Surgery versus sclerotherapy for the treatment of varicose veins (Review)

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[Intervention Review]

Surgery versus sclerotherapy for the treatment of varicose veins

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ABSTRACT

Background

Varicose veins are a relatively common condition and account for around 54,000 in-patient hospital episodes per year. The two most common interventions for varicose veins are surgery and sclerotherapy. However, there is little comparative data regarding their effectiveness.

Objectives

To identify whether the use of surgery or sclerotherapy should be recommended for the management of primary varicose veins.

Search strategy

Thirteen electronic bibliographic databases were searched covering biomedical, science, social science, health economic and grey literature (including current research). In addition, the reference lists of relevant articles were checked and various health services research-related resources were consulted via the internet. These included health economics and HTA organisations, guideline producing agencies, generic research and trials registers, and specialist sites.

Selection criteria

All studies that were described as randomised controlled trials comparing surgery with sclerotherapy for the treatment of primary varicose veins were identified.

Data collection and analysis

Two authors independently extracted and summarised data from the eligible studies using a data extraction sheet for consistency. All studies were cross-checked independently by the authors.

Main results

A total of 2306 references were found from our searches, 61 of which were identified as potential trials comparing surgery and sclerotherapy. However, only nine randomised trials, described in a total of 14 separate papers, fulfilled the inclusion criteria. Fifty trials were excluded and one trial is ongoing and is due for completion in 2004. The trials used a variety of outcome measures and classification systems which made direct comparison between trials difficult. However, the trend was for sclerotherapy to be evaluated

as significantly better than surgery at one year; after one year (sclerotherapy resulted in worse outcomes) the benefits with sclerotherapy were less, and by three to five years surgery had better outcomes. The data on cost-effectiveness was not adequately reported.

Authors' conclusions

There was insufficient evidence to preferentially recommend the use of sclerotherapy or surgery. There needs to be more research that specifically examines both costs and outcomes for surgery and sclerotherapy.

PLAIN LANGUAGE SUMMARY

Surgery versus sclerotherapy for the treatment of varicose veins

Sclerotherapy (injection of a substance into the vein) shows greater benefits than surgery in the short term but surgery has greater benefits in the longer term. Varicose veins are a relatively common problem. Two treatments available are surgery and sclerotherapy. Both involve removal of the vein either by stripping it out (surgery) or by injecting it with a solution that causes it to collapse and be absorbed into the surrounding tissues (sclerotherapy). Neither treatment adversely affects blood flow through the limb. This review found that sclerotherapy was better than surgery in terms of treatment success, complication rate and cost at one year, but surgery was better after five years. However, the evidence was not of very good quality and more research is needed.

BACKGROUND

Varicose veins have an overall prevalence of between 20 and 60%, and approximately 25% of the adult population have at least one varicose vein (Callam 1994). Varicose veins are one of the commonest conditions requiring surgical treatment with 54,000 hospital in-patient episodes per year in England alone (OHE 2000). They also constitute a large part of the elective surgical waiting list.

People can experience a wide range of symptoms associated with their varicose veins that may not be directly attributable to the veins themselves (Bradbury 1999). The extent of the visible veins does not correlate with the severity or number of symptoms experienced (Goldman 1994; Isaacs 1995). There also appears to be a complex interaction between cosmetic dislike and perception of symptoms (Robbins 1994). The literature divides the symptoms people experience into subjective and objective physical symptoms. Subjective symptoms can include heaviness, aching, itching and cosmetic appearance. Objective physical changes can include varicose eczema, pigmentation, bleeding, and varicose ulcers. The patient can experience, to a greater or lesser degree, all of these symptoms or none at all.

Treatment of primary (simple) varicose veins is considered appropriate by the majority of vascular surgeons if the veins are symptomatic (Lees 1999). Common symptoms attributable to varicose veins include poor cosmesis (cosmetic appearance), ache and itching. Less common problems include haemorrhage (bleeding) and thrombophlebitis (inflammation of the vein wall with associated blood clot). In seeking to manage demand for varicose vein treatments the National Institute for Clinical Excellence (NICE) has produced patient referral advice (NICE 2001) as the basis for referral to a specialist.

There are currently three distinct treatment options available for varicose veins. These are conservative treatment, sclerotherapy and surgery. Conservative treatment consists of lifestyle advice and the use of compression hosiery (graduated elasticated stockings). This avoids the need for any intervention but requires good patient compliance. Sclerotherapy involves the injection of a sclerosant (e.g. sodium tetradecyl sulfate) into the varicosities followed by a period of compression treatment using bandaging or compression hosiery. Many surgical treatments are practiced; these may involve ligation of the affected stem vein (long or short saphenous veins), stripping of the affected stem veins, and avulsions (tearing away) of the varicosities. Some surgeons use a combination of surgery and injection sclerotherapy. Newer surgical treatments include subfascial ligation and PIN stripping. Subfascial ligation is a procedure that involves cutting through the skin and deep fascia (a sheet of connective tissue) and ligating (tying off) the incompetent perforating veins that link the veins in the skin to the deep veins in the muscle. PIN-stripping (Perforate Invaginate stripping) is a technique that involves stripping the vein into itself in a manner similar to turning a stocking inside out. This results in a smaller exit wound.

Despite the prevalence of varicose veins and the vast numbers of people being treated, the criteria for each of the various treatments are not well defined (Lees 1999; Tremblay 1985). Furthermore, there is no general consensus over which intervention is the most effective (Robbins 1994). This systematic review is an attempt to

clarify whether there is sufficient data to determine the relative effectiveness of the surgical and sclerotherapy treatment options in the management of varicose veins.

OBJECTIVES

The main objective of this review is to compare the effectiveness of surgery against sclerotherapy in the management of primary varicose veins. This includes any different or new techniques used for either sclerotherapy or surgery.

METHODS

Criteria for considering studies for this review

Types of studies

All prospective randomised controlled trials (RCTs) of the treatment of varicose veins were sought where any comparisons were made between surgery and sclerotherapy.

Types of participants

All people having treatment for primary varicose veins. People being treated for cosmesis and/or symptomatic varicose veins (e.g. ache, itch, etc.) were included.

Trials including participants undergoing treatment for complications of varicose veins, venous ulceration, and chronic venous insufficiency were excluded. People undergoing treatment for recurrent varicose veins were also excluded as we considered that they were a distinct group that may have different outcomes, complications and recurrence rates to people with primary varicose veins.

Types of interventions

All interventions that evaluated any surgical treatment for primary varicose veins versus sclerotherapy. This included any combination of these techniques and new techniques.

Types of outcome measures

(1) Initial success of treatment as judged by various methods including:

(a) subjective improvement in symptoms attributable to the varicose veins using techniques such as Likert or visual analogue scales;

(b) assessment of improvement in appearance of the limb, judged subjectively by the patient and/or surgeon, or objectively by means such as measuring the reduction in number or appearance of veins;

(c) overall patient satisfaction however it may be reported;

(d) objective testing, e.g. duplex ultrasonography, photoplethysmography;

(e) formal quality of life measures or generic measures of health such as the SF-36 or disease specific measures.

(2) Early complications of an intervention (less than six weeks post-intervention).

Particular attention was paid to complications relating specifically to an intervention, e.g. nerve damage, skin pigmentation, infection, haemorrhage, thrombophlebitis and deep venous thrombosis. Where available, details about general complications and mortality were considered.

(3) Long term complications of an intervention (over six months postintervention).

Recurrence rates and reoperation rates were included when available.

(4) Economic analysis.

Where available, cost-effective analysis of treatments and resource usage was included.

Search methods for identification of studies

All publications describing (or which might describe) randomised controlled trials (RCTs) of surgery for the treatment of varicose veins were sought through computerised searches of electronic databases including the Cochrane Peripheral Vascular Diseases Review Group's Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* Issue 2, 2004, MEDLINE and EMBASE. In addition, handsearching of relevant journals using the search strategy described by the Cochrane Peripheral Vascular Diseases Group was performed. The full list of journals that have been handsearched, as well as the search strategies used are described in the 'Search strategies for the identification of studies' section within the editorial information about the Cochrane PVD Group in *The Cochrane Library,* http:/ / www.mrw.interscience.wiley.com/ cochrane/ clabout/ articles/ PVD/ frame.html

The last searches were carried out in June 2004.

Search strategy

The search aimed to identify all papers relating to surgery and sclerotherapy in the management of varicose veins. The searches were originally conducted during April 2000 although the major database searches were re-run in October 2000, March 2001 and November 2002.

Sources searched

Thirteen electronic bibliographic databases were searched covering biomedical, science, social science, health economic and grey literature (conference proceedings, unpublished trials, thesis, and current research). In addition, the reference lists of relevant articles were checked and various health services research-related resources were consulted via the internet. These included health economics and HTA organisations, guideline producing agencies, generic research and trials registers, and specialist sites.

Search restrictions

Where possible (e.g. in the smaller databases), searches were not restricted by publication type or study design. However, methodological filters aimed at identifying guidelines, systematic reviews, and clinical trials were applied in the larger databases such as MEDLINE. Date and language restrictions were not used. Further details of the sources searched and strategies used are given in Table 1; Appendix 1; Appendix 2; Appendix 3 and Appendix 4.

Table 1. Sources searched

Electronic databases	Other sources	Other sources (cont)
1. AMED 2. Best Evidence 3. Biological Abstracts 4. CCTR (Cochrane Controlled Trials Register) 5. CDSR (Cochrane Database of Systematic Reviews) 6. EMBASE 7. HMIC (Health Information Management Consortium - comprising DH-Data, the King's Fund Database, and Helmis) 8. MEDLINE 9. NHS DARE (Database of Assessments of Reviews of Effectiveness) 10. NHS EED (Economic Evaluations Database) 11. NHS HTA (Health Technology Assessment) 12. PubMed (last 180 days) 13. Science Citation Index	1. AHRQ (Agency for Healthcare Research and Quality) 2. ARIF (Aggressive Research Intelligence Facility) 3. Bandolier 4. CCOHTA (Canadian Co-ordinating Centre for Health Technology Assessment) 5. CCT (Current Controlled Trials) 6. CenterWatch Trials Register 7. ClinicalTrials.gov, NIH Clinical Trials Database 8. COIN (Department of Health Circulars) 9. CRiB (Current Research in Britain) 10. CRW (Current Research Worldwide) 11. Department of Health 12. eMC(Electronic Medicines Compendium) 13. Health Care Needs Assessment 14. Health Evidence Bulletins, Wales 15. HSTAT (Health Services/Technology Assessment Text, US National Library of Medicine) 16. INAHTA (International Network of Agencies for Health Technology Assessment) Clearinghouse 17. Index to Theses 18. ISTP (Index to Scientific and Technical Proceedings) 19. MRC (Medical Research Council) Funded Projects Database 20. National Guideline Clearinghouse	21. National Research Register 22. NCCHTA (National Co-ordinating Centre for Health Technology Assessment) 23. NHS CRD (Centre for Reviews and Dissemination), University of York 24. NHS R&D Programmes 25. OMNI (Organising Medical Networked Information) 26. POINT (Department of Health publications) 27. ReFeR (Research Findings Register) 28. ScHARR Library Catalogue 29. SIGN (Scottish Intercollegiate Guidelines Network) 30. SumSearch 31. Trent Working Group on Acute Purchasing 32. TRIP (Turning Research into Practice) Database 33. UK Official Publications 34. Uncover 35. Wessex DEC (Development and Evaluation Committee) Reports 36. West Midlands DES (Development and Evaluation Services) Reports

Data collection and analysis

Full papers were obtained for all studies identified as potentially relevant for inclusion. Kathryn Rigby and Simon Palfreyman independently decided whether each identified trial was suitable for inclusion or exclusion. All trials that were randomised, or described as randomised, were assessed to see if they met the inclusion criteria and then underwent data extraction. Any disagreements about inclusion or exclusion were adjudicated by Jonathan Michaels. Where data were missing, attempts were made to contact the authors to provide additional detail.

The methodological quality of the trials was assessed on the basis of key determinants of trial quality as identified by the NHS Centre for Reviews and Dissemination (2001):

(1) comparability of groups in control and intervention arms at

baseline;
(2) analysis of the results on an intention to treat basis;
(3) completeness of follow up;
(4) blinding and objectivity of outcome assessment;
(5) appropriateness and completeness of statistical analysis of the results.
External and internal validity was assessed and each study was given a Jadad score (Jadad 1996) in order to give a standardised impression of the quality of the trial.
All analysis was on an intention to treat basis. It was our intention to perform meta-analyses where sufficient homogeneity was found and to test for heterogeneity based on clinical judgement and the Chi-square test. However, as the data were not homogeneous, no meta-analyses could be performed.
For future updates of this review should sufficient homogeneous data become available, meta-analyses will be performed using the RevMan Analyses (RevMan 4.2.7) software.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.
A total of 2306 references were found from our searches, 61 of which were identified as potential trials comparing surgery and sclerotherapy. However, only nine randomised trials, described in a total of 14 separate papers, fulfilled the inclusion criteria. There were a total of 51 citations relating to 50 trials that were excluded; one trial is ongoing and is due for completion in 2004 (Michaels 2004).
A total of 3313 participants were included in the trials. All but one of the trials (deRoos 2003) had over 100 participants and three had 500 or more. The length of follow up ranged from two to five years.
Belcaro 2000 was a randomised controlled trial conducted in both Italy and England. Participants were randomised to receive one of three interventions:
(1) endovascular sclerotherapy and sclerotherapy: under local anaesthetic a catheter was introduced into the long saphenous vein (LSV) at the knee and advanced to the saphenofemoral junction (SFJ). The deep vein was occluded and sclerosant injected. Residual varicose veins had sclerotherapy over the following three months;
(2) surgery and sclerotherapy: SFJ ligation under general or spinal anaesthetic and collateral veins marked preoperatively only. Sclerotherapy was repeated for residual varicose veins over the following three months;
(3) surgery only: ligation of the SFJ and collaterals, and ligation of incompetent veins as marked by duplex ultrasonography.
One hundred and fifty participants were randomised; 39 had endovascular sclerotherapy (EVS), 40 had surgery and sclerotherapy, and 42 had surgery only. Twenty-nine refused treatment or follow up, or did not have the allocated treatment and were excluded. The three groups were comparable at inclusion for age, sex and clinical findings. Little information was given on the methods used to calculate the costs but compared to surgery EVS was 68% of the cost, and surgery and sclerotherapy was 122% of the cost.
Belcaro 2003 was a randomised controlled trial conducted in Italy, UK, Greece, France, Cyprus and South Africa. Participants were randomised between six interventions:
(1) sclerotherapy: veins larger than 3 mm in diameter were treated with 1 to 2 ml of 3% sclerosing agent, veins smaller than 3 mm with 2% solution (n = 148);
(2) high-dose sclerotherapy: same as Group 1 except volume of sclerosing agent greater, i.e. 3 to 6 ml of 3% sclerosing agent in larger veins (larger than 3 mm) (n = 136);
(3) ligation: flush ligation performed under general anaesthetic (GA), spinal or local anaesthetic (LA) using 'closed loop' technique (n = 155);
(4) stab avulsion: segments (2 to 5 cm) of vein removed (n = 144);
(5) foam sclerotherapy: injection of a 'tensioactive' substance (J&J-93FA) which produces a foam that displaces the blood in the vein (n = 150);
(6) surgery (stripping and ligation) plus sclerotherapy (n = 154).
Eight hundred and eighty-seven participants were randomised and followed up for 10 years. A total of 138 (16%) participants were lost to follow up with no statistically significant variations amongst the groups. The six groups were comparable for age and gender.
Beresford 1978; Chant 1972. These were two papers reporting one randomised controlled trial with the three-year and five-year outcome results. It was undertaken at the Royal Free Hospital, London, England. Participants were randomised to receive SFJ ligation, stripping of the LSV and ligation of perforators (or SPJ ligation), or injection/compression sclerotherapy (I/CST) by Fegan's method.
Three hundred and thirty-nine participants were seen in clinic and 249 (73%) were admitted into the trial. One hundred and fifteen participants had sclerotherapy and 100 had surgery. Ninety were excluded, 31 because they had had previous treatment and 27 because the interventions were contraindicated on medical or social reasons. The same observer conducted the follow-up examination and in the same way as on the first visit. Although the observer was blinded, he could see some of the incision wounds and this may have influenced the decision for more treatment. Participants were classified as improved or requiring further treatment including compression stockings. The percentage of participants seen at three years was 90% in the surgery groups and 97% in the sclerotherapy group. Fifteen participants were not seen (10 in the surgical groups and five in the sclerotherapy group). Thirty-nine of the surgery participants and 28 of the sclerotherapy participants received treatment to both legs, but only one leg was chosen at

random for analysis to reduce any bias. Outcome data were transformed using logit transformation (the natural log of the odds ratio) and analysed for the effect of class, sex type of treatment and number of legs treated. None of these effects were significant.

deRoos 2003 was a randomised controlled trial conducted in the Netherlands. Participants were randomised to either sclerotherapy or ambulatory phlebectomy. The unit of randomisation was the leg and not the patient. This meant that although 82 participants were included in the trial 98 operations were randomised - 49 legs were randomised to sclerotherapy and 49 to ambulatory phlebectomy. Only participants with lateral accessory varicose veins (LAVs) were included. These were defined as tortuous and dilated veins on the anterolateral side of the thigh, originating on the lateral side of the leg distal to the knee and draining 10 cm distal to the sapheno-femoral junction into the GSV or into the SF junction. Sclerotherapy was administered using the 'empty vein' technique which consists of the vein being emptied by stroking the overlying tissue while injecting the sclerosant. Ambulatory phlebectomy was performed under local anaesthetic. An incision of 2 mm diameter was made parallel to the vein and the vein extracted. Participants were followed up for two years. The outcome measures were recurrence and complication rates.

Doran 1975. This trial was conducted in Worcestershire, England, described as a random series, and allocated participants to receive surgery or injection/compression sclerotherapy (I/CST) by Fegan's method. If patients were born in a year with an even number they were allocated to sclerotherapy, whilst those born in a year with an odd number had surgery. Participants were included if they had varicose veins without ulceration and excluded if they had ulceration. A total of 331 participants met these criteria of which 182 had sclerotherapy and 149 had surgery. Ninety-eight participants in the sclerotherapy group and 73 in the surgery group had bilateral varicose veins (280 limbs in the sclerotherapy group and 222 limbs in the surgical group). The sclerotherapy method was clearly described but the surgery was not, although it appears to be SFJ ligation and stripping of the LSV. Participants were followed up for two years and the single outcome measure was success or failure, depending on the need for additional treatment at the end of each year.

Einarsson 1993. This trial had a five year follow up and was conducted at the University of Lund, Sweden. Participants were randomised to receive surgery or injection/compression sclerotherapy (I/CST) by Fegan's method. A total of 164 participants with symptomatic primary varicose veins were examined for the study. Participants were included if they had symptomatic primary varicose veins. Exclusion criteria were not clearly stated. Surgery comprised of SFJ or SPJ ligation and stripping of the LSV or SSV, multiple avulsions and resection of incompetent perforators. Sclerotherapy was undertaken in outpatients using Fegan's method and participants were seen at one and two weeks for further injections.

Outcomes measured were foot volumetry and objective clinical assessment of recurrence: graded as cured, improved (small recurrent or residual varicose veins) or failed (large varicose veins incompetent perforators or reflux in the saphenous veins). Participants were asked to describe themselves as cured, improved, unchanged or worse.

Hobbs 1968; Hobbs 1974; Hobbs 1984. These three papers described a randomised controlled trial with one-year, six-year and ten-year follow-up results and conducted at St Mary's Hospital, London. Participants were randomised to receive surgery or sclerotherapy. Participants were seen over a two-year period, however, the numbers included in the study differ between two papers. In the 1968 paper, 746 participants were seen, 35 refused to participate, 211 were rejected as they were unsuitable for surgery, 250 participants were allocated to surgery and 250 to sclerotherapy. Participants were clinically assessed, photographed and then randomised if they fitted the inclusion criteria and consented. Inclusion criteria were not clearly stated but exclusion criteria were defined as minor and superficial varicosities, ulcers, obesity, orthopaedic problems, serious medical problems, pregnancy, arterio-venous (AV) fistulae, lymphoedema and the use of the oral contraceptive pill. Each leg was classified as mild, moderate, or severe. They were also grouped according to the distribution of the varicose veins as:

* group 1 - LSV only;
* group 2 - SSV only;
* group 3 - LSV and incompetent perforating veins;
* group 4 - lower leg perforating veins.

Sclerotherapy was performed on outpatients using Fegan's method. Surgery consisted of SFJ ligation, stripping of LSV or SSV, multiple extrafascial ligations and subfascial ligations of perforators, and avulsions under general anaesthetic. Outcomes were assessed as cured, improved, or failed based on the poorest assessment by the patient or the surgeon. Participants were seen at six-monthly intervals for up to six years. Questionnaires were sent out at one and four years with returns of 96% and 78%.

Jakobsen 1979. This was a randomised controlled clinical trial conducted in Copenhagen, Denmark. Participants were randomised into one of three groups according to a stratified group comparative design. The groups were general anaesthetic surgery, local anaesthetic surgery and sclerotherapy, or sclerotherapy. The method of randomisation was not stated. A total of 516 participants were considered. Participants with primary varicose veins were included and those who had had previous treatment were excluded. Participants were registered according to age, sex, height, weight, type and degree of varicosity. The three groups were comparable on grounds of the above criteria and also in terms of symptoms and duration of illness. Thirty-three participants left the study prior to treatment because they moved or sought treatment elsewhere.

Participants were allocated to one of three interventions:

(1) SFJ or SPJ ligation, stripping of LSV or SSV, ligation of incompetent perforators and avulsions (161 participants);

(2) local anaesthetic ligation of SFJ or SPJ and incompetent perforators as an outpatient followed by sclerotherapy (165 partici-

pants);
(3) outpatient sclerotherapy (157 participants).
Participants were interviewed at their home, the hospital, or at work after three months and again after three years of treatment. The outcome measures used were objective evaluation of extent of varicose veins and subjective assessment of the outcome.
Rutgers 1994. This paper reported a randomised controlled trial with a three-year follow up and was conducted at State University, Maastricht, the Netherlands. Participants were randomised to receive general anaesthetic surgery (ligation and stripping) or injection/compression sclerotherapy (ligation and sclerotherapy) (I/CST) by Fegan's method. A total of 268 participants (536 limbs) were examined for the study. A history was taken from the participants and then they were clinically examined by vascular surgeons (inspection, palpation and tourniquet test) and had a Doppler ultrasound test. Inclusion criteria were stated as those with isolated incompetence of the LSV and local varicosities. Exclusion criteria were not clearly stated. Of the 268 participants examined, 156 (181 legs) were randomised. Seventy-eight participants (89 legs) were placed in the surgery group and 78 participants (92 legs) had ligation and sclerotherapy. Surgery included SFJ ligation, and stripping of the LSV from ankle to groin with multiple avulsions. The other group had SFJ ligation performed under local anaesthetic as an outpatient and sclerotherapy performed by Fegan's method. Both groups had recurrent or residual veins treated by sclerotherapy if requested. Both groups were comparable in terms of age and sex, both having 75% female participants.

Risk of bias in included studies

The overall quality of the studies was variable. The main criticism of these studies was that although all nine trials stated that they were randomised, only deRoos 2003; Einarsson 1993; Hobbs 1968 and Hobbs 1974 clearly stated their method of randomisation, in which the generation of the random sequence and the allocation of the interventions was adequate. Beresford 1978 stated that they used slips in sealed envelopes but the generation of these was not clear, and Doran 1975 used a pseudo-randomisation technique. This is a major failing and significantly affects the quality of the studies on critical appraisal. Specific inclusion criteria and exclusion criteria were not always recorded, although the exclusion criteria could sometimes be deduced from the inclusion criteria. The interventions were generally well described, however, in one paper (Hobbs 1968) there were discrepancies regarding the treatment that participants received. In their results, Hobbs 1974 reported that participants received sclerotherapy and a 'tie', although this is not mentioned as part of the interventions in the methods section.
The numbers of participants studied varied between 82 and 887, however, none of the trials estimated their sample size or included a power calculation in the published papers. In the two trials published in two papers, each with the initial and then late results, there was some discrepancy in the numbers of participants included (Beresford 1978; Chant 1972; Hobbs 1968; Hobbs 1974). In Hobbs 1968 the first results were published before the trial had finished recruiting which may be a potential source of bias. In Chant 1972, the initial numbers seen and considered for randomisation were different from the later publication (Beresford 1978) (339 versus 249) but the number who were actually randomised was consistent. Four of the nine trials examined the baseline groups for comparability. Outcome measures were generally reported well but in some cases their validity as a useful outcome measure can be criticised. Many of the measures used were subjective and may not be reproducible or comparable between studies. This is especially seen when subjective measures such as cosmesis are employed as endpoints. Follow-up procedures were generally well described, but only Chant 1972 and Beresford 1978 made any effort to comment on the blinding of their outcome assessor. In some cases, blinding of the observers may not have been possible but in those cases where it was, many of the studies did not clearly state whether they used blinding or not.
The quality of reporting of the results was also variable. The numbers lost to follow up were generally stated but very few papers stated the reasons why participants were lost or the methods used to reduce these losses. The explicit statement of analysis on an intention to treat basis varied and was only specifically alluded to in two trials (Doran 1975; Rutgers 1994). Most stated the statistical methods they used to analyse the results but this did not extend to using means, standard deviations and confidence intervals in the recording of the results. This influences the precision of the extent of the treatment effect.
On the whole, the conclusions drawn from the results were reasonable but internal validity was a problem with many of the studies. This was mainly due to a lack of reporting adequate generation methods of randomisation and concealment of allocation. This subsequently affects the study quality and estimation of treatment effects (Schulz 1996). External validity was generally good but again there were some doubts about the validity and reproducibility of the subjective outcome measures used. This is difficult to heavily criticise as it is widely accepted that there is a lack of good outcome measures within varicose vein assessment. Overall, only two trials (Chant 1972; Einarsson 1993) met the Jadad criteria for assessment of quality.

Effects of interventions

Our extensive search strategy found a total of nine randomised trials that were included in this review plus one study that is ongoing (Michaels 2004) and due for completion mid
2004.
Of the nine studies, six were directly comparable (Belcaro 2003; Chant 1972; Doran 1975; Einarsson 1993; Hobbs 1968; Jakobsen 1979). Belcaro 2000 compared a new technique for endovascular sclerotherapy against general anaesthetic surgery or local anaesthetic surgery and sclerotherapy. Rutgers 1994 compared general anaesthetic surgery with local anaesthetic surgery and sclerother-

apy. deRoos 2003 compared ambulatory phlebectomy and sclerotherapy. The exact surgical method used in Doran 1975 was not clearly stated but does not appear to involve ligation of incompetent perforators.

General anaesthetic surgery versus sclerotherapy

Belcaro 2003 used a complex trial design to compare different techniques of surgery and sclerotherapy. Standard sclerotherapy, high dose sclerotherapy and foam sclerotherapy were compared with 'closed-loop' surgical ligation, stab avulsion and surgery plus sclerotherapy. A total of 887 participants from 13 centres in six different countries were recruited. The study analysed recurrence of new veins and reflux/refilling times at five and 10 years. The recurrence of varicose veins at five years varied from 34% for surgery plus sclerotherapy to 48% for standard sclerotherapy. At 10 years this had increased to 37% and 56% for the same groups. The study analysed the result as ITT by considering treatment failures and losses to follow up. Stab avulsions had a significantly higher recurrence rate than the other treatments (41%; P < 0.02). A parallel group was included consisting of non-randomised participants who only underwent stripping but no details were given of the numbers or how they were recruited. However, the paper did state that the recurrence in this parallel group was 54% and significantly higher than the other groups. There was no reporting of reasons for withdrawal or losses to follow up, although the study states that they contacted 87% of the 'drop-outs' who "declared that they were asymptomatic". No cost data were reported but the authors stated that a cost-analysis report was underway.

Chant 1972 compared surgery and sclerotherapy in 249 participants. They analysed the success of treatment simply according to whether participants required further intervention. This study had a Jadad score of four. Only two major complications were reported, which were in the surgery group. These were myocardial infarction and pulmonary embolism but no deaths. The authors found that at three years, 14% of the surgery group and 22% of the sclerotherapy group had received more treatment (this included compression hosiery, 10 in each group). Three out of 13 participants in the surgery group had undergone sclerotherapy. Seven out of 14 in the sclerotherapy group had further sclerotherapy and seven out of 14 had surgery. When the loss to follow-up numbers were added and classed as treatment failures, the figures were 25% in the surgery group and 27% in the sclerotherapy group. No statistically significant differences were seen between the groups. By five years, the follow-up rate remained high and 12 surgical participants and 20 sclerotherapy participants had received sclerotherapy. Twenty-five sclerotherapy participants had undergone surgery. Thirty-three had support stockings bringing the total number of participants who were treatment failures to 40% in the sclerotherapy group and 24.2% in the surgery group. When these participants were broken down by age, in the 15 to 34 years age group there was no difference in the retreatment rates. In the age group 35 to 64 years the probability of more treatment was significantly less if they had undergone surgery (35 to 44 years P < 0.05; 45 to 64 years p < 0.001). Figures regarding retreatment rates related to age and signs of venous insufficiency (ankle oedema and flares) were also included. In participants without signs of venous insufficiency there was no difference in the retreatment rates regardless of age or initial intervention. In those with ankle oedema or flares, regardless of age, the need for more treatment was significantly greater for initial sclerotherapy (P < 0.01).

A cost assessment was carried out based on 1967 to 1968 costs. The cost of surgical treatment was estimated from the hospital costing returns, a work-study, and data from the participants' notes and individual costings. General overheads, e.g. laundry, lighting, were shared equally between all in-patients; nursing and medical staff costs particular to varicose vein surgery were estimated as two hours per patient for nurses and one hour per patient for doctors. The average cost of an operation was used as a reasonable approximation and other costs such as drugs were assessed from notes. The final estimate was £44.22 per patient for undergoing surgical treatment. For sclerotherapy patients, the cost of a session was estimated from the cost of an outpatient visit. This included medical, nursing, and secretarial costs and came to £41.50 per session. The average number of patients seen per session was 31, and the average number of sessions per patient was 7.3. The average cost of sclerotherapy per patient therefore was £9.77.

Costs to the community for people in employment were also assessed. Sclerotherapy patients had an average of 6.4 days off with a loss of earnings of £29, and surgical patients had 31.3 days off with a loss of £118. Travelling time was also calculated and involved 30 hours for sclerotherapy patients and 100 hours for surgical patients. Five years later (1977), the costs were re-evaluated and suggested costs to the NHS were £52 for sclerotherapy and £236 for surgery. Costs to the community were estimated at £100 for sclerotherapy and £405 for surgery. When assessing costs to the patient, only those in full time employment were considered. Housewives are an important element of the population that seeks treatment for varicose veins and do incur costs, such as childcare. This deficiency was acknowledged by the study.

Doran 1975 compared surgery and sclerotherapy. This study had a two year follow up and was the poorest quality trial in this group with a Jadad score of one. The single outcome measure was success or failure. At one year follow up, sclerotherapy had a significantly better success rate than surgery but by two years there was no significant difference between the two treatments. Results were hampered by large losses to follow up. The exact surgical method used was not clearly stated and did not appear to involve ligation of incompetent perforators.

Einarsson 1993 followed 164 participants randomised between surgery and sclerotherapy. Subjective and objective outcomes were measured, the objective outcome being quantitative. This study scored three on the Jadad scale. Complications in surgery were mainly wound infections (6%) and nerve injury (10%). Twenty-two per cent of participants in the sclerotherapy group had phlebitis and five of these participants had migrating throm-

bophlebitis which required surgery. This study found that both treatments had an immediate good clinical result that began to deteriorate by six months and more rapidly in the sclerotherapy group. By five years, the number of objective failures was 74% in the sclerotherapy group and 10% in the surgical group. Foot volumetry provided a quantitative estimate of treatment effect and showed that both treatments significantly improved calf muscle pump function, to a similar degree; by one year the values following sclerotherapy had fallen almost back to their original value. In the surgical group, the significant difference in improvement remained at five years and was significantly better than sclerotherapy. The results were similar when reflux was measured. Although the difference at five years in the surgical group was no longer significant compared to its original value, this difference was still significantly better than for sclerotherapy. There was also a difference seen in the mean sick leave of 20 days for surgery versus one day for sclerotherapy.

Hobbs 1968 this study had a ten year follow up of participants who were randomised between surgery and sclerotherapy. The study scored two on the Jadad scale. Complication rates were reported and included nerve injury and wound infection in the surgical group; deep vein thrombosis, pulmonary embolism and collapse also occurred. In the sclerotherapy group, the main side effects were skin staining and overdose effects, but no statistical analysis was carried out. There were few conclusions regarding the differences between the groups at one year mainly because of the way the results were reported and the lack of inclusion of any statistical analysis of the results. Reporting in the six year follow-up paper was clearer although no statistical analysis was recorded. Veins were graded as 'cured, improved or failed' (same or worse than before) according to the poorest assessment from the surgeon or patient. The graphs depicted that at one year, sclerotherapy had a very high cure rate but this rapidly fell after two years. Surgery had a lower cure rate initially at one year but the rate of its decline was much slower. At six years, 50 legs treated with sclerotherapy required surgery; 83 legs treated with surgery had sclerotherapy and eight required a second operation (seven out of the eight treated for short saphenous incompetence). The ten year results reported subjective assessment of surgery and sclerotherapy but did not report any reoperation rates. Participants were reclassified according to whether the long or short saphenous systems were involved, only perforator veins, or just dilated superficial veins. The authors concluded that dilated superficial veins and perforator veins were best treated by sclerotherapy but again figures were only given as percentages and absolute numbers were not provided. When the saphenous systems became involved, the initial success rate with sclerotherapy was high but this rapidly declined and surgery was more likely to provide a permanent cure.

Jakobsen 1979 had a three year follow-up period and compared three different interventions: general anaesthetic surgery, local anaesthetic surgery and sclerotherapy, or sclerotherapy. Both subjective and objective outcomes were measured with a good follow-up rate. There was one major complication of a pulmonary embolism in a patient who had bilateral surgery. There were no statistically significant differences in the complication rates between the groups. The degree of disability experienced was measured as time off work. This was significantly greater in the surgery only group than in the other two groups. On both subjective and objective evaluation, general anaesthetic surgery was significantly better than local anaesthetic surgery and sclerotherapy ($p < 0.0005$), which in turn was significantly better than sclerotherapy ($P < 0.0005$).

Rutgers 1994 looked at 156 participants over three years with objective and subjective outcome measures. This study scored 2 on the Jadad scale (Jadad 1996). General anaesthetic SFJ ligation and strip of the LSV to the ankle was compared with local anaesthetic SFJ ligation and sclerotherapy. Both groups were also offered sclerotherapy to any remaining varicose veins if requested. No comment was made on the numbers in each group who requested the additional sclerotherapy. Only two cases in the surgery group were reoperated on and both were for short saphenous vein incompetence. Five were operated on in the sclerotherapy group and in four cases it was for suspected LSV or SFJ reflux. An important outcome was the complication rates for surgery where 33% of participants had evidence of injury to the saphenous nerve. This led the authors to recommend that the nerve should only be stripped to the knee and they stated that this finding had changed their practice. Significant findings in favour of surgery were seen at three years in both the subjective and the objective outcome measures used. General anaesthetic surgery was significantly better than local anaesthetic surgery and sclerotherapy in terms of getting a good result as assessed by the patient, the surgeon, clinical examination and on Doppler findings (all $P < 0.05$). The authors concluded that this is because general anaesthetic allows for a better exposure and dissection of the SFJ and that stripping removes important perforators.

Ambulatory phlebectomy

deRoos 2003 compared ambulatory phlebectomy and sclerotherapy. They only included participants with lateral accessory varicose veins (LAVs). The ambulatory phlebectomy was performed under local anaesthetic. The unit of randomisation was the leg. A total of 82 participants were included with 16 participants having bilateral veins treated; no details of whether these participants had the same or different procedures on each leg were reported. The study had a two-year follow up. Recurrence rates at one year were 25% for sclerotherapy and 2.1% for the ambulatory phlebectomy. At two years, this had increased to 37.5% in the sclerotherapy group and no additional recurrences were reported in the phlebectomy group. The risk ratio for recurrence at two years was 18.0 (95% CI 2.5 to 129.53). Complications of blistering (31%) in the phlebectomy group were reported. The sclerotherapy group had a higher incidence of phlebitis (27% versus 12%) that was not statistically significant. In addition, if three sclerotherapy sessions were required (adjuvant sclerotherapy at two and four weeks), then there was a statistically significant increase in the likelihood of re-

currence at two years (3.37 times risk of recurrence p = 0.001). The study concluded that ambulatory phlebectomy was the treatment of choice for LAVs.

Endovascular sclerotherapy

Belcaro 2000 looked at a new technique of endovascular sclerotherapy (EVS) using local anaesthetic surgery compared to general anaesthetic surgery and sclerotherapy or general anaesthetic surgery alone. The study had a long follow-up period of 10 years and assessed 150 participants using objective outcomes. The Jadad score was 2. No significant complications were reported. Incompetence of below knee veins, measured by duplex ultrasonography, was found to be significantly improved in those who had undergone surgery compared with those who had undergone surgery and sclerotherapy. Arterio-venous pressure (AVP) at 10 years was also measured and showed that all three groups had significantly deteriorated from their initial values; there was no difference between sclerotherapy and surgery only but there was a significant difference between EVS and surgery with sclerotherapy in favour of the latter. It should be noted that surgery did not include stripping of the LSV and, therefore, it was not considered to be directly comparable with the other groups. A brief description of costs was given but no specific methods were included regarding the calculation of these figures.

Treatment success or failure

Treatment success or failure was assessed differently amongst the studies. Chant 1972 classified failure as anyone who had more treatment, including stockings. Einarsson 1993 defined it as those with large varicose veins or reflux in the saphenous veins. Hobbs 1968 defined failure as the leg being the same or worse than before treatment. However, a general trend can be established from the results based on data reported on assessment at follow up. At one year, three studies stated that sclerotherapy was significantly better than surgery (Doran 1975; Einarsson 1993; Hobbs 1968); in one study phlebectomy was better than sclerotherapy (deRoos 2003). After one year, the effectiveness of sclerotherapy rapidly declined so that by two years no significant differences were seen. At three years, one study reported that surgery was significantly better than sclerotherapy (Jakobsen 19796) but two others still found no significant difference at this point (Chant 1972; Hobbs 1968). By five years, three trials reported that surgery had a significantly better outcome than sclerotherapy (Beresford 1978; Einarsson 1993; Hobbs 1968). Irrespective of how it was defined in the various studies, all studies showed that sclerotherapy was worse than surgery.

Complication rates

We looked at the complication rates given for the interventions. One study (Doran 1975) did not give data and two (Belcaro 2000; Jakobsen 1979) stated that there was no statistically significant difference between interventions. Three studies (Einarsson 1993; Hobbs 1974; Jakobsen 1979) reported a pulmonary embolism rate that ranged between 0.48% and 1.25%. One trial reported a deep vein thrombosis (0.96%) (Hobbs 1968) and wound infection rates ranged between 6 and 7.25% (Einarsson 1993; Hobbs 1968). Three trials recorded saphenous nerve injury; in the two where the vein was stripped to the knee this was 10% (Einarsson 1993; Hobbs 1968) but in Rutgers 1994 the incidence rose to 33% when the vein was stripped to the ankle. Hobbs 1968 stated an overall complication rate from sclerotherapy as 6.6%, but the rate was as high as 22% for phlebitis in Einarsson 1993.

Costs

Costs were analysed in some studies but the methodology was not adequately stated (Belcaro 2000) and the figures are outdated (Piachaud 1972). Sclerotherapy was cheaper in terms of cost to the hospital and to the patient, measured in terms of money and days off work.

Although meta-analysis was precluded, a general trend of results was established. At one year, three studies stated that sclerotherapy was significantly better than surgery (Doran 1975; Einarsson 1993; Hobbs 1968). After one year its effectiveness rapidly declined so that by two years, no significant differences were seen. This evidence included data from Einarsson 1993, which measured an objective outcome, foot volumetry. At three years, one study reported that surgery was significantly better than sclerotherapy (Jakobsen 1979) but two others still found no significant difference (Beresford 1978; Hobbs 1974). By five years, all three trials reported that surgery had a significantly better outcome than sclerotherapy (Beresford 1978; Einarsson 1993; Hobbs 1974). However, the recommendations made by Beresford 1978 took age and evidence of venous insufficiency into account, and Hobbs (1974) stated that the presence of involvement in the saphenous system made a difference.

We attempted to look at the five year figures for treatment failure in the three studies; however, this again was difficult as each trial had used a different definition of treatment failure. Chant 1972 classified failure as anyone who had more treatment, including stockings. Einarsson 1993 defined it as those with recurrent large varicose veins or reflux in the saphenous veins, and in Hobbs 1968 failure was on the basis of if the leg was the same or worse than before. In spite of this, all showed that sclerotherapy had worse outcomes than surgery.

DISCUSSION

Varicose veins are a common problem and treatments have been around for decades. Extensive early research was conducted through a large randomised study in 1968 (Hobbs 1968). However, despite the volume of research and the extended period of investigation since, the evidence on the overall best treatment for varicose veins is still equivocal.

This review highlights many of the problems faced by researchers in this area. The population is large and easily accessible but, although a frequently recurrent problem, follow up can be difficult.

The next challenge is that of how to measure change in the state of the varicosities. Subjective measures are always open to bias and no single classification system has been uniformly adopted. Objective measures such as duplex ultrasonography and foot volumetry can be used but have not been universally employed in these trials, and their clinical validity is questionable.

A further consideration when evaluating the trials conducted in this area is that the population included in the trials is likely to be a selected group. Surgeons possibly use clinical criteria such as size, severity and symptoms for when they would 'offer' sclerotherapy. However, the trials are not clear whether any classification of symptoms, size, severity, for example, were used to screen participants for inclusion.

The overall quality of the trials included was generally poor, especially when recording the method of randomisation. Generation of the random sequence and allocation of the intervention was not always clearly described (only adequate for three out of seven trials), and little or no attempt was made at blinding the outcome assessors, all of which introduces potential bias. Although the sample sizes were large, (range 150 to 516 participants, mean 261) no power calculations to assess sample size were reported. Length of follow up for the trials was generally good with a range of 2 to 10 years, mean 4.86 years.

Results from statistical methods employed were not clearly documented in a fashion that allowed an accurate assessment of power or precision. This all precluded a formal meta-analysis. Even documentation on complication rates, which should have been recorded for all of these trials, was not always provided or given in a standard form. What is clear is that any intervention offered is not without real risk of complications. The majority of complications were minor, however, the major ones such as a pulmonary embolism are potentially life threatening. This is a significant risk to take for a non-life threatening illness.

A general trend seen in all the trials was only clarified when the follow-up period was extended to above three years. Of the five comparable trials, three showed that sclerotherapy was more effective in the first year. This outcome rapidly deteriorated so that by five years, surgery was the most effective intervention. Two of the trials (Chant 1972; Hobbs 1968) had findings that deviated slightly from this depending on age, venous insufficiency or the involvement of the saphenous system.

For the majority of participants with significant varicose veins, surgery, whether under local anaesthetic (as in deRoos 2003) or general anaesthetic, appeared to provide a more long-term benefit when compared with sclerotherapy, in terms of recurrence. However, when cost was included in the comparison, sclerotherapy had a clear initial advantage, although the data on which the costings were based were from the 1960s. Sclerotherapy also appeared to provide benefit in terms of participants not requiring hospital admission or as much time off work. This result was not surprising but what was not addressed was the true cost-effectiveness of these treatments, i.e. it is pointless having a cheap treatment if you have to have it repeatedly. A formal economic cost-effectiveness analysis is required to answer this question adequately.

Many of the trials evaluating sclerotherapy and surgery were relatively old and there have been several advances that may make surgical treatment safer, less expensive and more effective. These include day case surgery, stripping to the knee (as opposed to not stripping, or stripping to the ankle) and the use of tourniquets. None of the cost data took account of the advent of day case surgery, which has the potential to reduce the costs associated with surgery. Day case surgery also needs only one visit to hospital whilst sclerotherapy may require two or three, and may need repeating on a regular basis. Little comment can be given on this subject as up-to-date costing is required and the change in the surgical management of varicose veins needs to be addressed.

Quantitative power cannot be provided for this review or support its conclusions but a clear relationship between time, the intervention given and effect can be seen. This is in favour of surgery, but a clear assessment of the true relationship between surgery and sclerotherapy will require a cost-effectiveness analysis to be performed, preferably conducted alongside a randomised controlled clinical trial.

AUTHORS' CONCLUSIONS

Implications for practice

Until clearer quantitative evidence is produced there still appears to be a place for the use of both surgery and sclerotherapy in the management of varicose veins. There would appear to be a trade-off between lower costs and fewer serious complications, with sclerotherapy showing better early outcomes but surgical treatment showing more durable long-term benefits. The extent of the varicose veins, in particular the presence of venous changes and saphenous system reflux, on the basis of these trials, governs the intervention of choice. As the spectrum of signs and symptoms with which participants present is wide, it seems logical that no single treatment is universally employed. The exact lines between the use of one or the other are unclear. This evidence suggests that sclerotherapy should be offered to participants with minor superficial varicose veins not related to reflux in the saphenous systems.

Implications for research

Cost-effectiveness trials comparing surgery and sclerotherapy are needed that describe the extent of the varicose veins and use consistent criteria, evaluate validated outcome measures and include methodologically rigorous economic analyses.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Belcaro 2000

Methods	Method of randomisation: not stated. Setting and length of follow-up: evaluated at 10 days, 1, 3, 6 months initially, then every 2 years for 10 years. Duplex at every visit and ambulatory venous pressures (AVP) before and at 10 years.
Participants	150 participants: 39 EVS, 40 surgery and sclerotherapy, 42 surgery only. 29 refused treatment or follow-up and were excluded. Inclusion criteria: 40 to 60 years old, simple superficial incompetence. Exclusion criteria: Previous treatment, history of DVT, superficial thrombophlebitis, obesity, diabetes, bone or joint complaints, hypertension, CVS problems. Patients assessed by Duplex and AVP and refill times. Maximum venous outflow (MVO) also evaluated. Patients agreed not to have any venous treatment during the period of the trial.
Interventions	1) Endovascular sclerotherapy (EVS) and sclerotherapy. Under local anaesthetic a catheter was introduced into the LSV at the knee and advanced to the SFJ. The deep vein was occluded and sclerosant injected. Residual varicose veins had I/CST over the following 3 months. 2) Surgery and sclerotherapy. SFJ ligation under general or spinal anaesthetic and collateral veins marked pre-operatively only. Residual varicose veins had I/CST over the following 3 months. 3) SFJ ligation and collaterals and ligation of incompetent veins marked by Duplex.
Outcomes	Objective outcomes: Duplex, AVP. Statistics used: Sigma-Plot, nonparametric and chi-square test. No significant complications (DVT or superficial thrombosis). 96 of 121 patients completed follow-up at 10 years. Dropouts were for non medical reasons. The groups were comparable at inclusion for age, sex and clinical findings. At 10 years no SFJ incompetence was seen in those who had SFJ ligation. In group 1, 6 of 32 patients had incompetent SFJs. In group 1, 43.8% limbs had incompetent below knee veins compared to 16.1% in group 2 (P<0.05) and 36.4% in group 3 (P<0.05 versus group2 and P<0.05 versus group 1). Little information given on costs but compared to surgery, EVS cost 68% and surgery and sclerotherapy cost 122%. See additional Table 2 for further details.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Belcaro 2003

Methods	Method of randomisation: states that participants were randomised according to a random code and the code was opened after the intervention had been decided. Patients randomised between six interventions: Grp 1 - standard sclerotherapy, Grp 2 - high dose sclerotherapy, Grp 3 - multiple vein ligation, Grp 4 - stab avulsions, Grp 5 - foam sclerotherapy, Grp 6 - surgery plus sclerotherapy. Follow-up: 10 years.
Participants	887 patients seen Grp 1 - 148 patients Grp 2 - 136 patients Grp 3 - 155 patients Grp 4 - 144 patients Grp 5 - 150 patients Grp 6 - 154 patients Inclusion criteria: Age between 25 and 65 with uncomplicated primary varicose veins. Exclusion criteria: Pregnancy, obesity, post-thrombotic occlusion, history of thrombosis, coagulation disorders, diabetes, severe venous insufficiency, lipodermatosclerosis, ulcer, skin changes.
Interventions	1) Sclerotherapy. Veins larger than 3 mm in diameter were treated with 1 to 2 ml of 3% sclerosing agent, veins greater than 3 mm with 2% solution. Compression applied for 10 to 30 days post-sclerotherapy. 2) High dose slcerotherapy. Same as 1) except volume of sclerosing agent greater 3 to 6 ml of 3% sclero-agent in larger veins (greater than 3 mm). 3) Ligation. Flush ligation performed under general anaesthetic (GA), spinal or local anaesthetic (LA) using “closed loop” technique. 4) Stab avulsion. Segments (2 to 5 cm) of vein removed. 5) Foam sclerotherapy. Injection of a “tensioactive” substance (J&J-93FA) which produces a foam that displaces the blood in the vein. 6) Surgery (stripping and ligation) plus sclerotherapy.
Outcomes	Outcomes: recurrence at 5 and 10 years, Duplex, measurement of ambulatory venous pressure (AVP). See additional Table 3 for details.
Notes	States Group 4 had a failure rate equivalent to 41% of included patients (not ITT) which was significantly worse than the other groups (p<0.02).

Risk of bias

Item	Authors' judgement	Description

Belcaro 2003 (*Continued*)

Allocation concealment?	Unclear	B - Unclear

Chant 1972

Methods	Method of randomisation: consecutive slips drawn from concealed envelopes. Demographic data and a history of phlebitis, thrombosis, injury to legs and presenting symptoms such as visability, aching, itching, cramps, swelling, rashes or ulcers were collected. Patients also examined for presence of oedema, pigmentation, eczema and ulceration. Outcomes: examination by same observer, not blinded as the scars were still visible. Symptoms and signs recorded. Patients classified as improved or given further treatment. Follow up: 6 months, 1, 2 and 3 years. Age, address, occupation, parity and weight also recorded.
Participants	339 patients seen, 115 patients had sclerotherapy (I/CST), 100 patients had surgery, 90 patients were excluded. 5 year follow-up: 249 patients seen. 125 patients had sclerotherapy (I/CST), 124 patients had surgery. Inclusion criteria: varicose veins. Exclusion criteria: previous treatment (31 patients); excluded for medical and social reasons (27 patients); expressed a preference for treatment; age over 60; minimal varicose veins not warranting treatment. The two groups were similar in terms of age, height, weight, sex. Parity in women was similar. More women in CST were in social class IV and V.
Interventions	1) Surgery. SFJ / SPJ ligation, strip of LSV and ligation of incompetent perforating veins and short saphenous and lateral varicosities. 2) I/CST by Fegan's method. An economic analysis was also performed as part of the trial Cost assessment has been carried out along with this trial based on 1967-68 costs. Hospital costs: Surgery: hospital costing returns, a work-study, data from the patients' notes, individual costings. General overheads, eg. laundry, shared equally between all in-patients. Nursing and medical staff costs particular to varicose vein surgery: 2 hours per patient for nurses; 1 hour per patient for doctors. Average cost of an operation used as a reasonable approximation and other costs such as drugs were assessed from notes. Sclerotherapy: cost of a session estimated from the cost of an outpatient visit. This included medical, nursing, and secretarial costs and amounted to £41.50 per session. Average number of patients seen per session was 31; average number of sessions per patient was 7.3.
Outcomes	93% of those treated were seen at 3 years; 14% in the surgery group and 22% in I/CST group had had further treatment; there was no significant difference between the two treatments. See Table 4 and Table 5 for further details.

Chant 1972 (*Continued*)

	At 3 years, 90 of 100 patients in surgery group and 110 of 115 patients in sclerotherapy group were seen. 39 of surgery and 28 of sclerotherapy patients received treatment to both legs, but only one leg was chosen at random to be analysed, to reduce any bias. Outcome data was transformed using logit transformation and was analysed for the effect of class, sex, type of treatment and number of legs treated. None of these effects were significant. Complications: 15 surgery and 25 sclerotherapy patients had complications. Numbers weren't specified but mean outpatient attendance increased from 1.0 to 2.2. No deaths but one severe bronchospasm under general anaesthetic due to coronary artery occlusion. 34 patients accepted into trial did not have treatment [26 did not attend for treatment (18 surgery, 8 sclerotherapy) and 8 moved or were medically contraindicated]. The 26 who did not attend were judged to have needed more treatment and were added to the 3 year figures. This gives 31 in the surgical and 32 in the sclerotherapy group who needed further treatment. Waiting list time was similar between the two groups (no data), 2 moved out of the area, 6 excluded for medical reasons not apparent at time of randomisation. These patients were analysed for influence of bias and were found to be slightly but not significantly older than the treated group. 15 patients were not seen in follow up (10 surg and 5 CST). Cost: The final estimate was £44.22 for surgery. The average cost of sclerotherapy per patient was £9.77. Costs to the community: sclerotherapy patients had an average of 6.4 days off with a loss of earnings of £29. Surgical patients had an average of 31.3 days off with a loss of £118. Travelling time: sclerotherapy 30 hours, surgery 100 hours. 5 year follow-up study results: 40% of those treated by sclerotherapy and 24.2% treated by surgery had further treatment. 37 were re-treated, (25 in sclerotherapy, and 12 in surgery group). 5 initially treated by sclerotherapy went on to have surgery, the rest had sclerotherapy. 33 were given compression stockings. Authors recommended that patients under 35 years should have sclerotherapy, and those of any age who show no signs of venous insufficency have a similar outcome from either treatment. Also stated that those under 35 with signs of venous insufficency are likely to do better with surgical treatment. 2 patients collapsed during operation: one myocardial infarction (F) and one pulmonary embolism (M). Both recovered and were discharged 9 days later. 91.3% CST and 93.9% surgery were seen at 5 years. 10 in CST and 6 in surgery could not be traced.
Notes	Problems with using data on signs and symptoms (not reproducible) as an objective method and stated that there was no other reliable way.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

deRoos 2003

Methods	Method of randomisation: computer generated randomisation list in blocks of four and sealed envelopes. Outcomes: Recurrence rates at 1 and 2 years, complications. Patients were assessed using Doppler ultrasound and digital photo-plethysmography. Only patients with lateral accessory varicose veins (LAV) were included = tortuous veins on the anterolatero side of the thigh.
Participants	A total of 98 operations in 82 patients were randomised. In 16 patients both legs were included. Inclusion criteria: 18 years or over with primary LAV. Exclusion criteria: DVI, pregnancy, migrane, hypercoagulable state, dependant oedema, arterial disease, allergy to sclerosing agent or bandage.
Interventions	1) Sclerotherapy (n=49 operations). Sclerotherapy consisted of injection of 3% polidocanal solution equivalent to 1.5% sodium tetradecyl sulphate using empty vein technique. Class 1 compresison stockings applied immediately after injection and worn for 4 days and nights and Class 2 stockings during the day for 10 days. 2) Ambulatory phlebectomy (n=49 operations). Ambulatory phlebectomy consisted of injection of 1% prilocain with epinephrine as LA. 2mm stab incisions made parallel to marked veins and Oesch phlebectomy hooks used. Vein was then fixed with artery clamps and extracted until part of the varicose vein was either extracted or ruptured. This was repeated until vein extracted completely. Incisions closed using surgical tape only. Bandages applied and left in place for 5 days and Class 2 stockings worn for further 5 days.
Outcomes	See Table 6 for details.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Doran 1975

Methods	Method of randomisation: injection sclerotherapy for those who were born in a year with an even number, surgery for those born in a year with an odd number. Objective outcomes: no clear outcomes stated, judged to be success or failure depending on whether they had more treatment. 2 year follow-up at various intervals not stated.
Participants	331 patients, 182 had I/CST, 149 had surgery. In I/CST group: 98 had bilateral varicose veins. In surgery group: 73 had bilateral varicose veins. Total number of limbs - 502 (280 I/CST and 222 surgery). Inclusion criteria: primary varicose veins. Exclusion criteria: venous ulceration.

Doran 1975 (*Continued*)

Interventions	1) Fegan's method of I/CST compression for 6 weeks. 2) SFJ ligation, strip and avulsions.
Outcomes	49.6% of patients with varicose veins in the LSV region who had surgery required sclerotherapy at the end of year one, compared to 23.7% in the sclerotherapy group (no P values given). Authors suggested that it is hard to get a good result with I/CST if the limb is obese. No clear result between two groups due to large losses to follow-up. Further details in Table 7.
Notes	Statistical differences difficult due to large losses to follow-up. Only 66.9 % of patients seen at 2 years. 166 limbs lost. Method of randomisation is only pseudo-randomisation.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Einarsson 1993

Methods	Method of randomisation: blind drawing of pre-selected numbers for each treatment. Outcomes: recurrence of varicose veins and incomptent perforators and saphenous veins. Definitions used: Cured: no true varicose veins; Improved: small or reopened saphenous vein at injection site; Failed: large varicose veins, incompetent perforators or reflux in saphenous vein. Patients asked if leg had been cured, improved, unchanged or worse. Follow-up: before, 6 months, 1, 3, 5 years. Clinical tests: foot volumetry.
Participants	164 patients: 80 surgery, 84 I/CST. Baseline comparability: Surgery: 80 patients (82 legs); 58 female, 22 male; mean age 42 years (21- 65). Sclerotherapy: 84 patients (85 legs); 55 female, 29 male; age 41 years (21- 60). Site of incompetence: Surgery: LSV/SSV only 29, SV& perf. 44, perf only 9. Sclerotherapy: LSS/SSV 24, SV&perf. 53, perf only 8. Average 5 injections, range 2 to 16. Bandage used for 6 weeks longer if swelling. All but 2 patients operated on as day case.
Interventions	1) Surgery SFJ/ SPJ ligation strip and ligation of perforators and of local varicose veins. 2) Sclerotherapy using empty vein technique and compression bandages for 6 weeks.

Einarsson 1993 (*Continued*)

Outcomes	See Table 8 for attendance rate and 5 year results. Complications: See Table 9 for details. Mean sick leave: Surgery: 20 days; sclerotherapy: 1 day. Patients' subjective impression better than surgeon's objective impression as to degree of improvement. Immediate good clinical results deteriorated as early as 6 months and were worse in sclerotherapy group. Foot volumetry expelled volume (EV) at 6 months significantly increased but no difference between the groups. After 1 year mean value in sclerotherapy group had fallen almost back to values before treatment. In surgery group statistical improvement of EV remained after 5 years and was significantly better than sclerotherapy. Reflux only significantly better for 1 year in sclerotherapy group. In surgical group reflux still much improved but not statistically significant at 5 years. Difference between groups was significant.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Hobbs 1968

Methods	Method of randomisation: not clear. An envelope provided by a statistician was opened which stated intervention to be received. Patients classified as: Grp 1- LSV only, Grp 2- SSV only, Grp 3- LSV & perf veins, Grp 4 - lower leg perf. veins only. Then classified as: a) mild b) moderate c) severe. Outcomes: graded as cured, improved, same or worse. Clinically assessed. Photographed and classified. Questionnaires (90% return rate) asking which method of treatment they preferred. Follow-up: up to 27 months post treatment (average 12 months).
Participants	688 patients seen, allocated to one of four groups: Grp 1 refused (59 pat), Grp 2 rejected from trial (211), Grp 3 Surgery (207), Grp 4 I/CST (211). Six year follow-up study: 746 consecutive new patients seen and put in groups over a two year period. Grp 1 - 35 refused, Grp 2 - 211 unsuitable, Grp 3 - 250 surgery,

Hobbs 1968 (*Continued*)

	Grp 4- 250 injection. Inclusion criteria: not clear, says new patients. Exclusion criteria: minor or superficial varicose veins (115); stagnation/ ulcers with obesity or orthopaedic problems like arthritis (27); serious medical problems (20); deep vein problems (26); pregnant (11); AV fistulae (6); lymphoedema (4); on anticoagulants (2).
Interventions	1) I/CST. 287 legs in 211 patients. Both legs done in a special clinic by same doctor and nurse, 11 of these were on the oral contraceptive pill and 15 had leg ulcers. Average no. of injections was 10 per leg. 15% needed a 2nd set, (average number 4), 2% needed a 3rd set (average 2). The average number of visits was 6 per patient. 2) Surgery. SFJ ligation strip LSV/SSV and multiple extrafascial and subfascial ligation of perforating veins. (Tie appears to be ligation of termination of LSV/SSV under local anaesthetic prior to injection if there is gross incompetence).
Outcomes	Complications of surgery: cutaneous nerve injury 21, delayed wound healing 15, DVT 2, minor PE 1, anaesthestic collapse 1. Complications of I/CST: skin staining 6, overdose effects 1, acute flare up of rheumatism 1, recurrent boils 1. No of injections 21, 23, 20, 36 and 38 at a single session. In surgical group, 47% said they would have preferred I/CST. 95% of I/CST preferred that treatment. For details of 1 year results see Table 10. Six year follow up study results: No clear figures given. All results presented as graphs. At 1 year ICST more effective with a high cure rate but falls at 2 years and failure rate markedly increases in years 4, 5 and 6. This occurred even with repeated injections. At 1 year surgery showed a lower success rate but this did not fall with time. Differentiated into 3 groups: 1 - dilated superficial veins, 2 - incompetent lower leg perforator, 3 - involves LSV and SSV. Groups 1 and 2 best treated with I/CST. When superficial veins involved, early results (1 year) with I/CST are good but not maintained for longer than 2 or 3 years, so that by year 4 results are very poor. Surgery provides a more permanent cure when superficial veins involved. I/CST fails when there is gross incompetence of the SFJ. 60% of 746 pats had proximal incompetence and injection failed in third group. Cause of competence could not be obtained or maintained. Authors conclusions: surgery suitable for proximal LSV and SSV only. LSV best stripped to knee to stop nerve damage. Perforator veins best treated by I/CST. 5 weeks compression is adequate. Recommend surgery for incompetent LSV and SSV and I/CST for minor and cosmetic veins or perforator veins.
Notes	Withdrawals not stated. Comments on four different treatment types in the results, not stated in the methods section. No comment on the statistics used. Six year follow-up study results: Results slightly confusing as says it analysed 704 I/CST patients but 250 only in randomised trial. Numbers also different between the two trials.

Hobbs 1968 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Jakobsen 1979

Methods	Method of randomisation: stated as random and patients were divided into three groups according to a stratified group comparative design and randomised. Outcomes: Objective: A - no varicose veins, B - B a few less than 5 mm in diameter, C - Remaining or new veins greater than 5 mm. No main trunk or perforator incompetence, D - Main trunk or perforator incompetence. Subjective: A. no inconvenience, B. slight functional or cosmetic problem but satisfied, C. Appreciable functional or cosmetic problem better than before but dissatisfied with the result, D. Unaltered or greater inconvenience. Patients interviewed at home, hospital or work, 3 months and 3 years after treatment.
Participants	516 patients. 33 patients left study because they moved or sought treatment elsewhere prior to intervention. Grp 1 - 161 pats, Grp 2 - 165 pats, Grp 3 - 157 pats. Inclusion criteria: primary varicose veins. Exclusion criteria: previous treatment. Patients were registered according to age, sex, height, weight, type and degree of varicosity. The three groups were comparable.
Interventions	1) SFJ or SPJ ligation, strip of LSV or SSV, ligation of incompetent perforators and avulsions. 2) Local anaesthetic ligation of SFJ or SPJ and incompetant perforators as an outpatient, followed by sclerotherapy. 3: Outpatient sclerotherapy. Each extremity was evaluated separately and one limb eliminated by ballot in bilateral cases.
Outcomes	By 3 years, 5 patients had died and 3 patients were lost to follow-up. Follow-up was 100% and 98.1 % complete at these times with no significant difference between groups. Complications: one PE in group 1, but no significant difference in complications between the groups.

Jakobsen 1979 (*Continued*)

	Significant difference in time spent off work with median period of disability being 14.2, 7.6 and 0 days respectively. A Kruskal-Wallis test showed that radical surgery at 3 years was significantly better than combined treatment (P< 0.0005), and combined treatment was better than sclerotherapy (P< 0.0005).
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Rutgers 1994

Methods	Method of randomisation: not stated. Bilateral limbs treated the same. Done by two vascular surgeons: a) symptoms; b) clinical examination (inspection, palpation and tourniquet Doppler examination). Objective outcomes: Doppler ultrasound. Other endpoints: a) structured interview, b) clinical treatment, c) patient complaints (patients asked to grade them as absent, unchanged or worse), d) cosmetic result, excellent, moderate or poor. Rated by patient and one surgeon not involved in initial treatment as: 1) no visible or palp varicose veins, 2) visible or palpable varicose veins less than 5 mm, 3) varicose veins greater than 5 mm or visible incompetent main trunks. Finally grouped into good or bad. Setting and length of follow-up: 3 months, 1, 2, 3 years. Surgical Dept Netherlands.
Participants	156 patients; 181 limbs. Grp 1 - 78 pats (89 legs), 11pats bilateral. Grp 2 - 78 pats (92 legs), 14 pats bilateral. Inclusion criteria: Isolated incompetence of the LSV and local varicosities. Exclusion criteria: Not stated. 181 legs/156 pats had SFJI and local varicose veins only. Both groups were comparable for sex and age.
Interventions	1) General anaesthetic SFJ ligation strip from med malleolus to groin and avulsions. Compressive bandages for 1 day then stockings for 4 weeks. Admitted for 2/3 days. 2) I/CST first using 1% ethoxysclerol (12ml max). Local anaesthetic as an out-patient. Ligation of SFJ (crossectomy). In both groups residual varicose veins were treated by sclerotherapy if requested.

Rutgers 1994 (*Continued*)

Outcomes	Analysed on an intention-to-treat basis. Fischers exact test and Chi-square test used. Results: mostly given in graphs. Good result as judged by patient (72% versus 54%), by surgeon (61% versus 39) and for clinical examination (10% versus 47%) and for Doppler (15% versus 46%) (P<0.05). There was a significant association between the surgeon's assessment of cosmesis and Doppler assessment of reflux, but in one group only, P<0.05. No association between saphenous reflux and pats complaints or cosmetic assessment at 2 or 3 yrs. 27 limbs (33%) had saphenous nerve injury giving sensory loss of a neuritis (most neuralgia lasted for 1 year but 4 lasted for 3 years). Showed in group 2 that patient satisfaction was 90% but by 3 years 50% had developed Doppler recurrence or saphenous reflux remained. No correlation between reflux and patient's cosmetic assessment or complaints.
Notes	At 3 years, numbers available for follow up were: Grp 1 - 69/89 limbs (78%); Grp 2 - 73/92 limbs (79%). Authors stated that difference is due to a better groin exposure by general anaesthetic and clearence of important perforator tributaries by stripping. Also should only be stripped to knee.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

CST compression sclerotherapy
DVI deep venous insufficiency/deep vein incompetence
DVT deep vein thrombosis
EVS endovascular sclerotherapy
I/CST injection/compression sclerotherapy
LAV lateral accessory varicose veins
LSV long saphenous vein
PE pulmonary embolism
Perf. perforators
RT refill time
SFJ sapheno-femoral junction
SSV short saphenous vein
Tx treatment

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

Albiker 1991	Non-randomised study.
Ariyoshi 1996	Not examining outcomes identified in protocol.
Belcaro 1991	Does not fit inclusion criteria. All the patients may have surgery prior to being randomised to multiple ligations, sclerotherapy and SAVAS technique.
Belcaro 1992	Does not fit inclusion criteria. Selective saphenous vein repair and plication versus observation.
Belcaro 1993	Does not fit inclusion criteria. Selective saphenous vein repair and plication versus observation.
Berta 1980	Non-randomised study.
Bishop 1986	Non-randomised study.
Bradbury 1993	Non-randomised study.
Corcos 1996	Prospective cohort non-RCT.
Corcos 1997	Prospective cohort non-RCT, duplicate of above.
Creton 1999	Cohort study on recurrent varicose veins.
Dimakakos 1995	Retrospective cohort.
Dunn 1995	Cohort study.
Fentem 1976	Evaluating conservative treatments only.
Fischer 1973	Non-randomised study.
Fitridge 1999	Randomised but does not fit inclusion criteria.
Garde 1995	Retrospective cohort.
Georgiev 1990	Cohort study.
Gibbs 1999	Randomised but examines recurrent not primary varicose veins.
Greer 1990	Descriptive study.
Griffith 1989	Randomised but does not fit inclusion criteria.
Haeger 1967	Non-randomised systematic study.

(*Continued*)

Hilbe 1998	Non-randomised cohort study.
Jarvinen 1976	Non-randomised observational study.
Kodellas 1996	Descriptive study.
Lennihan 1975	Non-randomised study.
Liew 1994	Cohort study compares in-patient and day surgery only.
McAdam 1976	Observational study.
Melrose 1979	Randomised but does not fit inclusion criteria.
Natali 1992	Comparing sclerotherapy only.
Neglen 1986a	Non-randomised study
Neglen 1986b	Socio-economic evaluation not associated to any RCT
Neglen 1993	Partially randomised. The study populations are a combination of randomised patients and non-randomised patients.The non-randomised patients were the excluded patients in the trial (Einarsson 1993).
O'Leary 1996	Non-randomised study.
O'Shaughnessy 1989	Retrospective study.
Perrin 1993	Retrospective cohort on recurrent veins.
R'mond-Martimb'u1990	Prospective cohort non-randomised study.
Ramesh 1995	Prospective cohort.
Raraty 1999	Randomised but does not fit inclusion criteria.
Rautio 2002	Randomised but does not fit inclusion criteria.
Rintoul 1975	Retrospective study.
Rivlin 1975	Review of management, an observational study.
Schanzer 1994	Consecutive, non-randomised patients.
Seddon 1973	Non-randomised study.

(*Continued*)

Shouler 1989	Randomised but does not fit inclusion criteria.
Trempe 1991	Retrospective study.
Turton 1997	Observational study.
Twardowskasaucha1992	Non-randomised study.
Vin 1996	Prospective cohort.
Wagner 1996	Non-randomised study.
Yamaki 1998	Non-randomised cohort study.

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

Michaels 2003

Trial name or title	Assessment of cost-effectiveness of the treatment of varicose veins.
Methods	
Participants	Patients undergoing treatment for varicose veins.
Interventions	Three sub-groups of patients: conservative treatment, surgery and sclerotherapy.
Outcomes	Incremental cost effectiveness of each treatment based on patient's symptomatic, investigative and demographic features. Patient and societal priorities for treatment assessed using a 'willingness to pay' technique.
Starting date	01 Oct 1998
Contact information	Mr Jonathan Michaels Department of Vascular Surgery, Sheffield Vascular Institute, Northern General Hospital, Herries Road, Sheffield, UK. S5 7AU Tel. 0114 271 4968 Fax. 0114 271 4747 Email: michaels@aol.com
Notes	Single centre trial.

DATA AND ANALYSES

This review has no analyses.

WHAT'S NEW

Last assessed as up-to-date: 23 August 2004.

4 November 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 1, 1999

Review first published: Issue 4, 2004

15 November 2005	Amended	Edits made to acknowledgements and contribution of authors.
10 August 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Kathryn Rigby reviewed articles, extracted data, co-wrote the review.

Simon Palfreyman reviewed articles, extracted data, co-wrote the review.

Catherine Beverley searched databases, handsearched journals and extracted data.

Jonathan Michaels reviewed articles, arbitrated over unclear cases of inclusion/exclusion of articles and co-wrote the review.

DECLARATIONS OF INTEREST

Michaels JA and Palfreyman SJ are undertaking a study of the treatments of varicose veins, funded by the NHS Health Technology Assessment Programme.

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Internal sources

- Sheffield Vascular Institute, UK.

External sources

- NHS R&D HTA Programme, UK.
- Sheffield Vascular Institute, Northern General Hospital, Sheffield, UK.
- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK.

NOTES

This review is one of two concerning surgery for varicose veins on its own or compared with other techniques. The protocol for this review is called 'Surgery for varicose veins', unique ID 833499072911380755. The first review is called 'Surgery for varicose veins: use of tourniquet'.

INDEX TERMS

Medical Subject Headings (MeSH)

*Sclerotherapy; Randomized Controlled Trials as Topic; Varicose Veins [surgery; *therapy]

MeSH check words

Humans