-arrested human keratinocytes and fibroblasts) for venous leg ulcers. In 12 RCTs identified by the review, people also received compression bandaging. Two of these trials (102 people) compared a dressing with an autograft, two trials (45 people) compared fresh allografts with dressings, three RCTs (80 people) compared frozen allografts with dressings, and five trials (552 people) evaluated tissue-engineered products (summarised above). Seven RCTs compared different types of skin graft with each other. The review found insufficient evidence to determine whether skin grafting increased healing rates for venous ulcers because studies were small and generally of poor quality, therefore, no further data are reported here. The review excluded one RCT, that met *BMJ Clinical Evidence* inclusion criteria for this review and it is, therefore, reported below. [35]

Healing rates

Skin grafts compared with usual care We don't know how porcine extracellular matrix graft skin graft plus compression compares with compression alone at increasing healing of venous ulcers at 12 weeks ([low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
[35] RCT	120 people with chronic leg ulcer(s)	Proportion of people healed , at 12 weeks 55% with porcine extracellular matrix graft plus compression 34% with compression alone Absolute numbers not reported	RR 1.59 95% CI 1.06 to 2.42 RR reported for healing with matrix		matrix graft

Recurrence rates

No data from the following reference on this outcome. [35]

Quality of life

No data from the following reference on this outcome. [35]

Adverse effects

No data from the following reference on this outcome. ^[35]

Further information on studies

^[34] The review reported that there was no evidence of harm from tissue-engineered skin.

Comment: Porcine-derived products may not be acceptable to some patient groups. ^[36]

OPTION SUPERFICIAL VEIN SURGERY TO TREAT VENOUS LEG ULCERS

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- We don't know whether superficial vein surgery increases healing of ulcers in people treated with compression.

Benefits and harms

Perforator ligation versus no surgery or versus surgery plus skin grafting in the presence of compression:
 We found one RCT (47 people) comparing perforator ligation with no surgery or with surgery plus skin grafting. ^[37]
 All participants were also treated with a compression bandage.

Healing rates

Perforator ligation compared with no surgery or surgery plus skin grafting We don't know whether perforator ligation is more effective at increasing the proportion of ulcers healed at 1 year or at reducing time to ulcer healing compared with no surgery or surgery plus skin grafting (very low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
^[37] RCT 3-armed trial	47 people with compression	Proportion of ulcers healed , after 1 year with perforator ligation with no surgery with surgery plus skin grafting Absolute results not reported	P >0.05 The RCT did not perform an intention-to-treat analysis (ITT), and 7/47 (15%) people withdrew from the trial The RCT is likely to have been underpowered to detect a clinically important difference among groups	↔	Not significant
^[37] RCT 3-armed trial	47 people with compression	Time to complete ulcer healing with perforator ligation with no surgery with surgery plus skin grafting Absolute results not reported	P >0.05 The RCT did not perform an ITT analysis, and 7/47 (15%) people withdrew from the trial The RCT is likely to have been underpowered to detect a clinically important difference among groups	↔	Not significant

Recurrence rates

No data from the following reference on this outcome. ^[37]

Quality of life

No data from the following reference on this outcome. ^[37]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
^[37] RCT 3-armed trial	47 people	Postoperative complications 0 with perforator ligation 0 with no surgery 0 with surgery plus skin grafting The RCT did not perform an intention-to-treat analysis, and 7/47 (15%) people withdrew from the trial The RCT may have been too small to detect clinically important adverse effects	Significance not assessed		

Minimally invasive surgery versus compression bandages or usual care:

We found two RCTs (215 people), which compared [minimally invasive surgery](#) with compression bandages. ^[38] ^[39] In the first RCT, people randomised to surgery were treated with a compression bandage before surgery, ^[38] whereas in the second RCT they wore compression until ulcer healing. ^[39] The second RCT compared [subfascial endoscopic perforator surgery \(SEPS\)](#) plus superficial venous surgery as required with compression alone. ^[39]

Healing rates

Minimally invasive surgery compared with compression bandages or usual care We don't know how [minimally invasive surgery](#) and compression bandages or usual care compare for reducing time to complete healing and increasing ulcer healing rates ([low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
^[38] RCT	45 people	Healing rates 100% with surgery 96% with compression Absolute numbers not reported	Significance not assessed The RCT randomised legs rather than people		
^[38] RCT	45 people	Median time to complete healing 31 days with surgery 63 days with compression	P <0.005 The RCT randomised legs rather than people	○○○	surgery
^[39] RCT	170 people with venous leg ulcers	Proportion of ulcers healed 83% with SEPS plus superficial venous surgery as required 73% with compression alone Absolute numbers not reported	P = 0.24	↔	Not significant

Recurrence rates

No data from the following reference on this outcome. ^[38] ^[39]

Quality of life

No data from the following reference on this outcome. ^[38] ^[39]

Adverse effects

No data from the following reference on this outcome. ^[38] ^[39]

Venous surgery (based on duplex scan) plus compression versus compression alone:

We found one systematic review (search date 2000–2007 only, 5 RCTs, 896 people) comparing superficial venous surgery with compression therapy. ^[40]

Healing rates

Venous surgery (based on duplex scan) plus compression compared with compression alone Performing venous surgery (based on duplex scan) in people receiving compression is no more effective than compression alone at increasing healing rates at 24 weeks and at 3 years (**moderate-quality evidence**).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
^[41] RCT	341 people In review ^[40]	Healing rates , at 24 weeks 65% with surgery plus compression 65% with compression alone Absolute numbers not reported	HR for healing: 0.84 95% CI 0.77 to 1.24	↔	Not significant
^[42] RCT	341 people Further report of reference ^[41]	Healing rates , at 3 years 93% with surgery plus compression 89% with compression alone Absolute numbers not reported	P = 0.73	↔	Not significant
^[40] Systematic review	76 legs Data from 1 RCT	Healed ulcers 68% with surgery plus compression 64% with compression alone Absolute numbers not reported	P value not reported Reported as not significant	↔	Not significant
^[40] Systematic review	45 people Data from 1 RCT	Healed ulcers 100% with surgery plus compression 96% with compression alone Absolute numbers not reported	P value not reported Reported as significant	○○○	superficial venous surgery

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[40] Systematic review	500 legs Data from 1 RCT	Healed ulcers 93% with surgery plus compression 89% with compression alone Absolute numbers not reported	P value not reported Reported as not significant	↔	Not significant
[40] Systematic review	200 legs Data from 1 RCT	Healed ulcers 83% with surgery plus compression 73% with compression alone Absolute numbers not reported	P value not reported Reported as not significant	↔	Not significant

Recurrence rates

Venous surgery (based on duplex scan) plus compression compared with compression alone Superficial venous surgery seems more effective than compression therapy at reducing recurrence rates in people with venous leg ulcers (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[40] Systematic review	45 legs Data from 1 RCT	Recurrence 9% with surgery plus compression 38% with compression alone Absolute numbers not reported	Reported as significant P value not reported	○○○	superficial venous surgery
[40] Systematic review	500 legs Data from 1 RCT	Recurrence 31% with surgery plus compression 56% with compression alone Absolute numbers not reported	Reported as significant P value not reported	○○○	superficial venous surgery
[40] Systematic review	200 legs Data from 1 RCT	Recurrence 22% with surgery plus compression 23% with compression alone Absolute numbers not reported	Reported as not significant P value not reported	↔	Not significant

No data from the following reference on this outcome. [41] [42]

Quality of life

No data from the following reference on this outcome. [40] [41] [42]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[41] RCT	341 people In review [40]	Adverse effects , 24 weeks with surgery plus compression with compression alone Absolute results not reported Adverse events were minimal and about equal in each group	Significance not assessed		

No data from the following reference on this outcome. [42]

Open perforator surgery versus subfascial endoscopic perforator surgery:

We found one systematic review (search date 2003, 1 RCT). [43]

Healing rates

Open perforator surgery compared with subfascial endoscopic perforator surgery We don't know how open perforator surgery and *subfascial endoscopic perforator surgery* (SEPS) compare at increasing ulcer healing rates at 4 months (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
[43] Systematic review	39 people Data from 1 RCT	Healing rates , 4 months 17/20 (85%) with SEPS 17/19 (89%) with open surgery	Reported as not significant	↔	Not significant

Recurrence rates

No data from the following reference on this outcome. [43]

Quality of life

No data from the following reference on this outcome. [43]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[43] Systematic review	39 people Data from 1 RCT	Wound infection rates 0% with SEPS 53% with open surgery Absolute numbers not reported	P <0.001	○○○	SEPS

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
[43] Systematic review	39 people Data from 1 RCT	Adverse effects with SEPS with open surgery Absolute numbers not reported Deep vein thrombosis occurred in 1%, wound infection in 6%, neuralgia in 7%, and haematoma in 9% of all people with venous ulcers having surgical treatment involving SEPS	Significance not assessed		

Comment: Several operative approaches are commonly used, including [perforator ligation](#), saphenous vein stripping, and a combination of both procedures. The RCT comparing open perforator surgery with [subfascial endoscopic perforator surgery \(SEPS\)](#) found that hospital stay was shorter with SEPS (4 days with SEPS v 7 days with open surgery).^[44] About 25% of people who were offered venous surgery in one study refused it.^[45]

OPTION THERAPEUTIC ULTRASOUND

- For GRADE evaluation of interventions for Venous leg ulcers, [see table, p 34](#).
- We don't know whether therapeutic ultrasound is effective, as results from trials were too inconsistent to draw conclusions.

Benefits and harms

Therapeutic ultrasound versus no or sham ultrasound:

We found one systematic review (search date 2010, 8 RCTs) comparing [therapeutic ultrasound](#) with no ultrasound or sham ultrasound for venous leg ulcers.^[46] Ultrasound improved ulcer healing in all studies, but a significant difference was found in only four of the eight RCTs, and heterogeneity precluded pooling the RCTs.^[46] We also found one subsequent RCT (337 people) comparing low-dose, high-frequency ultrasound plus standard care with standard care alone.^[47]

Healing rates

Therapeutic ultrasound compared with standard care Therapeutic ultrasound plus standard care seems to be no more effective than standard care alone at reducing time to healing at 12 weeks and increasing the proportion of people with healed ulcers at 12 months ([high-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
[47] RCT	337 people	Time to healing , 12 weeks with ultrasound plus standard care with standard care alone Absolute results not reported	HR 0.99 95% CI 0.70 to 1.40 P = 0.97	↔	Not significant
[47] RCT	337 people	Proportion of people with healed ulcers , 12 months 72/168 (43%) with ultrasound plus standard care 78/169 (46%) with standard care alone	P = 0.39	↔	Not significant

Recurrence rates

Therapeutic ultrasound compared with standard care Therapeutic ultrasound plus standard care is no more effective than standard care alone at reducing recurrence rates (moderate-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[47] RCT	337 people	<p>Recurrence</p> <p>17/31 (55%) with ultrasound plus standard care</p> <p>14/31 (45%) with standard care alone</p> <p>A total of 31 reference ulcers recurred in the 124 people successfully followed up with photographically confirmed healing of reference ulcer; unclear how many of the people analysed were from each group</p>	P = 0.68	↔	Not significant

Quality of life

No data from the following reference on this outcome. [47]

Adverse effects

No data from the following reference on this outcome. [47]

Further information on studies

[46] Mild and severe erythema, local pain, and small areas of bleeding were reported in RCTs [48] [49] identified by the review.

Comment: None.

QUESTION	What are the effects of organisational interventions for venous leg ulcers?
OPTION	LEG ULCER CLINICS

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- We don't know whether leg ulcer clinics increase healing of ulcers.
- Leg ulcer clinics and leg clubs may only be suitable for mobile people.

Benefits and harms

Leg ulcer clinics versus usual care:

We found one systematic review (search date 2001, 1 RCT) [50] and two subsequent RCTs. [51] [52]

Healing rates

Leg ulcer clinics compared with usual care We don't know whether leg ulcer clinics are more effective at increasing ulcer healing rates compared with usual care ([very low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Healing					
[50] Systematic review	People with leg ulcers Data from 1 RCT	Likelihood of healing with high-compression bandaging in a leg ulcer clinic with usual care Absolute results not reported	Cox model: ulcers were 1.65 times more likely to heal when attending a leg ulcer clinic 95% CI 1.15 to 2.35		high-compression bandaging in a leg ulcer clinic
[51] RCT	33 people	Reduction in ulcer area with community-based 'Leg clubs' with usual care Absolute results not reported	P = 0.004		community-based 'Leg clubs'
[51] RCT	33 people	Proportion of people healed, 12 weeks 7/16 (44%) with community-based 'Leg clubs' 4/17 (24%) with usual care	Reported as not significant P value not reported		Not significant
[52] RCT	126 mobile people with leg ulcers	Healing rate, 3 months 58% with clinic care 57% with home care Absolute numbers not reported Care was given by trained nurses in both groups	P = 0.5		Not significant

Recurrence rates

Leg ulcer clinics compared with home care We don't know whether leg ulcer clinics are more effective than home care at reducing recurrence rates in people with venous leg ulcers ([low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[52] RCT	126 mobile people with leg ulcers	Recurrence, 1 year 25% with clinic care 22% with home care Absolute numbers not reported Care was given by trained nurses in both groups.	P = 0.42		Not significant

No data from the following reference on this outcome. [\[50\]](#) [\[51\]](#)

Quality of life

No data from the following reference on this outcome. [\[50\]](#) [\[51\]](#) [\[52\]](#)

Adverse effects

No data from the following reference on this outcome. ^[50] ^[51] ^[52]

Further information on studies

^[50] All people attending the leg ulcer clinic were treated with high-compression bandaging, whereas only half the people receiving usual care at home were treated with some type of compression bandaging. Compression bandaging is known to be beneficial in the treatment of leg ulcers, and so increased improvement rates in those attending the leg clinic would be expected.

Comment:

Clinical guide

Leg ulcer clinics and leg clubs may only be suitable for mobile people.

QUESTION

What are the effects of advice about self-help interventions in people receiving usual care for venous leg ulcers?

OPTION

ADVICE TO ELEVATE LEG

- For GRADE evaluation of interventions for Venous leg ulcers, [see table, p 34](#) .
- We found no RCT evidence about advice to elevate legs, although the intervention makes sense as venous insufficiency is corrected if the leg is elevated above the heart.
- Many people with venous leg ulcers have mobility and joint problems, which may make this intervention impractical.

Benefits and harms

Advice to elevate leg versus standard care alone:

We found no systematic review or RCTs.

Comment:

Clinical guide

We found no RCT evidence to support the elevation of the leg, although this intervention makes sense as venous insufficiency is corrected if the leg is elevated above the heart. The advantages of leg elevation, such as reduced oedema and increasing venous return, must be weighed against the potential for harm if the cardiovascular system cannot cope with a sudden increase in circulating volume. Many people with venous disease have joint or other mobility problems that mitigate against their being able to elevate their legs for long periods.

OPTION

ADVICE TO KEEP LEG ACTIVE

- For GRADE evaluation of interventions for Venous leg ulcers, [see table, p 34](#) .
- We found no RCT evidence about the effects of advice to keep the leg active, although this intervention makes sense, as venous insufficiency can be reduced by activation of the calf muscle pump.
- Many people with venous disease have joint or other mobility problems that may mitigate against increasing their activity levels.

Benefits and harms

Advice to keep leg active versus standard care alone:

We found no systematic review or RCTs.

Comment: **Clinical guide**

Potential advantages of activity may include reduced leg oedema and increasing venous return.

QUESTION What are the effects of interventions to prevent recurrence of venous leg ulcers?

OPTION COMPRESSION (BANDAGES AND STOCKINGS) TO PREVENT RECURRENCE

- For GRADE evaluation of interventions for Venous leg ulcers, see table, p 34 .
- Compression (bandages and stockings) reduces recurrence of ulcers compared with no compression, and should ideally be worn for life.
- Although compression hosiery should ideally be worn for life, arterial sufficiency and changes in leg shape should be regularly assessed prior to provision of replacement hosiery.

Benefits and harms

Compression stockings versus no compression:

We found one systematic review (search date 2012), [53] which found one RCT [54] comparing compression stockings with no compression.

Recurrence rates

Compression stockings compared with no compression Compression stockings are more effective than no compression at reducing ulcer recurrence rates at 6 months; however, we only found one RCT of 153 people (high-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[54] RCT	153 people In review [53]	Recurrence , at 6 months 21% with compression stockings 46% with no compression stockings Absolute numbers not reported	RR 0.46 95% CI 0.28 to 0.76 NNT for 6 months' treatment 2 95% CI 2 to 5		compression stockings

Quality of life

No data from the following reference on this outcome. [54]

Adverse effects

No data from the following reference on this outcome. [54]

Compression stockings versus other forms of compression:

We found one systematic review (search date 2012, 2 RCTs). [53] The first RCT identified by the review compared two brands of UK class 2 stockings. The second RCT identified by the review compared class 2 and class 3 stockings (see Comment). We found one subsequent RCT. [55]

Recurrence rates

Compression stockings compared with other forms of compression High-compression stockings (UK class 3) seem no more effective than moderate-compression stockings (UK class 2) at reducing recurrence at 5 years ([moderate-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
^[53] Systematic review	166 people Data from 1 RCT	Recurrence , after 18 months 22/92 (24%) with Medi stockings 27/74 (36%) with Scholl stockings	RR 0.74 95% CI 0.45 to 1.20	↔	Not significant
^[53] Systematic review	300 people Data from 1 RCT	Recurrence , after 5 years 59/151 (39%) with class 2 elastic compression 48/149 (32%) with class 3 compression Intention-to-treat analysis This analysis may underestimate the effectiveness of class 3 stockings, as a significant proportion of people changed from class 3 to class 2	RR 0.82 95% CI 0.61 to 1.12	↔	Not significant
^[55] RCT	93 people	Percentage of recurring ulcers 14% with moderate-compression stockings 9% with high-compression stockings	P = 0.651	↔	Not significant

Quality of life

No data from the following reference on this outcome. ^[53] ^[55]

Adverse effects

No data from the following reference on this outcome. ^[53] ^[55]

Further information on studies

^[53] Both RCTs found that non-compliance with compression stockings was associated with recurrence.

Comment: The application of high compression to limbs with reduced arterial supply may result in ischaemic tissue damage and, at worst, amputation. ^[26]

Compression hosiery is classified according to the magnitude of pressure exerted at the ankle; the UK classification states that class 2 stockings are capable of applying 18 mmHg to 24 mmHg pressure and class 3 are capable of applying 25 mmHg to 35 mmHg pressure at the ankle. Other countries use different classification systems. Stockings reduce venous reflux by locally increasing venous pressure in the legs relative to the rest of the body. This effect only takes place while hosiery

is worn. The association between non-compliance with compression and recurrence of venous ulceration provides some indirect evidence of the benefit of compression in prevention. People are advised to wear compression stockings for life, and they may be at risk of pressure necrosis from their compression stockings if they subsequently develop arterial disease. Regular re-assessment of the arterial supply is considered good practice, but we found no evidence about the optimal frequency of assessment. Other measures designed to reduce leg oedema, such as resting with the leg elevated, may be useful (see [Comment on Advice to elevate legs, p 26](#)).

OPTION SUPERFICIAL VEIN SURGERY TO PREVENT RECURRENCE

- For GRADE evaluation of interventions for Venous leg ulcers, see [table, p 34](#) .
- Superficial vein surgery may reduce recurrence of venous leg ulcers.
- Endoscopic surgery may be more effective than open surgery.

Benefits and harms

Surgery plus compression versus compression alone:

We found one systematic review (search date 1997, 1 RCT),^[56] three subsequent RCTs,^{[38] [39] [41]} and one long-term follow-up report.^[42]

Recurrence rates

Surgery plus compression compared with compression alone Superficial vein surgery plus compression seems more effective than compression alone at reducing ulcer recurrence rates at 12 months to 3 years ([moderate-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
^[56] Systematic review	30 people Data from 1 RCT	Recurrence , after 18 months 5% with surgery plus compression stockings 24% with compression stockings alone Absolute numbers not reported	RR 0.21 95% CI 0.03 to 0.80 The RCT was poorly controlled, and its results should be interpreted with caution		surgery plus compression stockings
^[38] RCT	45 people	Recurrence rates , over 3 years 2/21 (10%) with minimally invasive surgery 9/24 (38%) with compression bandages People randomised to surgery wore compression stockings immediately after surgery, and people randomised to compression wore compression stockings after ulcer healing was achieved	P <0.05 The RCT randomised legs rather than people		surgery
^[41] RCT	500 people	Recurrence rates , after 12 months 12% with superficial vein surgery plus compression 28% with compression alone Absolute numbers not reported Subgroup of 428 people with healed ulcers in this analysis	HR -2.76 95% CI -4.27 to -1.78 P <0.0001		surgery plus compression
^[42] RCT	500 people with leg ulcers Further report of reference ^[41]	Recurrence rates , 4 years 31% with superficial vein surgery plus compression 56% with compression alone Absolute numbers not reported	Reported as significant P <0.001		surgery plus compression

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
		442 people in this analysis			
[39] RCT	170 people	Recurrence rates , 27 months 22% with subfascial endoscopic perforator surgery plus compression 23% with compression alone Absolute results reported graphically	Reported as not significant	↔	Not significant

Quality of life

No data from the following reference on this outcome. [38] [39] [41] [42] [56]

Adverse effects

No data from the following reference on this outcome. [38] [39] [41] [42] [56]

Open versus endoscopic surgery:

We found one systematic review (search date 2003, 1 RCT), [43] which compared open surgery with [subfascial endoscopic perforator surgery](#) (SEPS), and a subsequent long-term follow-up report [57] of the RCT identified by the review. We found one RCT that gave information on adverse effects. [44]

Recurrence rates

Open compared with endoscopic surgery Open surgery may be less effective than endoscopic surgery at reducing ulcer recurrences at 12 months ([low-quality evidence](#)).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Recurrence					
[57] RCT	39 people Further report of reference [43]	Recurrences , at 12 months 4 (22%) with open surgery 2 (12%) with SEPS	P = 0.044	○○○	SEPS

No data from the following reference on this outcome. [44]

Quality of life

No data from the following reference on this outcome. [43] [44] [57]

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[57] RCT	39 people Further report of reference [43]	Adverse effects with open surgery with SEPS Absolute numbers not reported Deep vein thrombosis was reported in 1%, wound infection in 6%, neuralgia in 7%, and haematoma in 9% of people having surgical treatment involving SEPS	Significance not assessed		
[44] RCT	People with leg ulcers	Wound infection rates 53% with open surgery 0% with SEPS Absolute numbers not reported	P <0.001	○○○	SEPS

Comment: Although vein surgery has the usual risks of surgery and anaesthesia, advances in surgical techniques are likely to make this an increasingly acceptable treatment option for patients with venous leg ulcers.

GLOSSARY

Minimally invasive surgery Surgery in which small incisions are made in the skin, and the use of surgical instruments with cameras or direct viewing through eyepieces allows the surgeon to operate. Often performed under local anaesthetic and as a day case.

Charing Cross Venous Ulcer Questionnaire A 21-item questionnaire normally used in conjunction with the Short Form-36 (SF-36) to assess health-related quality of life when venous ulceration is present.

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Multilayer elastomeric high-compression bandages Usually a layer of padding material followed by one to four additional layers of elastomeric bandages.

Perforator ligation A procedure that involves tying off the blood vessels that link the deep and superficial venous systems. The one-way valves in these veins prevent flow from the deep to the superficial system. Malfunctioning perforator vessels may be responsible for increasing venous pressure in the superficial venous system, leading to ulceration.

Short Form (SF-12) A generic, multi-purpose short-form survey with 12 questions selected from the SF-36 Health Survey. The responses, when combined, scored, and weighted, result in two scales of mental and physical functioning and overall health-related quality of life.

Subfascial endoscopic perforator surgery A minimally invasive endoscopic procedure that eliminates the need for a large incision in the leg. An endoscope is used to visualise directly and tie off incompetent medial calf perforating veins, to decrease venous reflux and reduce ambulatory venous pressure.

Therapeutic ultrasound Application of ultrasound to a wound, using a transducer and a water-based gel. Prolonged application can lead to heating of the tissues; but, when used in wound healing, the power used is low and the transducer is constantly moved by the therapist, so that the tissue is not heated significantly.

Topical negative pressure Negative pressure (suction) applied to a wound through an open-cell dressing (e.g., foam, felt).

Unna's boot An inner layer of zinc oxide-impregnated bandage, which hardens as it dries to form a semirigid layer against which the calf muscle can contract. It is usually covered in an elastomeric bandage.

Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Compression (bandages and stockings) to prevent recurrence One systematic review updated^[53] and one RCT added.^[55] Categorisation unchanged (beneficial).

Compression (bandages and stockings) versus no compression One systematic review updated^[8] and one RCT added.^[9] Categorisation unchanged (beneficial).

Compression stockings versus compression bandages One systematic review updated^[8] and two RCTs added.^[14]^[15] Categorisation unchanged (likely to be beneficial).

Pentoxifylline (oral) One systematic review updated.^[26] Categorisation unchanged (beneficial).

Skin grafting One systematic review updated.^[34] Categorisation unchanged (unknown effectiveness).

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GRADE Evaluation of interventions for Venous leg ulcers.

Important outcomes	Healing rates, Quality of life, Recurrence rates									
	Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
<i>What are the effects of treatments for venous leg ulcers?</i>										
	5 (707) ^[8] ^[9]	Healing rates	Compression (bandages and stockings) versus no compression	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results in some RCTs
	1 (140) ^[8]	Recurrence rates	Compression (bandages and stockings) versus no compression	4	-1	-1	-1	0	Very low	Quality point deducted for sparse data; consistency point deducted for conflicting results; directness point deducted for inclusion of compression in control group
	1 (321) ^[9]	Quality of life	Compression (bandages and stockings) versus no compression	4	-2	0	0	0	Low	Quality points deducted for incomplete reporting of results (baseline scores not available) and for lack of statistical analysis of between-group difference
	3 (1119) ^[13] ^[14] ^[15] ^[17] ^[18] ^[19]	Healing rates	Compression stockings or tubular garments versus compression bandages	4	-2	0	-2	0	Very low	Quality points deducted for incomplete reporting of data and methodological flaws; directness points deducted for inclusion of people with different severities of ulcers and for differences in treatment regimens in both groups, affecting generalisability of results
	1 (138) ^[16]	Recurrence rates	Compression stockings or tubular garments versus compression bandages	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
	1 (60) ^[25]	Healing rates	Topical negative pressure versus usual care	4	-1	0	-2	0	Very low	Quality point deducted for sparse data; directness points deducted for inclusion of people with non-venous ulcers and for uncertainty about generalisability of results outside a hospital setting
	1 (60) ^[25]	Recurrence rates	Topical negative pressure versus usual care	4	-1	0	-2	0	Very low	Quality point deducted for sparse data; directness points deducted for inclusion of people with non-venous ulcers and for uncertainty about generalisability of results outside a hospital setting
	7 (659) ^[26]	Healing rates	Oral pentoxifylline versus placebo	4	0	0	-1	0	Moderate	Directness point deducted for pentoxifylline being combined with compression
	7 (301) ^[27] ^[29] ^[30] ^[31] ^[32] ^[33]	Healing rates	Low-level laser treatment versus sham treatment or control	4	-2	0	-2	0	Very low	Quality points deducted for incomplete reporting of results and for differences in length of follow-up; directness points deducted for treatment inconsistencies between groups and for assessing different measures of healing
	1 (120) ^[35]	Healing rates	Skin grafts versus usual care or versus each other	4	-1	0	-1	0	Low	Quality point deducted for sparse data; directness point deducted for intervention combined with compression

Important outcomes			Healing rates, Quality of life, Recurrence rates						
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
1 (47) ^[37]	Healing rates	Perforator ligation versus no surgery or versus surgery plus skin grafting in the presence of compression	4	-3	0	0	0	Very low	Quality points deducted for sparse data, incomplete reporting of results, and no intention-to-treat analysis
2 (215) ^{[38] [39]}	Healing rates	Minimally invasive surgery versus compression bandages or usual care	4	-1	-1	0	0	Low	Quality point deducted for incomplete reporting of results; consistency point deducted for conflicting results
5 (at least 341 people) ^[40]	Healing rates	Venous surgery (based on duplex scan) plus compression versus compression alone	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (745 legs) ^[40]	Recurrence rates	Venous surgery (based on duplex scan) plus compression versus compression alone	4	-1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
1 (39) ^[43]	Healing rates	Open perforator surgery versus subfascial endoscopic perforator surgery	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results
1 (337) ^[47]	Healing rates	Therapeutic ultrasound versus no or sham ultrasound	4	0	0	0	0	High	
1 (62) ^[47]	Recurrence rates	Therapeutic ultrasound versus no or sham ultrasound	4	-1	0	0	0	Moderate	Quality point deducted for sparse data
<i>What are the effects of organisational interventions for venous leg ulcers?</i>									
4 (at least 159 people) ^{[50] [51] [52]}	Healing rates	Leg ulcer clinics versus usual care	4	-1	0	-2	0	Very low	Quality point deducted for incomplete reporting of results; directness points deducted for differences in treatments received by both groups and uncertainty about generalisability of results
2 (246) ^[52]	Recurrence rates	Leg ulcer clinics versus usual care	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of data
<i>What are the effects of interventions to prevent recurrence of venous leg ulcers?</i>									
1 (153) ^[54]	Recurrence rates	Compression stockings versus no compression	4	-1	0	0	+1	High	Quality point deducted for sparse data; effect-size point added for RR <0.5
3 (559) ^{[53] [55]}	Recurrence rates	Compression stockings versus other forms of compression	4	0	0	-1	0	Moderate	Directness point deducted for change-over of a large proportion of people from class 3 to class 2 grade of stocking
4 (at least 673) ^{[38] [39] [41] [42] [56]}	Recurrence rates	Surgery plus compression versus compression alone	4	-1	0	0	0	Moderate	Quality point deducted for methodological flaws
1 (39) ^{[43] [57]}	Recurrence rates	Open versus endoscopic surgery	4	-2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting

Important outcomes		Healing rates, Quality of life, Recurrence rates							
Studies (Participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
			<p>We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.</p>						