Endovenous Laser Treatment (EVLT™) for Varicose Veins

November 2003

MSAC application 1059

Assessment report

ISBN 0 64282283 2

ISSN (Print) 1443-7120

ISSN (Online) 1443-7139

First printed August 2004

Electronic copies of this report can be obtained from the Medical Service Advisory Committee's internet site at:

http://www.msac.gov.au/

Hard copies of the report can be obtained from:

The Secretary
Medical Services Advisory Committee
Department of Health and Ageing
Mail Drop 107
GPO Box 9848
Canberra ACT 2601

Enquiries about the content of the report should be directed to the above address.

The Medical Services Advisory Committee is an independent committee which has been established to provide advice to the Commonwealth Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform Government decisions about which medical services should attract funding under Medicare.

This report was prepared by the Medical Services Advisory Committee with the assistance of Ms Linda Mundy, Dr Petra Bywood, Ms Tracy Merlin, Mr Brent Hodgkinson and Professor Janet Hiller from the Health Technology Assessment Unit, Department of Public Health, University of Adelaide; and Mr Rob Fitridge, Department of Surgery, University of Adelaide. Ms Jo Mason from Mason Edit edited this report. The report was endorsed by the Commonwealth Minister for Health and Ageing on August 10th 2004.

Publication approval number: 3285

Contents

Tables

Figures

Executive summary

The procedure

The proposed intervention is endovenous laser treatment of varicose veins (EVLT™). EVLT™ is minimally invasive and can be performed in an outpatient setting under local anaesthetic. The procedure involves the insertion of a laser fibre into the lumen of the saphenous vein, followed by the application of thermal energy, which occludes the vein. The laser fibre is gradually withdrawn, occluding the entire length of the vein and hence abolishing venous reflux.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Commonwealth Government to strengthen the role of evidence in health financing decisions in Australia. The MSAC advises the Commonwealth Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. A team from the Health Technology Assessment Unit, Department of Public Health, University of Adelaide was engaged to conduct a systematic review of the literature on endovenous laser treatment for varicose veins. An advisory panel with expertise in this area then evaluated the evidence and provided advice to the MSAC.

The MSAC's assessment of endovenous laser treatment (EVLT™) for varicose veins

Level IV evidence (case series) on endovenous laser treatment (EVLT™) for varicose veins was available for inclusion in this assessment. None of these studies included a control group.

In the absence of controlled studies, data on clinical outcomes from EVLT™ were indirectly compared to the stripping and junction ligation arm of randomised controlled trials.

An indirect comparison can only provide a simple presentation of the safety and effectiveness outcome rates for both EVLT™ and stripping procedures, and should not be used as a method of determining the comparative effectiveness of the two procedures. To make a sound comparison of EVLT™ and stripping, patients should be selected in the same way, operations should occur under similar conditions and in the same time period, and discharge and treatment protocols and clinical outcomes should be assessed and defined in the same manner. Uncontrolled studies are affected by bias and confounding and are potentially misleading; valid conclusions regarding their effectiveness cannot be made.

There is a real need for a randomised controlled trial to be conducted in this area, in view of the number of patients undergoing varicose vein surgery and on waiting lists, and the lack of currently available comparative data. The National Institute for Clinical Excellence (NICE) has reported that a randomised controlled trial of EVLT™ versus conventional stripping surgery was scheduled to start in June 2003 at Leeds, United Kingdom.

Clinical need

There were no studies available that describe the prevalence of varicose veins in the general Australian population. The estimated prevalence in the general population of countries of similar ethnic composition to Australia ranges from 10.4 to 23.0 per cent for men, and from 29.5 to 39.0 per cent for women. The wide range may be due to inter-study variability concerning three key features: the age structure of the population, the definition of varicose veins and the methodology used to measure venous disorders. From July 2001 to June 2002 the Medicare Benefits Schedule (MBS) processed 11,965 claims for the combined treatment options of stripping and/or junction ligation of the sapheno-femoral and/or the sapheno-popliteal vein. This is the comparator on the MBS and may indicate the level of clinical need for the procedure under review.

Safety

Good quality data were not available to assess the safety of endovenous laser treatment for varicose veins in comparison with vein stripping and ligation. However, all case series assessed in this review did report fully on the outcomes of enrolled EVLT™ patients. Self-limiting symptoms such as pain, ecchymosis, induration and phlebitis were common adverse events associated with endovenous laser treatment. More serious adverse events such as deep vein thrombosis and incorrect placement of the laser in vessels were uncommon. Deep vein thrombosis occurred in one patient and was an ongoing problem at the end of follow-up, requiring long-term administration of medication. Incorrect laser placement occurred in two patients, ie 0.3 per cent of total limbs treated in the full studies. This serious operator error resulted in no long-term harmful effects; however, the potential for significant damage was real.

Paraesthesia, infection, bruising and haematoma were common adverse events associated with stripping of the saphenous vein. The highest paraesthesia rate of 30.3 per cent was reported after ankle to groin surgery at 1 year. The more serious thrombotic adverse events were uncommon, with one pulmonary embolism and superficial venous thrombosis reported in three patients. Although infection was a common adverse event, reported rates within studies were low, ranging from 2 to 8 per cent of limbs.

It would appear from the available literature that EVLT™ is as safe as the current practices of stripping and/or junction ligation.

Effectiveness

There were no studies available that assess the effectiveness of endovenous laser treatment for varicose veins in comparison with saphenous vein stripping and junction ligation.

From the low-level case series evidence available, it would appear that EVLT™ is of benefit to the majority of patients in the short term. However, the main treatment outcome of

abolition of reflux is assessed differently in the two procedures, and is therefore not comparable. Reflux is assessed in the saphenous vein alone after EVLT™, but in the entire limb after stripping and junction ligation. In addition, there is confusion regarding the definition of recurrent varicose veins, which may be true recurrent veins, residual incompetent veins or new incompetent veins.

Peer reviewed studies have reported the occlusion of saphenous veins and the abolishment of venous reflux in 80 to 100 per cent of limbs treated with EVLT™. The study with the longest follow-up period (24 months) reported occlusion of the greater saphenous vein in 93.4 per cent of limbs treated with EVLT™. Re-treatment of patients is low, with reported rates between 1.3 and 4.0 per cent; rates for recanalisation are similarly low. Symptoms associated with varicose veins, such as pain and oedema, were reduced after EVLT™.

Abolition of reflux was observed in 85.9 to 92.2 per cent of limbs that had undergone ankle to groin stripping; and in 57.1 to 100 per cent of limbs that had undergone groin to knee stripping. The study with the longest follow-up period (5 years) reported abolition of reflux in 85.9 per cent of limbs after groin to ankle stripping. Recurrent varicose veins in the absence of reflux were reported at rates of 12.5 to 33.3 per cent after stripping and junction ligation.

Whether EVLT™ is as, or more, effective than the stripping and ligation procedure cannot be determined.

Cost-effectiveness

An analysis of the cost-effectiveness of this procedure was not possible due to a lack of high quality evidence on clinical effectiveness. It should be emphasised that the EVLT™ procedure does not treat tributary varicosities, and patients will require follow-up treatment for these. During the stripping procedure, tributary varicosities are ligated and avulsed. Therefore, a formal cost analysis would need to account for the whole procedure, including follow-up treatment of tributary vessels.

Recommendation

Endovenous laser treatment for varicose veins appears to be safe in comparison to stripping of varicose veins but there is insufficient evidence pertaining to effectiveness and cost-effectiveness, therefore MSAC recommended that public funding should not be supported for this procedure at this time.

The Minister for Health and Ageing accepted this recommendation on August 10th 2004.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of endovenous laser treatment (EVLT™), which is a therapeutic technology for varicose veins. The MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. The MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

The MSAC's terms of reference and membership are at Appendix A. The MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

An advisory panel with expertise in vascular surgery, radiology, general practice and consumer issues was established to evaluate the evidence and provide advice to the MSAC from a clinical perspective. Membership of the advisory panel is provided at Appendix B.

This report summarises the assessment of current evidence for endovenous laser treatment (EVLT™) of varicose veins.

Background

Endovenous laser treatment (EVLT™) for varicose veins

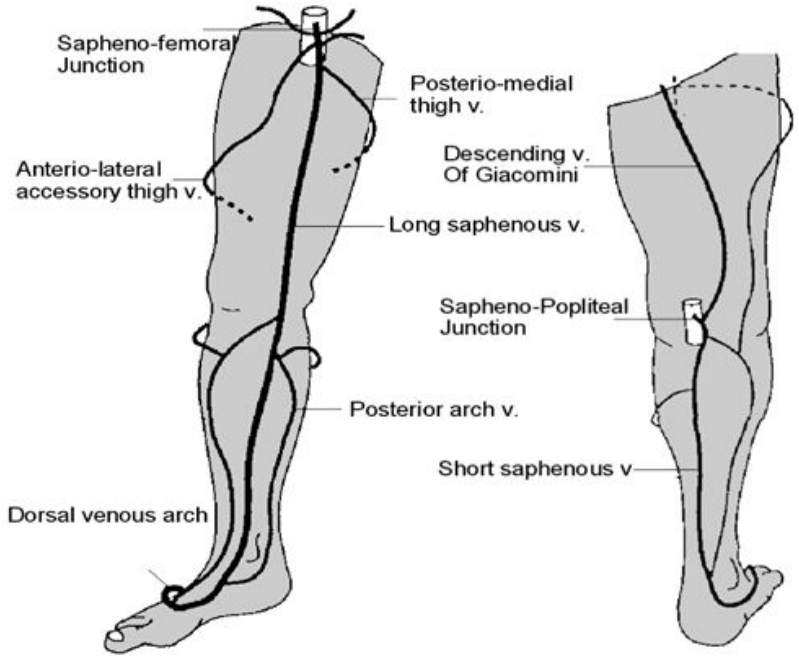
There is no universal clinical definition of varicose veins. In general, the term varicose veins refers to incompetent veins of the greater or lesser saphenous systems, that appear distended, tortuous and often protuberant (Lofgren 1985). The greater or long saphenous vein (GSV) begins along the inner arch of the foot and ascends along the inner side of the leg, through the thigh, to the femoral vein. The lesser or small saphenous vein (LSV) begins at the outer arch and ascends along the Achilles' tendon to the popliteal vein (Gabella 1995) (Figure 1). Blood returning to the heart from the legs must work against gravity. Muscle contractions in the lower legs, aided by elastic vein walls, pump blood back to the heart, and one-way valves in the veins close to prevent back flow. Varicose veins generally occur when there is impaired function of the valves and the vein walls are inelastic, resulting in retrograde blood flow. Leaky valves cause the blood to reflux away from the heart. As a consequence, blood pools in the veins, giving them an enlarged and distended appearance, a condition known as venous reflux or incompetency. Varicose veins can, however, occur without significant incompetency of the veins (Harrison 2001; Lofgren 1985).

The exact cause of varicose veins is unknown. Several risk factors have been identified, including increasing age, gender, family history, obesity and pregnancy (Callam 1994). Frequently reported symptoms include localised swelling, heaviness, cramp and aches, chronic localised fatigue, itching and tingling. One or more of these symptoms and the presence of clinically demonstrated reflux are indications for surgical intervention (Bradbury et al 1999). More serious symptoms, eg thrombophlebitis[1], bleeding, venous dermatitis and skin pigmentation as a prelude to venous ulceration[2], also require surgical intervention (Wolf & Brittenden 2001). Symptoms may be exacerbated by prolonged periods of standing or sitting (Bradbury et al 1999; Lofgren 1985; Tisi & Beverley 2003). Varicose veins should be differentiated from superficial telangiectasias, commonly referred to as spider or thread veins (NICE 2000).

[1] Thrombophlebitis is the formation of a blood clot (thrombus) inside the inflamed vein.

[2] Venous insufficiency may result in the exudation of blood from the veins into the surrounding tissue, causing oedema. The level of oxygenation is reduced in the tissue and ulceration may occur.

Figure 1 Greater and lesser saphenous veins

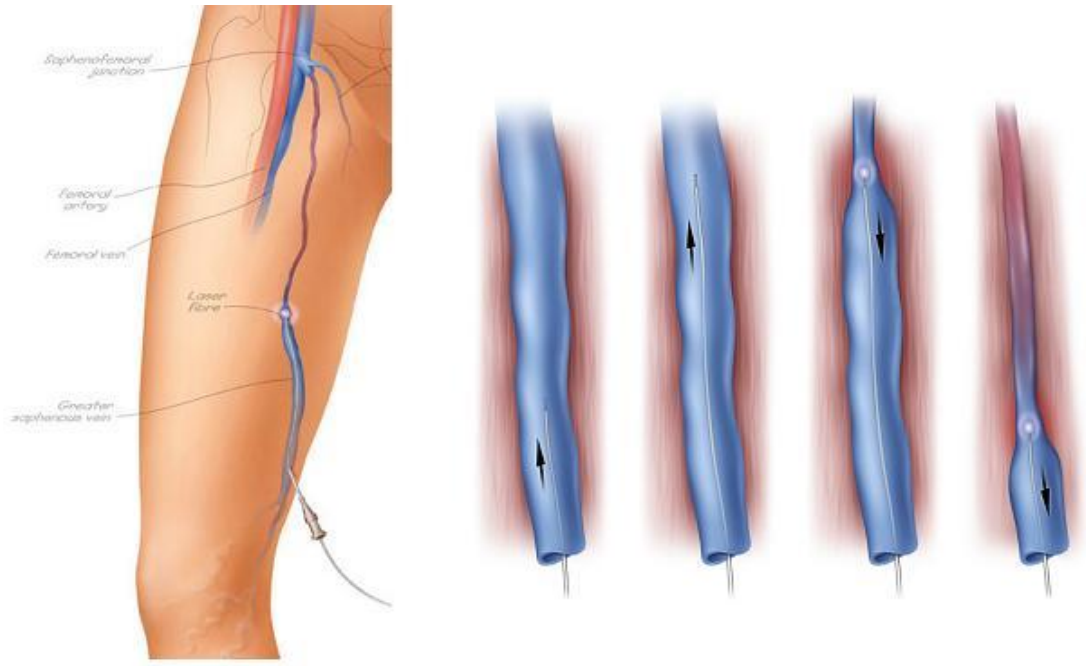


Source: Cuzzilla 2003, printed with permission

The use of endovenous lasers is a recent development in minimally invasive techniques for the treatment of varicose veins. EVLT™ may be performed in an outpatient setting with the patient receiving local anaesthesia or light sedation. Patients undergo a duplex ultrasound examination to determine the source(s) of reflux and venous incompetency. The distance between the point of entry and the sapheno-femoral or sapheno-popliteal junction is also determined by ultrasound.

Access to the greater or smaller saphenous veins is achieved via a percutaneous incision at the ankle or below the knee, either by needle puncture or the stab wound-Mueller hook approach. A guide wire or cannula is introduced into the vein and manoeuvred towards the junction, under ultrasound guidance. A catheter is introduced along the guide wire. The guide wire is then removed. Patients receive perivascular tumescent infiltration of anaesthetic along the length of the vein, which dissipates the heat generated during the procedure, reducing tissue damage. A diode laser fibre is then inserted into the catheter to approximately 1–2 cm below the sapheno-femoral or sapheno-popliteal junction, with positioning confirmed by ultrasound. Thermal laser energy is applied along the length of the vein and the laser fibre is withdrawn slowly in 3–5 mm increments. Compression is applied by hand to accomplish vein wall apposition. The laser fibre is removed, followed by the catheter, and the wound is cleaned and dressed (Figure 2). Graduated compression stockings are applied and patients are instructed to walk immediately following the procedure. Tributary varicosities cannot be treated during the EVLT™ process and will always require follow-up treatment with sclerotherapy approximately 4 weeks after the EVLT™ procedure (Diomed Ltd 2001; Min et al 2001; Navarro et al 2001).

Figure 2 Endovenous laser treatment of varicose veins, insertion of laser fibre and withdrawal, showing vein ablation



Source: Diomed 2001, used with permission

Intended purpose

Endovenous laser treatment for varicose veins is indicated for adult patients with clinically documented primary venous reflux, confirmed by duplex ultrasound, of the greater or lesser saphenous veins. These patients have exhausted other conservative treatment measures and sclerotherapy is considered unlikely to be successful.

The device is contraindicated in patients:

- who are pregnant;
- with deep vein thrombosis;
- who are breast-feeding;
- who are unable to ambulate;
- with known hypercoagulability;
- with arterial occlusive disease; and
- who are in general poor health.

Furthermore, patients with tortuous veins or atypical venous anatomy may not be suitable candidates for EVLT™.

Clinical need / burden of disease

Venous disease includes a spectrum of disorders from varicose veins to chronic leg ulcerations, and has been described as 'one of the most common conditions affecting humankind' (Callam 1994). Prevalence rates of varicose veins have been reported in several narrative reviews on the epidemiology of varicose veins (Adhikari et al 2000; Callam 1994; Fowkes et al 2001). However, since many of the studies that were included in these reviews were conducted in selected groups of workers, clinic patients or populations in developing countries, prevalence rates from these studies may not be representative of Australian populations. For this review, literature examining the prevalence of varicose veins in adult populations in developed countries was assessed using the strict criteria provided in Box 1.

Box 1 Study selection criteria for prevalence

Research question

What is the prevalence of varicose veins in the general Australian population?

Selection criteria	Inclusion criteria
Population	General population over the age of 18 years in developed countries
Outcome	Prevalence — proportion of the population with varicose veins
Study design	Cohort studies, cross-sectional surveys (with random sampling), whole population studies

In total, nine studies evaluating the prevalence of varicose veins in the general community were assessed for this review. Profiles of these studies are provided in Appendix C. Four studies were conducted in Europe, one in Israel, one in the USA, one in New Zealand and two in Britain. Several papers were published by the Edinburgh Vein Study group (Allan et al 2000; Bradbury et al 1999; Evans et al 1997, 1998, 1999; Ruckley et al 2002), which contained the same data on prevalence. Only one paper from this group, containing the most relevant data, was included for analysis (Evans et al 1999). Eight of the studies assessed were cross-sectional surveys with response rates ranging from 53.8 to 90.0 per cent. There was one prospective cohort study (Brand et al 1988).

Prevalence rates for men and women in developed countries are shown in Table 1. Studies reported prevalence rates for varicose veins in the general community ranging from 6.8 to 39.7 per cent in men and from 24.6 to 39.0 per cent in women. This wide range in prevalence rates may reflect the inter-study variability of three key factors: the age structure of the study population, the definition of varicose veins, and the methodology used to measure venous disorders.

The age structure of the study populations varied markedly between studies. The upper age limits in all studies ranged from 60 to 90+ years, whereas the lower age limits typically ranged from 18 to 45 years (Abramson et al 1981; Brand et al 1988; Evans et al 1999; Franks et al 1992; Laurikka et al 1993; Preziosi et al 1999; Prior et al 1970; Sisto et al 1995). One study examined varicose veins in an older population, aged 66–96 years (Canonico et al 1998).

Apart from the one Finnish study (Sisto et al 1995), which had lower prevalence rates for both men (6.8%) and women (24.6%), most of the studies showed prevalence rates of 10.4 to 23.0 per cent in men and 29.5 to 39.0 per cent in women. Evans et al described much

higher rates for men (39.7%) and women (32.2%) in subjects aged 18–64 (Evans et al 1999). Most studies reported an increase in the prevalence of varicose veins with age. However, this was not apparent across studies and it is possible that age effects were masked by the differences in methodology.

Table 1 Prevalence of varicose veins in the general population

Study	Location	Study design	Age group	Prevalence (%)	
				Men	Women
Abramson et al (1981)	Israel	Survey	>20	10.4	29.5
Brand et al (1988)	USA	Cohort study	40–89	23.0	29.9
Canonico et al (1998)	Italy	Survey	66–96	17.0	35.2
Evans et al (1999)	Scotland	Survey	18–64	39.7	32.2
Franks et al (1992)	England	Survey	35–70	17.0[a]	31.0[a]
Laurikka et al (1993)	Finland	Survey	>40	18.0	32.0
Preziosi et al (1999)	France	Survey	45–60	18.3	30.6
Prior et al (1970)	New Zealand	Survey	20–70+	20.0	39.0
Sisto et al (1995)	Finland	Survey	>30	6.8	24.6

[a] Data were calculated from the paper

Although there is no standard definition of varicose veins, most studies described varicose veins as 'dilated (or distended), tortuous veins'. One study selected a broad definition that included any dilated, tortuous veins (Canonico et al 1998), three studies specifically excluded minor varicosities, such as hyphenwebs and reticular veins (Abramson et al 1981; Brand et al 1988; Laurikka et al 1993), and four studies failed to provide a definition (Franks et al 1992; Preziosi et al 1999; Prior et al 1970; Sisto et al 1995). In one population of 18 to 64-year-olds, prevalence was 32.2 per cent in women and 39.7 per cent in men when only pronounced varicosities were considered and 80 per cent when isolated reticular and hyphenweb veins were included (Evans et al 1999). The degree of severity is likely to influence the extent to which subjects are classified as having varicose veins, either in a self-administered questionnaire or by clinical examination.

The methodology used to assess varicose veins also varied between studies, from simple subjective assessment (self-administered questionnaires) to a range of more objective measures including clinical examination, photographic validation, and more recent quantification of venous function such as continuous wave Doppler ultrasonography and duplex scanning. Abramson et al (1981) demonstrated a poor correlation between questionnaire results and subsequent examination. Studies that rely on questionnaires alone may give misleading data on prevalence. For example, some questionnaires included only one question, such as 'Have you had anything wrong with your legs?', 'Do you have varicose veins?' or 'Have you ever had large veins or varicose veins in your legs?' (Franks et al 1992; Madar et al 1986). Studies that rely on clinical examinations alone may also be subject to observer error. For example, inter-observer variability between 12 physicians who examined varicose veins in Paris policemen ranged from 14.0 to 40.0 per cent (De Backer 1997). More

recent methods of assessing venous reflux include continuous wave Doppler ultrasonography or duplex scanning, which are objective, non-invasive and repeatable. However, the greater sensitivity of the duplex scanning technique, which narrows the distinction between normal and abnormal venous function, may lead to increased detection of asymptomatic subjects; this may underlie the relatively high rate of prevalence reported in the Edinburgh Vein Study (Evans et al 1999).

Except for the Edinburgh Vein Study (Evans et al 1999), most studies reported higher prevalence rates in women. Higher female prevalence may be attributable to longer life expectancy in women or to the impact of previous or existing pregnancies. In Australia it is predominantly women who seek treatment for varicose veins, as shown by the preponderance of claims processed by the Health Insurance Commission (HIC) for the different varicose vein services (HIC data 2002–03). The demand for treatment peaks in the 45–54 years age group for both men and women. An example of the age and gender distribution of the number of claims processed by the Medical Benefits Scheme (MBS) for two items is shown in Table 2, specifically items 32508 and 32511, as defined in pages 11 and 12 of this report.

Table 2 Number of claims processed by HIC for MBS items 32508 and 32511 (combined) for the treatment of varicose veins, July 2002 to June 2003

Age range	Male	Female	Total number of claims
5-14	9	7	16
15–24	83	83	166
25–34	278	769	1,047
35–44	624	1,988	2,612
45–54	958	2,092	3,050
55–64	891	1,542	2,433
65–74	424	648	1,072
75–84	104	209	313
>=85	2	14	16
Total	3,373	7,352	10,725

Although varicose veins are not life threatening and rarely a serious problem, complications from venous disease can be disabling. Moreover, it is a dynamic disease process and recurring treatment for chronic varicose veins may place considerable demand on health services. For example, Table 3 shows the number of claims processed by HIC for the re-treatment of varicose veins using the current 'gold standard', vein stripping and junction ligation (HIC data 2002–03, MBS items 32514 and 32517, defined on pages 11 and 12).

Table 3 Number of claims processed by HIC for MBS items 32514 and 32517 for the re-treatment of varicose veins, July 2002 to June 2003

Age range	Item 32514	Item 32517	Total number of claims
15–24	5	3	8
25–34	51	14	65
35–44	273	72	345
45–54	531	135	666
55–64	529	185	714
65–74	277	87	364
75–84	56	24	80
>=85	4	0	4
Total	1,726	520	2,246

Data describing the prevalence of varicose veins in an Australian population were not available. The international literature indicates that varicose veins are relatively common. A 'best estimate' of prevalence rates was determined from three studies that used a similar definition of varicose veins and included a clinical examination of subjects aged over 20 years. These studies reported prevalence rates ranging between 10.4 and 23.0 per cent in men and 29.5 and 39.0 per cent in women (Abramson et al 1981; Brand et al 1988; Prior et al 1970). The degree of severity of varicose veins is likely to influence the demand for health services. Although the prevalence rate of milder forms of varicose veins is high, this may not necessarily translate to clinical burden. Clearer definitions of varicose veins that reflect degrees of severity are needed to determine prevalence rates and more accurately assess the clinical burden on the community.

Existing procedures

The clinical decision-making process concerned with the treatment and diagnosis of patients with varicose veins is presented in Figure 3.

A broad range of treatment options for varicose veins is available depending on the severity of symptoms and the clinical assessment of the patient. Patients require a physical examination to determine the source of venous incompetency, frequently followed by a duplex scan examination which will confirm if reflux is present (Wolf & Brittenden 2001).

Relief of symptoms may be achieved with self-help mechanisms such us exercise, weight loss, elevation of limbs, avoidance of long periods of time sitting or standing, and the use of compression stockings (NICE 2000).

Sclerotherapy[3] (the ablation of the vessel by the injection of a sclerosing agent) is the treatment of choice for telangiectasias or primary varicose veins where reflux has not been demonstrated. However, in varicose veins where reflux has been demonstrated to be the cause of vascular insufficiency, it is suggested that sclerotherapy is unlikely to give a durable result (Bergan et al 2001). A novel approach to the ablation of the saphenous vein is the technique of echo-sclerotherapy, where the sclerosing agent is forcibly mixed with air to

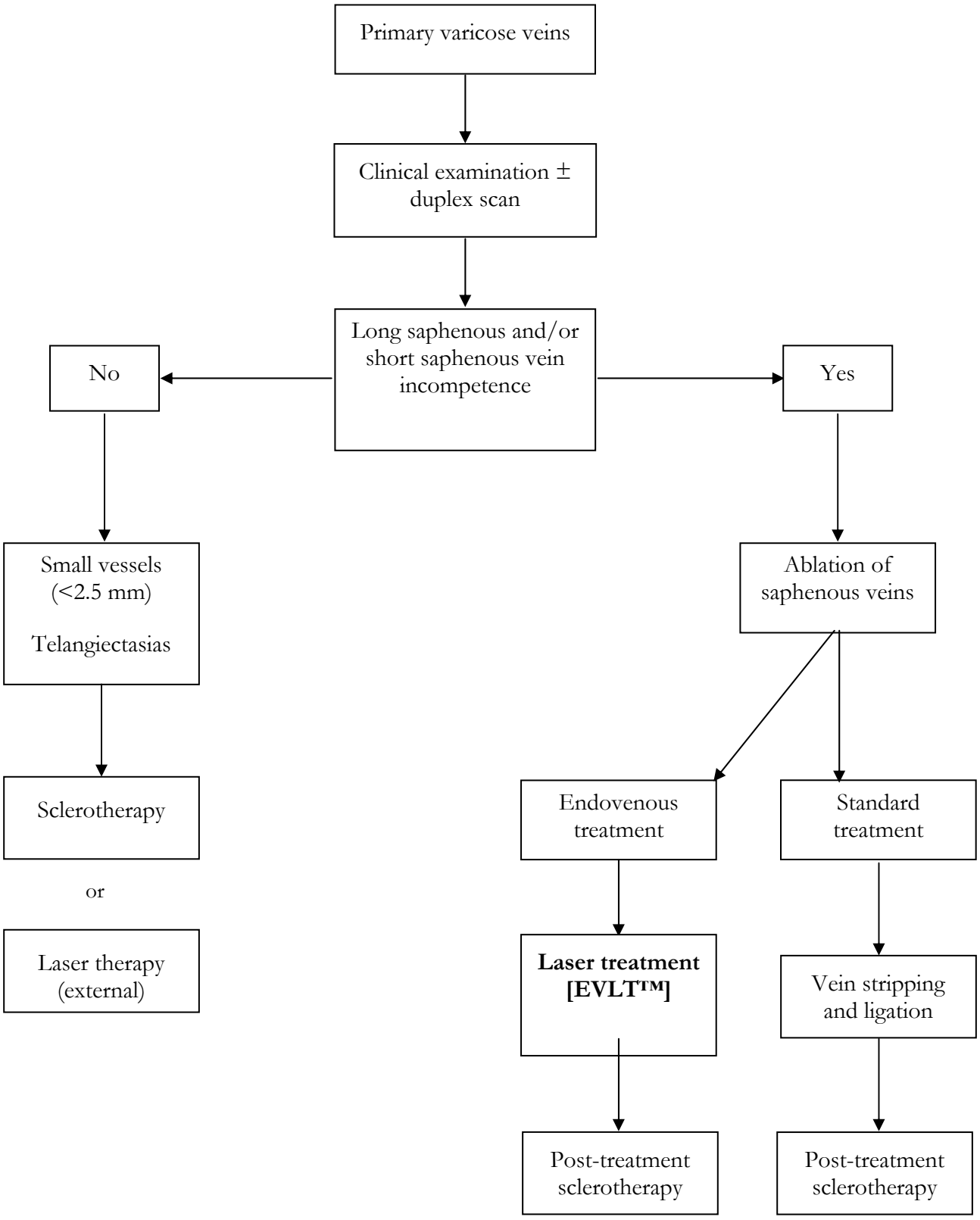
[3] MBS item numbers 32500 and 32501

produce a foam which is then injected, under ultrasound guidance, into the incompetent varicose vein (Campbell 2002). This technique has yet to receive widespread acceptance with vascular clinicians. Similar results for small varicosities (<1 mm diameter) may be achieved with hand-held lasers applied externally (Weiss & Dover 2002b). In addition, small non-reflux varicose veins on the surface of the leg may be treated under local anaesthetic using ambulatory phlebectomy (American College of Phlebology 1998; Bergan et al 2001).

A similar technique to EVLT™ is the VNUS Medical Technologies' closure system, which utilises radio-frequency wavelengths. A heat-generating catheter is inserted into the vein and positioned below the sapheno-femoral junction. The catheter is heated to 85°C and slowly withdrawn down the length of the vein, causing contraction of the vein wall and, ultimately, destruction of the vessel (Manfrini et al 2000; Sybrandy & Wittens 2002). This technique is not listed on the MBS.

The mechanisms of occlusion differ between the techniques. The EVLT™ and VNUS Medical Technologies' systems occlude the vein by generating heat, causing the vein to shrink and collapse. In sclerotherapy, a sclerosing agent (saline or sodium tetradecyl sulphate) irritates the endothelium of the treated vein, causing it to thrombose. External compression assists in collapsing and sealing the vessel, which is eventually absorbed by the surrounding tissue.

Figure 3 Clinical decision tree for endovenous laser treatment (EVLT™) for varicose veins



Comparator

Endovenous laser treatment is suggested after self-help mechanisms and primary interventions have been exhausted and have failed to ease pain and prevent further damage. Therefore, the most appropriate comparator is the standard intervention currently used to treat these types of patients, specifically vein stripping and junction ligation.

Ligation[4] involves tying off the vessel at either the sapheno-popliteal or the sapheno-femoral junction (Ruckley 1983; Wolf & Brittenden 2001). Ligation alone usually results in a high recurrence of the varicose vein, which may then be treated using sclerotherapy (Bergan et al 2001). In most cases ligation is performed in conjunction with stripping.

Surgical stripping of varicose veins is seen by many to be the treatment of choice (Wolf & Brittenden 2001). Stripping of varicose veins involves making one or two incisions, under general anaesthetic, one in the patient's groin and, if necessary, one at the knee or ankle. The uppermost section of the saphenous vein is ligated flush with the femoral vein and the tributary veins are ligated and avulsed, reducing the need for secondary follow-up treatment such as sclerotherapy. Since recurrence is likely to occur in the communicating veins, ligation of the collaterals is a key factor in limiting the rate of re-treatment of varicose veins (Chandler et al 2000b). The stripper is inserted into the lumen of the vein and passed either down from the incision in the groin or up from the incision at the knee. The excised end of the saphenous vein is placed over the head of the stripper and the gentle withdrawal of the shaft pulls the saphenous vein towards the point of entry, from where it can subsequently be removed (Bergan et al 2002; Lofgren 1985). Occasionally it may be difficult to pass the stripper down to the knee due to the tortuous nature of the vein and only a small section of the vein can be dissected at its origin (Lofgren 1985). Perforate invagination (PIN) is a modification of conventional stripping. PIN stripping inverts the vein and thus avoids the tissue trauma associated with pulling the conventional stripper down the vein. Rates of neuralgia, paraesthesia and haematoma appear to be reduced using the PIN method (Durkin et al 1999).

Marketing status of the technology

Endovenous laser treatment (EVLT™) is registered on the Australian Register of Therapeutic Goods (TGA listing AUSTL 80993 and AUSTL 80938).

Current reimbursement arrangement

Currently there is no listing on the MBS for EVLT™. Stripping and junction ligation of the greater and/or lesser saphenous vein are listed on the MBS
(1 November 2002) under the following item numbers:

Item 32508:	Complete dissection at the sapheno-femoral OR sapheno-popliteal junction – 1 leg – with or without either ligation or stripping, or both, of the long or short saphenous veins, for the first time on the same

[4] MBS item numbers 32508 and 32511

leg, including excision or injection of either tributaries or incompetent perforating veins, or both (Anaes.) (Assist.)
Fee: $432.65

Item 32511: As above but complete dissection at the sapheno-femoral AND sapheno-popliteal junction
Fee: $643.20

Item 32514: Ligation of the long or short saphenous vein on the same leg, with or without stripping, by re-operation for recurrent veins in the same territory – 1 leg – including excision or injection of either tributaries or incompetent perforating veins, or both (Anaes.) (Assist.)
Fee: $751.40

Item 32517: As above but ligation of the long AND short saphenous vein on the same leg in either territory.
Fee: $967.55

Approach to assessment

Review of literature

The medical literature was searched to identify relevant studies and reviews for the period between 1966 and September 2003. Table 4 describes the electronic databases that were used for this search.

Table 4 Bibliographic databases

Electronic database	Time period
AustHealth	1997 – 9/2003
Australian Medical Index	1996 – 9/2003
Australian Public Affairs Information Service (APAIS) - Health	1990 – 9/2003
Cinahl	1977 – 9/2003
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	1966 – 9/2003
Current Contents	1993 – 9/2003
Embase	1974– 9/2003
Pre-Medline and Medline	1966 – 9/2003
ProceedingsFirst	1993 – 9/2003
PsycInfo	1983 – 9/2003
Web of Science – Science Citation Index Expanded	1995 – 9/2003

Three separate literature searches were conducted to encompass outcomes for EVLT™, stripping and/or junction ligation, and prevalence of varicose veins. The search terms used are listed in Table 5. The full search strategies (based on a PubMed platform) are provided in Appendix D.

Table 5 Search terms utilised

Area of inquiry	Search terms
EVLT search	MeSH Venous insufficiency, Saphenous vein, Varicose veins, Ultrasonography-doppler, Laser surgery, Vascular surgery Text words Saphenous near vein*, varicose vein*, venous insuff*, varicose near vein*, endovenous*, endovasc*, venous near (reflux or incomp* or insuff*), laser*, EVLT
Stripping search	MeSH Venous insufficiency, Saphenous vein, Varicose veins, Vascular surgery, Randomized controlled trial, Meta-analysis Text words Saphenous near vein*, varicose vein*, venous insuff*, varicose near vein*, venous near (reflux or incomp* or insuff*), junction near lig*, strip*
Prevalence	MeSH Prevalence, Cross-sectional studies, Incidence, Cohort studies, Epidemiology, Natural history, Population characteristics, Risk Text words epidemiol*, prevalen*, inciden*, natural histor*, risk*, cohort*, population, registry or register

The following electronic internet databases were searched for relevant literature up until September 2003:

- NHMRC- National Health and Medical Research Council (Australia) http://www.health.gov.au/nhmrc/
- Australian Department of Health and Ageing http://www.health.gov.au/
- Scirus – for Scientific Information Only http://www.scirus.com
- Trip database http://www.tripdatabase.com
- Current Controlled Trials metaRegister http://controlled-trials.com/
- International Network for Agencies for Health Technology Assessment http://www.inahta.org/
- National Library of Medicine Health Services / Technology Assessment Text http://text.nlm.nih.gov/
- National Library of Medicine Locator Plus database http://locatorplus.gov
- New York Academy of Medicine Grey Literature Report http://www.nyam.org/library/greylit/index.shtml
- US Department of Health and Human Services (reports and publications) http://www.os.dhhs.gov/

More recent listings of reports were located and searched at the websites of health technology assessment agencies and specialist vascular websites up until September 2003 (see Appendix E).

All reference lists of included articles were searched for additional relevant source material.

Inclusion criteria

Due to the lack of comparative data between EVLT™ and stripping and/or junction ligation, an indirect comparison of the two procedures was conducted. Separate searches were conducted for EVLT™ and stripping and/or junction ligation. Due to the wealth of literature on stripping and/or junction ligation, only data from meta-analyses or the stripping arm of randomised controlled trials were assessed.

The following inclusion criteria were applied to the identified citations for assessing the safety and effectiveness of EVLT™:

- adult patients over the age of 18 years, with clinically documented primary venous reflux of the greater or lesser saphenous veins in whom sclerotherapy is unlikely to be successful;
- the proposed intervention uses endovenous laser treatment as described by Diomed (Diomed Ltd 2001) for the treatment of varicose veins;
- the studies were conducted on humans; and
- there were no language restrictions.

The following inclusion criteria were applied to the identified citations for assessing the safety and effectiveness of stripping and/or junction ligation of varicose veins:

- adult patients over the age of 18 years, with clinically documented primary venous reflux of the greater or lesser saphenous veins;
- only the stripping and/or junction ligation arm of meta-analyses of randomised controlled trials or individual randomised controlled trials;
- the studies were conducted on humans; and
- the language was restricted to English for assessing safety and effectiveness.

The selection criteria for assessing the prevalence of varicose veins are given in Box 1. Publication language was restricted to English for these studies.

The study selection process went through six phases (Figure 4).

Figure 4 Study selection process

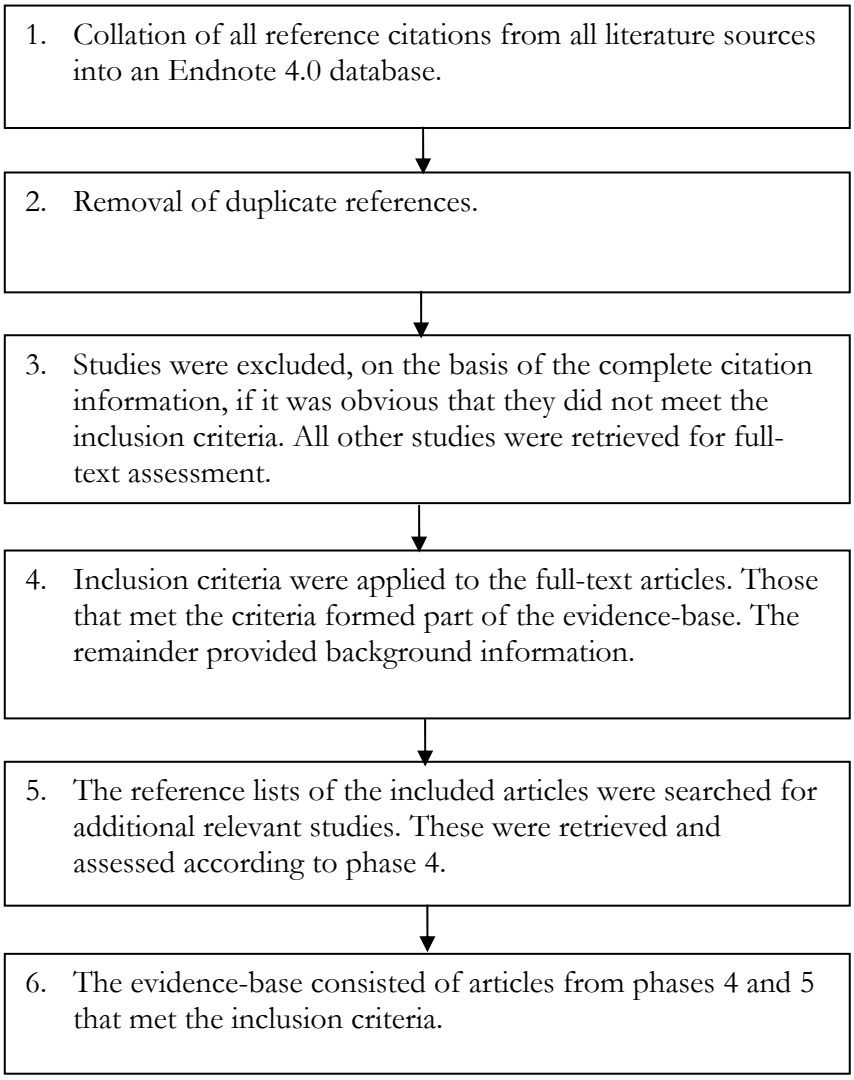


Table 6 provides a breakdown of the study selection process in terms of the number of citations retrieved and retained at each phase.

Table 6 Number of citations initially retrieved and then retained at each phase

Search	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6
Prevalence	7,359	5,644	77	9	0	9
EVLT™ safety and effectiveness	7,523	5,855	71[a]	17[a]	0[b]	17
Stripping safety and effectiveness	1,164	966	64	18	0[b]	18
Total	16,046	12,465	212	44	0	44

[a] Total includes 8 abstracts; [b] No pearling references were relevant

Seventeen safety and effectiveness studies, including eight abstracts from conference proceedings, satisfied the inclusion criteria for EVLT™ and were assessed. Abstracts from conference proceedings did not contain enough information to be critically appraised.

Outcomes were assessed from these abstracts but presented separately. Fifty-four papers were excluded after phase 3.

Eighteen safety and effectiveness studies satisfied the inclusion criteria for stripping and/or junction ligation and were assessed. Outcomes were assessed and presented separately from the EVLT™ outcomes. Forty-six papers did not meet the inclusion criteria and were excluded after phase 3.

Details of those studies which did not answer the inclusion criteria for EVLT™ and stripping studies are outlined in Appendix F.

Data extraction and analysis

Data were extracted from the included articles by a single researcher using tables developed *a priori* and outcome definitions provided in the original protocol.

Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes in the individual studies, including numerator and denominator information.

Differences in the frequency of pre- and post-EVLT™ outcomes were calculated using McNemar's chi square test, where applicable, at $p<0.05$.

All statistical calculations and testing were undertaken using the biostatistical computer package Stata version 7.0 (Stata Corporation 2001).

Critical appraisal

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000).

These dimensions (Table 7) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature identified as informing a particular intervention. The last two require expert clinical input as part of their determination.

Table 7 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design.*
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *p*-value or, alternatively, the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of only clinically important effects in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

*See Table 8

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in Table 8.

Table 8 Designations of levels of evidence*

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials
II	Evidence obtained from at least one properly-designed randomised controlled trial
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group
IV	Evidence obtained from case series, either post-test or pre-test/post-test

*Modified from NHMRC 1999

The appraisal of controlled trials pertaining to EVLT™ for varicose veins would have been undertaken using a checklist developed by Downs and Black (1998). This checklist is suitable for trials and cohort studies and has been psychometrically assessed to have overall high internal consistency, good test–retest and inter-rater reliability, and high criterion validity (Downs & Black 1998). However, no controlled trials were available for assessment. Uncontrolled studies were assessed for their quality using the checklist developed by Young and colleagues for case series (Appendix G) (Young et al 1999). In addition, this checklist was used to assess the stripping arm of the randomised controlled trials included in this assessment. The size of the effect and the clinical relevance of the evidence cannot be determined without the presence of a control group.

Expert advice

An advisory panel with expertise in vascular surgery, radiology, general practice and consumer issues was established to evaluate the evidence and provide advice to the MSAC from a clinical perspective. In selecting members for advisory panels, the MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the advisory panel is provided at Appendix B.

Results of assessment

The literature revealed that no studies compared the use of EVLT™ with that of conventional stripping and/or junction ligation. An indirect comparison of the two procedures was therefore conducted with the results presented separately. An indirect comparison provides a simple presentation of the safety and effectiveness outcome rates for both procedures. It should not be used as a method of determining the comparative effectiveness of the procedures, as the results may be potentially misleading. To compare two procedures, patients should be selected in the same way, operations should occur under similar conditions and in the same time period, and discharge and treatment protocols and clinical outcomes should be assessed and defined in the same manner. The only circumstance whereby indirect comparisons may be valid for determining effectiveness is when two interventions are compared through their relative (adjusted) effect versus a common comparator (usually from two randomised controlled trials). Naive (unadjusted) indirect comparisons, in which the results of individual arms between trials are compared as if from a single trial, are liable to bias and 'should be avoided wherever possible' (Song et al 2003).

Seventeen studies were identified for inclusion in this assessment of the safety and effectiveness of EVLT™. Nine of these studies were presented as full, descriptive studies (Boné & Navarro 2001; Chang & Chua 2002; Gérard et al 2002; Min et al 2001, 2003; Navarro et al 2001; Proebstle 2002b; Proebstle, Lehr et al 2002; Proebstle et al 2003) and the remaining eight were abstracts presented at scientific meetings (Goldman 2002; Mackay 2002; Min 2001, 2003a, 2003b, 2003c; Navarro & Boné 2001, 2002). The eight abstracts did not contain enough information to be critically appraised so their safety outcomes were assessed and presented separately. All of these studies were descriptive case series and therefore of low methodological quality (level IV evidence). Sample sizes in the full studies ranged from 20 to 423 patients, with 20 to 504 saphenous veins treated, respectively. Sample sizes in the eight abstract studies ranged from 20 to 344 patients, with 20 to 389 saphenous veins treated, respectively. Profiles of these studies are provided in Appendix C.

All the full studies performed EVLT™ on the greater saphenous vein, with the exception of Proebstle et al (2003), who conducted EVLT™ on the lesser saphenous vein. Of the abstract studies, only Mackay (2002) and Min (2003c) carried out EVLT™ on the lesser saphenous vein. In addition, Min (2003c) presented outcomes of EVLT™ on anterior-lateral tributaries.

Possible duplication of results may have occurred in the studies by Min (Min et al 2001, 2003; and abstracts 2001, 2003a), Boné and Navarro (2001; and Navarro and Boné abstracts 2001, 2002) and Proebstle (2002b; and Proebstle, Lehr et al 2002). However, this was not clearly stated. The study by Chang and Chua (2002) used ligation at the sapheno-femoral junction in addition to EVLT™ of the greater saphenous vein. Three studies required translation into English: the study by Boné and Navarro (2001) from Spanish, Gérard et al (2002) from French, and Proebstle, Sandhofer et al (2002) from German.

Eighteen studies were identified for inclusion in this assessment of the safety and effectiveness of stripping and/or junction ligation (Butler et al 2002; Campanello et al 1996; Durkin et al 1999, 2001; Dwerryhouse et al 1999; Fitridge et al 1999; Hammarsten et al 1990; Jones et al 1996; Lacroix et al 1999; Lurie et al 2003; Munn et al 1981; Neglén et al 1993; Rautio, Ohinmaa et al 2002; Rutgers & Kitslaar 1994; Sarin et al 1992, 1994; Sykes et

al 2000; Wilson et al 1997). All of these studies were the stripping and/or junction ligation arm of a randomised controlled trial. The analysis of the stripping arm of randomised controlled trials, in isolation, results in these studies being considered as case series and as such, any data extracted from them is Level IV evidence. Most of these trials did not report conventional effectiveness outcomes such as those reported in the EVLT™ studies. The majority of stripping studies compared the finer points of surgical technique, such as the amount of blood loss or the degree of bruising, and therefore follow-up was short-term. Sample sizes in the stripping studies ranged from 13 to 100 greater saphenous veins treated. Follow-up ranged from 1 week to 5 years. Profiles of these studies are provided in Appendix C.

Twelve of the stripping studies were performed on the greater saphenous vein from groin to knee and five studies were performed on the greater saphenous vein from ankle to groin. No stripping studies were performed on the lesser saphenous vein. The study by Neglén et al (1993) did not report the numbers of patients who experienced groin to knee or ankle to groin surgery.

The studies by Durkin et al (2001), Dwerryhouse et al (1999) and Sarin et al (1994) were longer-term follow-up studies to those of Durkin et al (1999), Jones et al (1996) and Sarin et al (1992), respectively.

Is it safe?

Post-operative infection

EVLT™

None of the EVLT™ studies, including abstracts, reported any cases of post-operative infection.

Stripping

Seven of the 18 stripping studies reported post-operative infection. Five of these studies concerned groin to knee stripping (Table 9). The better quality study by Sarin et al (1992) reported infection in one limb out of 49 (2.0%). A poorer quality study by Durkin et al (1999) reported 2.7 per cent of limbs with post-operative infection in addition to 5.4 per cent of limbs with post-operative cellulitis. Over all the studies, infection was reported to occur in 2 to 8 per cent of limbs.

Table 9 Number of infection events after stripping

Study	Level of evidence	Quality score	Length of follow-up	Population	Post-operative infection rate
Groin to knee stripping					
Sarin et al (1992)	II	3/3	Follow-up of 3 months	49 GSV[a] in 33 patients	1/49 (2.0%) limbs
Lurie et al (2003)	II	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	72 hours 2/36 (5.6%) limbs 1 week 1/36 (2.8%) limbs 3 weeks 1/36 (2.8%) limbs
Wilson et al (1997)	II	2/3	Follow-up of 6 weeks	14 GSV[a]	1 week 1/14 (7.1%) limbs
Sykes et al (2000)	II	1/3	Follow-up of 6 weeks	25 GSV[a] in 25 patients	1/25 (4.0%)
Durkin et al (1999)	II	1.5/3	33/37 (89.2%) limbs followed up for 1 week	37 GSV[a]	Infection 1/37 (2.7%) Cellulitis 2/37 (5.4%)
Ankle to groin stripping					
Munn et al (1981)	II	1.5/3	57/100 (57%) patients followed up for 2.5–3.5 years	100 GSV[a] in 100 patients with bilateral varicose veins	8/100 (8.0%) limbs[b]
Both groin to knee and ankle to groin stripping					
Neglén et al (1993)	II	2.5/3	59/74 (80%) limbs followed up for 1 year 57/74 (77%) limbs followed up for 5 years	74 GSV[a]	4/74 (5.4%) limbs

[a] GSV = greater saphenous vein, [b] results reported as infection/haematoma, see Table 16

Laser-related adverse events

EVLT™

Three of the nine full EVLT™ studies reported laser-related adverse events (Table 10). The better quality study by Proebstle et al (2003) reported that treatment could not be completed in one patient out of 33 (3.0%) due to the incorrect placement of the laser into the popliteal vein instead of the lesser saphenous vein. This patient required administration of low molecular weight heparin for 10 days post-treatment. Gérard et al (2002) also reported one patient out of 20 (5.0%) in whom the laser was incorrectly positioned in the superficial femoral vein instead of the greater saphenous vein. Both of these patients reported no long-term harmful effects. Only one study, by Chang and Chua (2002), reported laser-related burns in 12 out of 252 (4.8%) patients, which healed by the end of the follow-up period (mean 19 months).

None of the abstract studies reported laser-related adverse events.

Table 10 EVLT™ laser-related adverse events

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of adverse events
Proebstle et al (2003)	IV	2.5/3	Median follow-up 6 months (range 3–12 months)	41 LSV[a] in 33 patients	Incorrect positioning of the laser 1/33 (3.0%) patients 1/41 (2.4%) limbs
Chang & Chua (2002)[b]	IV	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[c] in 149 patients	Burns 3 weeks 12/252 (4.8%) limbs 6 months 6/252 (2.4%) limbs Final outcome 12–28 months 0/252 (0.0%) limbs
Gérard et al (2002)	IV	2/3	Follow-up of 30 days	20 GSV[c] in 20 patients	Incorrect positioning of the laser 1/20 (5.0%) patients

[a] LSV = lesser saphenous vein, [b] study by Chang & Chua (2002) used ligation in addition to laser treatment,
[c] GSV = greater saphenous vein

Stripping

Laser-related adverse events are not a relevant side effect of the stripping procedure.

Thrombotic events

EVLT™

Only one of the nine full-text studies reported a thrombotic event (Table 11). Proebstle et al (2003) reported one case of deep vein thrombosis, five weeks after EVLT™ in the lesser saphenous vein. This patient, who had a pre-existing thrombophilic condition, polycythemia vera, and had previously experienced thrombotic events, may represent poor patient selection. The patient was treated with low molecular weight heparin and the oral anticoagulant, phenprocoumon. The condition was ongoing at the end of the study's follow-up period.

Table 11 Rate of thrombotic events post-EVLT™

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of thrombotic events
Proebstle et al (2003)	IV	2.5/3	Median follow-up 6 months (range 3–12 months)	41 LSV[a] in 33 patients	Deep vein thrombosis 1/41 (2.4%) limbs Ongoing at end of follow-up

[a] LSV = lesser saphenous vein

Stripping

Thrombotic events were reported in two of the 18 stripping studies (Table 12). A good quality study by Lurie et al (2003) reported superficial venous thrombosis in one to two limbs (2.8 to 5.6%), stripped groin to knee, depending on the time of follow-up. An equally good study by Neglén et al (1993) reported one patient who experienced a pulmonary embolism.

Table 12 Rate of thrombotic events after stripping

Study	Level of evidence	Quality score	Length of follow-up	Population	Rate of thrombotic events
Groin to knee stripping					
Lurie et al (2003)	II	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Superficial venous thrombosis 72 hours 1/36 (2.8%) limbs 1 week 2/36 (5.6%) limbs 3 weeks 1/36 (2.8%) limbs
Both groin to knee and ankle to groin stripping					
Neglén et al (1993)	II	2.5/3	59/74 (80%) limbs followed up for 1 year 57/74 (77%) limbs followed up for 5 years	74 GSV[a]	Pulmonary embolism 1 patient, cannot ascertain total number of patients

[a] GSV = greater saphenous vein

Pain

EVLT™

Five of the nine full-text EVLT™ studies reported low to moderate pain (Table 13). The better quality study by Proebstle, Lehr et al (2002) reported that all enrolled patients experienced pain. The other good quality study by Min et al (2001) reported that 6 per cent of patients experienced pain and required the use of analgesics for 1 to 2 weeks, when all symptoms were resolved. Another good quality study by Min et al (2003) found that 90 per cent of patients experienced discomfort in the form of a tightness or pulling sensation along the course of the treated GSV, 3 to 10 days after EVLT™.

One of the eight abstract studies (Min 2003b) reported that patients experienced tenderness and discomfort in 92 per cent of limbs, 4 to 7 days after EVLT™ (Table 13). It stated neither how long symptoms persisted nor if patients were prescribed analgesics.

Table 13 Pain associated with EVLT™

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of pain events
Min et al (2001)[a]	IV	3/3	Mean follow-up of 6 months (range 1–9 months)	90 GSV[b] in 84 patients	5/84 (6.0%) patients Required analgesics for 1–2 weeks
Proebstle, Lehr et al (2002)	IV	3/3	Follow-up of 28 days	31 GSV[b] in 26 patients	26/26 (100.0%) patients experienced slight to moderate pain
Min et al (2003)[a]	IV	2.5/3	Mean follow-up of 17 ± 11 months (range 1–39 months)	504 GSV[b] Results only presented for 499 limbs in 423 patients	381/423 (90.0%) patients experienced tightness or pulling
Proebstle et al (2003)	IV	2.5/3	Median follow-up 6 months (range 3–12 months)	41 LSV[c] in 33 patients	20/41 (48.8%) limbs were painful Median duration 1 week (range 0.2–4 weeks) 18/33 (54.5%) patients required analgesics
Gérard et al (2002)	IV	2/3	Follow-up of 30 days	20 GSV[b] in 20 patients	20/20 (100.0%) low to moderate pain requiring an average of 8 analgesic tablets up until day 8
Min (2003b)[a]	IV	Abstract	Follow-up of 12 months	150 GSV[b] in 131 patients	138/150 (92.0%) limbs were tender 4–7 days after EVLT™

[a] Possible duplication of results between studies, [b] GSV = greater saphenous vein, [c] LSV = lesser saphenous vein

Stripping

Pain or tenderness was reported by three of the 18 stripping studies (Table 14). The better quality study by Rautio, Ohinmaa et al (2002) only reported the average number of analgesics required by patients who had undergone knee to groin stripping, not the number of individual patients who experienced pain. The other two studies reported that patients experienced pain or tenderness in 14.0 to 28.0 per cent of limbs.

Table 14 Incidence of pain or tenderness from stripping

Study	Level of evidence	Quality score	Length of follow-up	Population	Rate of pain or tenderness
Groin to knee stripping					
Rautio, Ohinmaa et al (2002)	II	3/3	Mean follow-up of 50 days	13 GSV[a]	Average daily number of analgesics required[b] 1.3 ± 1.09 tablets for 14 days
Lurie et al (2003)	II	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Tenderness 72 hours 9/36 (25.0%) limbs 1 week 10/36 (27.8%) limbs 3 weeks 9/36 (25.0%) limbs
Ankle to groin stripping					
Munn et al (1981)	II	1.5/3	57/100 (57%) patients followed up for 2.5–3.5 years	100 GSV[a] in 100 patients with bilateral varicose veins	Pain 14/100 (14.0%) limbs

[a] GSV = greater saphenous vein, [b] analgesic administered was 600 mg ibuprofen

Bleeding complications

EVLT™

Three of the nine full-text EVLT™ studies reported bleeding complications associated with EVLT™ (Table 15). Chang and Chua (2002) and Gérard et al (2002) both recorded the development of a haematoma immediately after EVLT™ in 4.8 and 100 per cent, respectively, of limbs enrolled in their studies. Chang and Chua (2002) reported that at 6 months follow-up, haematomas had still not resolved in 2.4 per cent of limbs. The lower rate of bleeding complications reported by Chang and Chua (2002) compared to Gérard et al (2002) may be due to the concomitant use of ligation and EVLT™. The follow-up period in the study by Gérard et al (2002) was too short to ascertain if all symptoms had been successfully resolved. The better quality study by Min et al (2003) reported 24 per cent of limbs experienced bruising at 1-week follow-up, with all symptoms resolved by the 1-month follow-up.

One of the eight abstract studies by Min (2003b) reported bruising, other than bruising around the site of laser entry, after EVLT™ at 1-week follow-up, in 36 out of 150 (24.0%) limbs (Table 15).

Table 15 Rate of bleeding complications associated with EVLT™

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of bleeding complication events
Min et al (2003)[a]	IV	2.5/3	Mean follow-up of 17 ± 11 months (range 1–39 months)	504 GSV[b] Results only presented for 499 limbs in 423 patients	Bruising 121/504 (24.0%) limbs
Chang & Chua (2002)[c]	IV	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[b] in 149 patients	Haematoma 3 weeks 12/252 (4.8%) limbs 6 months 6/252 (2.4%) limbs Final outcome 12–28 months 0/252 (0.0%) limbs
Gérard et al (2002)	IV	2/3	Follow-up of 30 days	20 GSV[b] in 20 patients	Haematoma 20/20 (100.0%) limbs
Min (2003b)[a]	IV	Abstract	Follow-up of 12 months	150 GSV[b] in 131 patients	Bruising 1 week 36/150 (24.0%) limbs

[a] Possible duplication of results, [b] GSV = greater saphenous vein, [c] Study by Chang & Chua (2002) used ligation in addition to laser treatment

Stripping

Seven of the 18 stripping studies reported bleeding complications (Table 16). The better quality study by Rautio, Ohinmaa et al (2002) reported 30.8 per cent of limbs with a haematoma after knee to groin stripping. Three studies reported the mean or median blood loss for the total patient group rather than the number of individual patients who experienced that outcome. Blood loss ranged from 49.5 to 125.0 mL during groin to knee stripping; however, one study (Sykes et al 2000) reported a range of 20 to 300 mL. Four studies reported the mean or median area of bruising for the total patient group rather than the number of individual patients who experienced that outcome. Bruising ranged from 91.5 to 195.5 cm^2 in limbs that had undergone groin to knee stripping. In five studies haematoma was reported to occur in 4.0 to 52.9 per cent of limbs at the end of follow-up which ranged from 1 week to 4 months.

Table 16 Rate of bleeding complications associated with stripping

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of bleeding complications
Groin to knee stripping					
Rautio, Ohinmaa et al (2002)	II	3/3	Mean follow-up of 50 days	13 GSV[a]	Haematoma 4/13 (30.8%)
Lurie et al (2003)	II	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Haematoma 72 hours 14/36 (38.9%) 1 week 18/36 (50.0%) 3 weeks 12/36 (25.0%) 4 months 3/36 (8.3%)
Butler et al (2002)	II	2/3	Follow-up of 1 week	68 GSV[a]	Haematoma 36/68 (52.9%) Median blood loss for patient group as a whole 50 mL (IQR[b] 30–80) Median area of bruising for patient group as a whole 166 cm^2 (IQR[b] 77–261)
Wilson et al (1997)	II	2/3	Follow-up of 6 weeks	14 GSV[a] in 14 patients	Bleeding from wound in groin 1 week 1/14 (7.1%) Bruising 6 weeks 1/14 (7.1%) Median area of bruising for patient group as a whole 195.5 cm^2 (range 89–301)[c] Mean blood loss for patient group as a whole 49.5 mL (range 17–75)[c]
Durkin et al (1999)	II	1.5/3	33/37 (89.2%) limbs followed up for 1 week	37 GSV[a]	Mean area of bruising for patient group as a whole 91.5 cm^2 (IQR[b] 68–153)
Sykes et al (2000)	II	1/3	Follow-up of 6 weeks	25 GSV[a] in 25 patients	Haematoma 1/25 (4.0%) Median area of bruising for patient group as a whole 179 cm^2 (range 24–669) Median blood loss for patient group as a whole 125 mL (range 20–300)

Ankle to groin stripping					
Munn et al (1981)	II	1.5/3	57/100 (57%) patients followed up for 2.5–3.5 years	100 GSV[a] in 100 patients with bilateral varicose veins	Infection/ haematoma 8/100 (8.0%) limbs[d]

[a] GSV = greater saphenous vein, [b] IQR = inter-quartile range, [c] results are median (range), [d] results reported as infection/haematoma, see Table 9

Ecchymosis

EVLT™

Seven of the nine full EVLT™ studies reported ecchymosis, or discolouration, beneath the skin in patients during the early post-EVLT™ period (Table 17). Most of the symptoms were viewed as self-limiting, with a duration of 1 to 4 weeks. The three better quality studies by Min et al (2001), Proebstle (2002b) and Proebstle, Lehr et al (2002) reported that 100 per cent of patients enrolled in their studies experienced ecchymosis. The two studies by Proebstle (2002b) and Proebstle, Lehr et al (2002) each reported one patient who experienced hyper-pigmentation. This may be the same patient, as the population of these two studies may overlap. Proebstle, Lehr et al (2002) reported that ecchymosis was still visible at the end of the 28-day follow-up period. In the lower quality study by Chang and Chua (2002), symptoms in two limbs (0.8%) persisted beyond 6 months due to hyper-pigmentation.

None of the abstract studies reported on ecchymosis outcomes.

Table 17 Incidence of ecchymosis post-EVLT™

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of ecchymosis events
Min et al (2001)	IV	3/3	Mean follow-up 6 months (range 1–9 months)	90 GSV[a] in 84 patients	90/90 (100.0%) limbs 84/84 (100.0%) patients 1–2 weeks duration
Proebstle (2002b)[b]	IV	3/3	Does not state follow-up period	95 GSV[a] in 77 patients	2 weeks post-EVLT™ 77/77 (100.0%) patients 95/95 (100.0%) limbs 1/95 (1.1%) limbs experienced hyper-pigmentation.
Proebstle, Lehr et al (2002)[b]	IV	3/3	Follow-up of 28 days	31 GSV[a] in 26 patients	26/26 (100.0%) patients 1/26 (3.8%) patients experienced hyper-pigmentation still visible at end of follow-up.
Proebstle et al (2003)	IV	2.5/3	Median follow-up of 6 months (range 3–12 months)	41 LSV[c] in 33 patients	17/41 (41.5%) limbs Median duration 2 weeks (range 1–4 weeks)

Boné & Navarro (2001)	IV	2/3	Follow-up of 12 months	125 GSV[a] in 105 patients	24 hours 125/125 (100.0%) limbs 7 days 125/125 (100.0%) limbs 1 month 0/125 (0.0%) limbs
Chang & Chua (2002)[d]	IV	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[a] in 149 patients	3 weeks 58/252 (23.0%) limbs 2/252 (0.8%) limbs with hyper-pigmentation 6 months 2/252 (0.8%) limbs with hyper-pigmentation Final outcome 12–28 months 0/252 (0.0%) limbs
Navarro et al (2001)	IV	2/3	Mean follow-up of 4.2 months (range 7 days – 14 months)	40 GSV[a] in 33 patients	33/33 (100.0%) patients

[a] GSV = greater saphenous vein, [b] possible duplication of patients between the studies by Proebstle (2002b) and Proebstle, Lehr et al (2002), [c] LSV = lesser saphenous vein, [d] study by Chang & Chua (2002) used ligation in addition to laser treatment

Stripping

Ecchymosis and erythema (redness of the skin produced by the congestion of capillaries) were reported in only one of the 18 stripping studies (Table 18). The good quality study by Lurie et al (2003) reported 2.8 to 5.6 per cent of limbs affected by ecchymosis and erythema, respectively, at the end of the 4-month follow-up period, after knee to groin stripping surgery.

Table 18 Incidence of ecchymosis or erythema after stripping

Study	Level of evidence	Quality score	Length of follow-up	Population	Rate of ecchymosis or erythema
Groin to knee stripping					
Lurie et al (2003)	II	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Ecchymosis 72 hours 19/36 (52.8%) 1 week 23/36 (63.9%) 3 weeks 7/36 (19.4%) 4 months 1/36 (2.8%) Erythema 72 hours 3/36 (8.3%) 1 week 1/36 (2.8%) 3 weeks 3/36 (8.3%) 4 months 2/36 (5.6%)

[a] GSV = greater saphenous vein

Paraesthesia

Paraesthesia can be described as damage to the saphenous nerve that may result in abnormal sensations along the length of the site of treatment. Sensations may include feelings of burning, itching or prickling. The saphenous nerve runs alongside the greater saphenous vein and may be damaged in the treatment of varicose veins using either the EVLT™ or the conventional stripping procedure. The risk of damage to the saphenous nerve is increased during ankle to groin, compared to groin to knee, stripping due to the proximity of the nerve to the vein in the calf region (Bergan et al 2002; Ruckley et al 2002).

EVLT™

Four of the nine full-text EVLT™ studies reported paraesthesia (Table 19). The better quality studies by Min et al (2001) and Proebstle (2002b) reported paraesthesia rates in 1.2 per cent of patients and 1.1 per cent of limbs, post-EVLT™ on the greater saphenous vein. Min recorded that paraesthesia resolved after 6 weeks duration but Proebstle (2002b) did not state the length of duration of symptoms or length of follow-up.

The lower quality study by Chang and Chua (2002) noted the highest rate of paraesthesia, at 3 weeks follow-up, with 36.5 per cent of limbs experiencing paraesthesia after EVLT™ on the greater saphenous vein, in combination with junction ligation. This rate was reduced to 2.8 per cent of limbs at 6 months and all symptoms were resolved by the end of follow-up.

The study by Proebstle et al (2003) reported that paraesthesia occurred in 4 out of 41 (9.8%) limbs after EVLT™ of the lesser saphenous vein, and symptoms persisted for between 3 and 8 weeks.

None of the abstract studies reported paraesthesia associated with EVLT™.

Table 19 Rate of paraesthesia post-EVLT™

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of paraesthesia events
Min et al (2001)	IV	3/3	Mean follow-up of 6 months (range 1–9 months)	90 GSV[a] in 84 patients	1/84 (1.2%) patients 6 weeks duration
Proebstle (2002b)	IV	3/3	Does not state follow-up period	95 GSV[a] in 77 patients	1/95 (1.1%) limbs
Proebstle et al (2003)	IV	2.5/3	Median follow-up of 6 months (range 3–12 months)	41 LSV[b] in 33 patients	4/41 (9.8%) limbs Median duration 6.5 weeks (range 3–8 weeks)
Chang & Chua (2002)[c]	IV	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[a] in 149 patients	3 weeks 92/252 (36.5%) limbs 6 months 7/252 (2.8%) limbs Final outcome 12–28 months 0/252 (0.0%) limbs

[a] GSV = greater saphenous vein, [b] LSV = lesser saphenous vein,
[c] study by Chang & Chua (2002) used ligation in addition to laser treatment

Stripping

Ten of the 18 stripping studies reported cases of paraesthesia; six of these studies performed groin to knee stripping and three were ankle to groin (Table 20). At the end of follow-up, rates of paraesthesia ranged from 4.1 to 23.0 per cent for limbs that had undergone groin to knee stripping and 4.5 to 19.0 per cent for limbs that had undergone ankle to groin stripping. The better quality study by Rautio, Ohinmaa et al (2002) reported 3 out of 13 (23.0%) limbs with paraesthesia. The good quality study by Rutgers and Kitslaar (1994) recorded the highest rate of paraesthesia, at 1-year follow-up, with 30.3 per cent of limbs experiencing saphenous nerve damage after ankle to groin stripping. This rate had decreased at the end of the 3-year follow-up to 4.5 per cent; however, only 77.5 per cent of limbs were followed up for this period.

Table 20 Rate of paraesthesia after stripping

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of paraesthesia events
Groin to knee stripping					
Rautio, Ohinmaa et al (2002)	II	3/3	Mean follow-up of 50 days	13 GSV[a]	3/13 (23.0%) limbs
Sarin et al (1992)	II	3/3	Follow-up of 3 months	49 GSV[a] in 33 patients	2/49 (4.1%) limbs
Lacroix et al (1999)	II	2/3	Follow-up of 30 days	30 GSV[a] in 30 patients with bilateral varicose veins	5/30 (16.7%) limbs
Lurie et al (2003)	II	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	72 hours 2/36 (5.6%) limbs 1 week 5/36 (13.9%) limbs 3 weeks 2/36 (5.6%) limbs
Durkin et al (1999)	II	1.5/3	33/37 (89.2%) limbs followed up for 1 week	37 GSV[a]	3/37 (8.1%) limbs
Sykes et al (2000)	II	1/3	Follow-up of 6 weeks	25 GSV[a] in 25 patients	2/25 (8.0%) limbs
Ankle to groin stripping					
Jones et al (1996)	II	2.5/3	55/64 (85.9%) limbs followed up for a mean of 31 months (range 28–33 months)	64 GSV[a]	6 weeks 3/64 (4.7%) limbs
Rutgers & Kitslaar (1994)	II	2.5/3	69/89 (77.5%) limbs followed up for 3 years	89 GSV[a] in 78 patients	1 year 27/89 (30.3%) 3 years 4/89 (4.5%)
Munn et al (1981)	II	1.5/3	57/100 (57%) patients followed up for 2.5–3.5 years	100 GSV[a] in 100 patients with bilateral varicose veins	Post-operative period 19/100 (19.0%) limbs
Both groin to knee and ankle to groin stripping					
Neglén et al (1993)	II	2.5/3	59/74 (80%) limbs followed up for 1 year 57/74 (77%) limbs followed up for 5 years	74 GSV[a]	Post-operative period 7/74 (9.5%) limbs

[a] GSV = greater saphenous vein

Induration

EVLT™

Five of the nine full EVLT™ studies reported induration, or hardening of the skin, along the length of the saphenous vein (Table 21). Of these studies, those concerned with EVLT™ of the greater saphenous vein reported induration in 100 per cent of limbs or patients at initial follow-up after treatment. Symptoms, however, were of limited duration, typically 3 to 4 weeks.

The study by Proebstle et al (2003) reported that induration occurred in 14 out of 41 (34.1%) limbs after EVLT™ of the lesser saphenous vein, and symptoms persisted between 1 and 4 weeks.

None of the abstract studies reported induration associated with the EVLT™ procedure.

Table 21 Proportion of patients, or limbs, with post-EVLT™ induration

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of induration events
Proebstle (2002b)[a]	IV	3/3	Does not state follow-up period	95 GSV[b] in 77 patients	95/95 (100.0%) limbs, duration of 3 weeks
Proebstle, Lehr et al (2002)[a]	IV	3/3	Follow-up of 28 days	31 GSV[b] in 26 patients	26/26 (100.0%) patients Resolved at end of follow-up.
Proebstle et al (2003)	IV	2.5/3	Median follow-up 6 months (range 3–12 months)	41 LSV[c] in 33 patients	14/41 (34.1%) limbs Median duration 4 weeks (range 1–4 weeks)
Boné & Navarro (2001)	IV	2/3	Follow-up of 12 months	125 GSV[b] in 105 patients	24 hours 105/105 (100.0%) patients 7 days 105/105 (100.0%) patients 1 month 0/105 (0%) patients
Navarro et al (2001)	IV	2/3	Mean follow-up of 4.2 months (range 7 days – 14 months)	40 GSV[b] in 33 patients	33/33 (100.0%) of patients

[a] Possible duplication of patients between the studies by Proebstle (2002b) and Proebstle, Lehr et al (2002),
[b] GSV = greater saphenous vein, [c] LSV = lesser saphenous vein

Stripping

Induration is not a relevant side effect of the stripping procedure.

Phlebitis

Inflammation of the outer coating of the vein or the tissue surrounding the vein was described in some studies as either phlebitis or periphlebitis. Other studies described thrombophlebitis, inflammation of the vein associated with thrombus formation. All of these conditions were combined into the one category of phlebitis.

EVLT™

Of the nine full EVLT™ studies included for assessment, five reported phlebitis after EVLT™ (Table 22). The two better quality studies by Proebstle (2002b) and Proebstle, Lehr et al (2002) reported that 7.7 per cent of patients and 3.2 per cent of limbs, respectively, experienced phlebitis. The majority of patients in these studies with phlebitis were prescribed the anti-inflammatory diclofenac. Proebstle, Lehr et al (2002) recorded that all symptoms were resolved by the end of follow-up (28 days) but the study by Proebstle (2002b) did not give this information. Min et al (2003) did not state the exact number of patients who required anti-inflammatory medication, nor the duration of symptoms.

The lower quality study by Proebstle et al (2003) yielded a similar rate of 7.3 per cent of limbs affected by phlebitis after EVLT™ in the lesser saphenous vein, with symptoms being resolved between 1.5 and 4 weeks.

Similarly, Chang and Chua (2002), who used EVLT™ and junction ligation of the greater saphenous vein, reported the lowest rate of 1.6 per cent of limbs affected by phlebitis, with limbs clear of phlebitis by the 6-month follow-up.

Of the eight abstract studies included for assessment, the two studies by Navarro and Boné (2001, 2002) recorded phlebitis after EVLT™ in 1.3 and 1.0 per cent of limbs, respectively (Table 22). The length of duration of symptoms was not reported, nor whether patients received any anti-inflammatory medication.

Table 22 Incidence of phlebitis post-EVLT™

Study	Level of evidence	Quality score	Length of follow-up	Population	Total number of phlebitis events
Proebstle (2002b)[a]	IV	3/3	Does not state follow-up period	95 GSV[b] in 77 patients	3/95 (3.2%) limbs Patients required diclofenac
Proebstle, Lehr et al (2002)[a]	IV	3/3	Follow-up of 28 days	31 GSV[b] in 26 patients	2/26 (7.7%) patients Patients required diclofenac Resolved at end of follow-up.
Min et al (2003)	IV	2.5/3	Mean follow-up of 17 ± 11 months (range 1–39 months)	504 GSV[a] Results only presented for 499 limbs in 423 patients	21/423 (5.0%) patients
Proebstle et al (2003)	IV	2.5/3	Median follow-up of 6 months (range 3–12 months)	41 LSV[c] in 33 patients	3/41 (7.3%) limbs Patients required diclofenac Median duration 1.5 weeks (range 1.5–4 weeks)
Chang & Chua (2002)[d]	IV	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[b] in 149 patients	3 weeks 4/252 (1.6%) limbs 6 months 0/252 (0.0%) limbs Final outcome 12–28 months 0/252 (0.0%) limbs
Navarro & Boné (2001)[e]	IV	Abstract	Follow-up of 24 months (mean 12.09 months)	150 GSV[b] in 128 patients	2/150 (1.3%) limbs
Navarro & Boné (2002)[e]	IV	Abstract	Follow-up of 36 months (mean 23.6 months	200 cases of GSV[b]	2/200 (1.0%) limbs

[a] Possible duplication of patients between the studies by Proebstle (2002b) and Proebstle, Lehr et al (2002), [b] GSV = greater saphenous vein, [c] LSV = lesser saphenous vein, [d] study by Chang & Chua (2002)used ligation in addition to laser treatment
[e] possible duplication of patients between the 2001 and 2002 studies

Stripping

Phlebitis is not a relevant side effect of the stripping procedure.

Summary of safety outcomes

From the available literature, it would appear that the EVLT™ procedure is as safe as the conventional stripping procedure.

Is it effective?

The main treatment outcome of EVLT™ was the abolition of reflux in the saphenous vein, demonstrated by the complete occlusion or obliteration of the vein, and confirmation by Doppler and colour duplex ultrasound examination. Following the EVLT™ procedure, reflux is assessed in the saphenous vein but not in other veins in the limb. Only the full-text EVLT™ studies were included to assess effectiveness outcomes.

The main treatment outcome of the stripping procedure was the abolition of reflux achieved by the removal of the saphenous vein. Following the stripping procedure, reflux cannot be assessed in the absent saphenous vein; however, the presence or absence of reflux is assessed in the entire limb and confirmed by Doppler, colour duplex ultrasound examination and plethysmography.

The aim of the outcomes in the two studies, in respect to reflux, are so diverse that they are not comparable.

Abolition of reflux

EVLT™

At the end of follow-up, all the EVLT™ studies evaluating EVLT™ of the greater saphenous vein, reported that between 90 and 100 per cent of limbs were fully occluded, although some of these limbs required re-treatment (Table 23). Follow-up ranged from a minimum of 28 days in the study by Proebstle, Lehr et al (2002) to 24 months in the study by Min et al (2003). The good quality study by Min et al (2003) presented preliminary results, probably building on the results of their 2001 study. Min et al (2003) is a longitudinal study, where 121 limbs were initially recruited and treated, and therefore had the longest follow-up period of 24 months. The authors reported that 40 patients were followed up for 36 months but did not supply accurate follow-up data for these patients. At 12 months a further 197 limbs had been treated, giving a total of 318 limbs. Enrolment continued until there were 504 limbs in total that could be assessed at a minimum of 1-month follow-up. This study reported that 97.2 per cent of limbs were successfully occluded at 1-month follow-up; however, this includes the nine (1.8%) limbs receiving re-treatment at the 1-week evaluation, eight of which were successful. Due to the nature of enrolment in this study, it is impossible to determine the length of follow-up for these limbs. In addition, five patients were lost to follow-up and it is unclear when this occurred. Min et al (2001) reported a gradual reduction in the diameter of the GSV after treatment: 32 per cent reduction at 1 month, 55 per cent at 3 months, 73 per cent at 6 months, and 81 per cent at 9 months post-EVLT™. The two good quality studies by Proebstle (2002b) and Proebstle, Lehr et al (2002) indicated that occlusion occurred in 97.0 per cent of limbs, although the follow-up period was short or not stated.

Proebstle et al (2003) reported the complete occlusion of the lesser saphenous vein, post-EVLT™, in 94.9 per cent of limbs and 93.8 per cent of patients. Treatment could not be completed in one patient in this study due to pronounced tortuosity of the LSV, which may reflect poor patient selection. In addition, one patient in this study, on whom EVLT™ was performed on both limbs, died from mesenteric infarction. This outcome was unrelated to the EVLT™ procedure and the total patient numbers in the study were adjusted accordingly.

The study by Chang and Chua (2002), which used ligation in addition to EVLT™ in the greater saphenous vein, reported 244 out of 252 (96.8%) limbs were completely occluded at 6 months follow-up. The eight limbs with partial occlusion were treated with sclerotherapy, resulting in 100 per cent complete occlusion at the end of the follow-up period.

Table 23 Occlusion of the vein after EVLT™

Study	Quality score	Length of follow-up	Population	Total number of occluded vessels
Min et al (2001)[a]	3/3	Mean follow-up of 6 months (range 1–9 months)	90 GSV[b] in 84 patients	1 week 87/90 (96.7%) limbs 3/90 (3.3%) re-treated [c] 1 month 90/90 (100.0%) limbs 3 months 82/83 (98.8%) limbs 6 months 61/62 (98.4%) limbs 9 months 26/27 (96.3%) limbs
Proebstle (2002b)[c]	3/3	Does not state follow-up period	95 GSV[b] in 77 patients	92/95 (96.8%) limbs
Proebstle, Lehr et al (2002)[c]	3/3	Follow-up of 28 days	31 GSV[b] in 26 patients	30/31 (97%) limbs
Min et al (2003)[a]	2.5/3	Mean follow-up of 17 ± 11 months (range 1–39 months)	504 GSV[a] Results only presented for 499 limbs in 423 patients	1 month 490/504 (97.2%) limbs 9/504 (1.8%) re-treated 3 months 444/447 (99.3%) limbs 6 months 390/369 (98.5%) limbs 9 months 351/359 (97.8%) limbs 12 months 310/318 (97.5%) limbs 24 months 113/121 (93.4%) limbs
Proebstle et al (2003)	2.5/3	Median follow-up of 6 months (range 3–12 months)	41 LSV[d] in 33 patients	37/39 (94.9%) limbs[e] 30/32 (93.8%) patients 1/39 (2.6%) limbs reported treatment failure due to incorrect positioning of laser

Boné & Navarro (2001)[f]	2/3	Follow-up of 12 months	125 GSV[b] in 105 patients	119/125 (95.2%) limbs
Chang & Chua (2002)[g]	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[b] in 149 patients	6 months 244/252 (96.8%) limbs 141/149 (94.6%) patients 8/252 (3.2%) limbs were treated with sclerotherapy Final outcome 12–28 months 252/252 (100.0%) limbs
Gérard et al (2002)	2/3	Follow-up of 30 days	20 GSV[b] in 20 patients	18/20 (90.0%) limbs totally occluded 1/20 (5.0%) limbs partially occluded 1/20 (5.0%) limbs reported treatment failure due to incorrect positioning of laser
Navarro et al (2001)	2/3	Mean follow-up of 4.2 months (range 7 days – 14 months)	40 GSV[b] in 33 patients	40/40 (100.0%) limbs

[a] Possible duplication of patients between studies, [b] GSV = greater saphenous vein, [c] possible duplication of patients between studies, [d] LSV = lesser saphenous vein, [e] patient on whom EVLT™ had been performed on 2 limbs died in this study, and total patient and limb numbers were therefore adjusted, [f] possible duplication of patients between studies, [g] study by Chang & Chua (2002) used ligation in addition to laser treatment

Stripping

The majority of the stripping studies were concerned with minor improvements in surgical technique aimed at reducing outcomes such as blood loss, bruising and pain. Many of the stripping studies had short-term follow-up periods that assessed these outcomes but did not report on the reflux status of the enrolled patients.

Six out of the 18 stripping studies explicitly reported on the reflux or venous insufficiency status of enrolled patients, with the follow-up period ranging from 3 months to 5 years (Table 24). Four of these studies were groin to knee procedures and the remaining two were ankle to groin procedures. The better quality study by Fitridge et al (1999) reported reflux in 11.8 per cent of limbs stripped groin to knee, after a short follow-up period of 3 months and on a small number of limbs. In another good quality study Jones et al (1996) reported the lowest rate of reflux in 5 out of 64 (7.8%) limbs stripped ankle to groin, after a long-term mean follow-up period of 31 months. This patient population was followed up by Dwerryhouse et al (1999), who reported an increase in the number of limbs experiencing reflux over 5 years, to 9 out of 64 (14.1%). The percentages of limbs assessed at the end of follow-up in these two studies were 85.9 and 81.3 per cent respectively. The highest rate of 42.9 per cent was reported by Sarin et al (1994) in limbs stripped groin to knee that had been followed up for a median of 21 months. This was a follow-up of their previous 1992 study, which reported reflux in 18.4 per cent of limbs after a 3-month follow-up.

In addition to reported reflux rates, 6 of the 18 stripping studies reported on venous function in limbs pre- and post-surgery using plethysmography (Table 25), which records changes in the volume of the limb as blood moves in and out of it with each cardiac cycle. Several techniques of plethysmography have been used in the past but the method is characterised by difficulties in obtaining reproducible results. More accurate methods, such

as Doppler, are currently used to assess reflux, and therefore plethysmography is of limited use. However, it can be used to calculate the venous volume of the leg; the venous filling index (VFI), which is a measurement of the rate of venous reflux; and the ejection fraction (EF), which is an indicator of calf muscle function. The refilling flow rate is directly related to venous reflux, with a reduced post-operative value indicating reduced venous reflux (Fitridge et al 1999). Normal healthy veins have a venous refill time >25 seconds, with slight, moderate and severe venous insufficiency having venous refill times of 20–24, 10–19 and <10 seconds, respectively (Goldman et al 1994).

The better quality studies by Campanello et al (1996) and Hammarsten et al (1990) reported statistically significant improvements in venous return time ($p<0.001$). In addition, Fitridge et al (1999) reported a statistically significant improvement in the venous filling index, indicating a reduction in venous reflux after groin to knee stripping.

Table 24 Reported reflux or venous insufficiency after stripping

Study	Quality score	Length of follow-up	Population	Reported reflux pre-stripping	Reported reflux post-stripping
Groin to knee stripping					
Fitridge et al (1999)	3/3	Follow-up of 3 months	17 GSV[a]		2/17 (11.8%) limbs
Sarin et al (1992)	3/3	Follow-up of 3 months	49 GSV[a] in 33 patients	SFJ[b] reflux 49/49 (100.0%) limbs GSV[a] reflux 49/49 (100.0%) limbs	SFJ[b] reflux 0/49 (0.0%) limbs GSV[a] reflux 9/49 (18.4%) limbs
Lurie et al (2003)	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]		72 hours 0/36 (0.0%) limbs 1 week 0/36 (0.0%) limbs
Sarin et al (1994) Follow-up study of patients from 1992 study	2.5/3	43/49 (87.8%) limbs in 29/33 patients followed up for a median of 21 months	49 GSV[a] in 33 patients	49/49 (100.0%) limbs	21/49 (42.9%) limbs
Ankle to groin stripping					
Dwerryhouse et al (1999) Follow-up to study by Jones et al (1996)	2.5/3	52/64 (81.3%) limbs followed up for 5 years	64 GSV[a]		GSV[a] reflux 9/64 (14.1%) limbs Sapheno-femoral incompetency 15/64 (23.4%) limbs
Jones et al (1996)	2.5/3	55/64 (85.9%) limbs followed up for a mean of 31 months (range 28–33 months)	64 GSV[a]		5/64 (7.8%) limbs

[a] GSV = greater saphenous vein, [b] SFJ = sapheno-femoral junction

Table 25 Results of plethysmography after stripping

Study	Quality score	Length of follow-up	Population	Mean value pre-operatively	Mean value post-operatively	Statistical result
Groin to knee stripping						
Campanello et al (1996)	3/3	Mean follow-up of 48 ± 42 months (range 3–94 months)	18 GSV[a] in 18 patients with bilateral varicose veins	VRT (t-50)[bc] 3.8 (0.3) seconds	VRT (t-50)[bc] 10.3 (1.1) seconds	$p < 0.001$[d]
Fitridge et al (1999)	3/3	Follow-up of 3 months	17 GSV[a]	VV[e] 145 ± 83 mL VFI[f] 30 ± 2.0 mL EF[g] 61 ± 15 %	VV[e] 122 ± 65 mL VFI[f] 1.2 ± 0.9 mL EF[g] 80 ± 30%	$p = 0.026$[h] $p = 0.001$[h] $p = 0.001$[h]
Sarin et al (1992)	3/3	Follow-up of 3 months	49 GSV[a] in 33 patients	PPG[i] 11 (7–16)[j] seconds	PPG[i] 12 (8–16)[j] seconds	
Sarin et al (1994) Follow-up study of patients from 1992 study	2.5/3	43/49 (87.8%) limbs in 29/33 patients followed up for a median of 21 months	49 GSV[a] in 33 patients	PPG[i] 11 (7–16)[j] seconds	PPG[i] 20 (13–27)[j] seconds	
Ankle to groin stripping						
Hammarsten et al (1990)	3/3	Mean follow-up of 52 ± 5 months (range 43–60 months)	24 GSV[a]	VRT[b] 5.2 ± 0.4 seconds	VRT[b] 8.1 ± 0.5 seconds	$p < 0.001$[d]
Both ankle to groin and groin to knee stripping						
Neglén et al (1993)	2.5/3	59/74 (80%) limbs followed up for 1 year 57/74 (77%) limbs followed up for 5 years	74 GSV[a]	(n = 74) EV[k] 10.4 ± 0.6 mL Q/EV_{rel}[l] 4.4 ± 0.3	(n = 57) EV[k] 14.9 ± 0.8 mL Q/EV_{rel}[l] 2.3 ± 0.2	$p<0.001$[d] $p<0.05$[d]

[a] GSV = greater saphenous vein, [b] VRT t-50 = venous return time: time in which 50% of the refilled volume is regained, [c] values are mean (SEM), [d] authors' statistical analysis using Wilcoxon rank sum test, *p* values only, no statistics given, [e] VV = venous volume (ml), [f] VFI = venous filling index (mL), [g] EF = ejection fraction (%), [h] authors' statistical analysis using paired t-test, [i] PPG = 95% refilling time, [j] median (inter-quartile range), [k] EV = expelled volume (mL), [l] Q/EV_{rel} = the refilling flow ratio (min^{-1})

Rate of re-treatment or recurrent varicose veins

In the literature there is considerable confusion in defining recurrent varicose veins. Many papers do not explicitly state whether the recurrent varicose veins are true recurrences, residual incompetent veins, or new incompetent veins which were previously normal.

EVLT™

The EVLT™ procedure does not treat tributary varicosities, which will always require follow-up treatment with sclerotherapy approximately 4 weeks after the EVLT™ procedure. This follow-up sclerotherapy is not reported in the EVLT™ studies as re-treatment.

None of the EVLT™ studies explicitly reported the rate of recurrent varicose veins. However, initial follow-up examination with duplex ultrasound found some saphenous veins to be only partially occluded and therefore still presenting with reflux. These veins were eligible for re-treatment. Two of the nine full-text studies, with possible overlapping patient populations, reported on limbs that required re-treatment. The good quality study by Min et al (2003), with a mean follow-up period of 17 months (range 1–39 months), reported nine limbs (1.8%) that required re-treatment after EVLT™ (Table 26). Eight of these (88.9%) greater saphenous veins were successfully occluded after re-treatment.

Table 26 Rate of re-treatment or recurrent varicose veins post-EVLT™

Study	Quality score	Length of follow-up	Population	Total number of re-treatment events
Min et al (2001)[a]	3/3	Mean follow-up of 6 months (range 1–9 months)	90 GSV[b] in 84 patients	3/90 (3.3%) limbs
Min et al (2003)[a]	2.5/3	Mean follow-up of 17 ± 11 months (range 1–39 months)	504 GSV[a] Results only presented for 499 limbs in 423 patients	9/504 (1.8%) limbs 8/9 (88.9%) successful

[a] Possible duplication of patients between studies, [b] GSV = greater saphenous vein

Stripping

Six of the 18 stripping studies reported recurrent varicose veins as an outcome (Table 27). Two of these studies assessed groin to knee stripping and the remaining four ankle to groin stripping. The better quality studies, by Campanello et al (1996) and Hammarsten et al (1990), reported 22.2 and 33.3 per cent of limbs, respectively, that experienced recurrent varicose veins after stripping, with a mean long-term follow-up of approximately 50 months. The good quality study by Dwerryhouse et al (1999), which had the longest follow-up period of 5 years, reported 17.2 per cent of limbs with recurrent varicose veins after ankle to groin stripping.

Only the study by Rutgers and Kitslaar (1994) reported on the re-treatment of limbs after ankle to groin stripping surgery (Table 27).

Table 27 Rate of re-treatment or recurrent varicose veins after stripping

Study	Quality score	Length of follow-up	Population	Rate of re-treatment or recurrent varicose veins
Groin to knee stripping				
Campanello et al (1996)	3/3	Mean follow-up of 48± 42 months (range 3–94 months)	18 GSV[a] in 18 patients with bilateral varicose veins	4/18 (22.2%) limbs
Sarin et al (1994) Follow-up study of patients from 1992 study	2.5/3	43/49 (87.8%) limbs in 29/33 patients followed up for a median of 21 months	49 GSV[a] in 33 patients	15/49 (30.6%) limbs
Ankle to groin stripping				
Hammarsten et al (1990)	3/3	Mean follow-up of 52 ± 5 months (range 43–60 months)	24 GSV[a] in 24 patients	8/24 (33.3%) limbs
Dwerryhouse et al (1999)Follow-up to study by Jones et al (1996)	2.5/3	52/64 (81.3%) limbs followed up for 5 years	64 GSV[a]	11/64 (17.2%) limbs
Jones et al (1996)	2.5/3	55/64 (85.9%) limbs followed up for a mean of 31 months (range 28–33 months)	64 GSV[a]	8/64 (12.5%) limbs
Munn et al (1981)	1.5/3	57/100 (57%) patients followed up for 2.5–3.5 years	100 GSV[a] in 100 patients with bilateral varicose veins	21/100 (21.0%) limbs
Rutgers & Kitslaar (1994)	2.5/3	69/89 (77.5%) limbs followed up for 3 years	89 GSV[a] in 78 patients ankle to groin	2/89 (2.2%) re-operated 12/89 (13.5%) required sclerotherapy at a mean time of 10 months

[a] GSV = greater saphenous vein

Recanalisation or neovascularisation

EVLT™

Recanalisation is the spontaneous restoration of the lumen of the saphenous vein after occlusion by EVLT™ has taken place. Four of the nine full EVLT™ studies reported on the recanalisation status of enrolled patients (Table 28). Of these, the two studies by Boné and Navarro (2001) (follow-up 12 months) and Navarro et al (2001) (mean follow-up 4.2 months) reported recanalisation results of 4.8 and 0.0 per cent, respectively, after EVLT™

on the greater saphenous vein. Patients in the study by Boné and Navarro (2001) were treated successfully with sclerotherapy.

The study by Chang and Chua (2002), which used ligation in addition to EVLT™ on the greater saphenous vein, also reported no cases of recanalisation at the end of the follow-up period (mean follow-up 19 months).

Proebstle et al (2003) performed EVLT™ on 39 lesser saphenous veins and reported no occurrence of recanalisation.

Table 28 Rate of recanalisation post-EVLT™

Study	Quality score	Length of follow-up	Population	Total number of recanalisation events
Proebstle et al (2003)	2.5/3	Median follow-up 6 months (range 3–12 months)	41 LSV[a] in 33 patients	0/39 (0.0%) limbs[b]
Boné & Navarro (2001)[c]	2/3	Follow-up of 12 months	125 GSV[d] in 105 patients	6/125 (4.8%) limbs Treated with sclerotherapy
Chang & Chua (2002)[e]	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[d] in 149 patients	0/252 (0.0%) limbs
Navarro et al (2001)	2/3	Mean follow-up of 4.2 months (range 7 days – 14 months)	40 GSV[d] in 33 patients	0/40 (0.0%) limbs

[a] LSV = lesser saphenous vein, [b] patient on whom EVLT™ had been performed on 2 limbs died in this study, and total patient and limb numbers were therefore adjusted, [c] possible duplication of patients between studies, [d] GSV = greater saphenous vein, [e] study by Chang & Chua (2002) used ligation in addition to laser treatment

Stripping

Neovascularisation after the stripping procedure is described as the proliferation of blood vessels in tissue where the saphenous veins have been removed. Neovascularisation is not necessarily clinically significant but may be a cosmetic issue for patients. Only one of the 18 stripping studies, the follow-up study by Dwerryhouse et al (1999), reported a high rate of neovascularisation (40.6%) 5 years after ankle to groin stripping surgery (Table 29).

Table 29 Rate of neovascularisation after stripping

Study	Quality score	Length of follow-up	Population	Rate of neovascularisation
Ankle to groin stripping				
Dwerryhouse et al (1999) Follow-up to study by Jones et al (1996)	2.5/3	52/64 (81.3%) limbs followed up for 5 years	64 GSV[a]	26/64 (40.6%) limbs

[a] GSV = greater saphenous vein

Reduction of symptoms

EVLT™

Two of the nine full-text EVLT™ studies reported on the reduction of symptoms associated with varicose veins after EVLT™ (Table 30). The study by Proebstle et al (2003) of EVLT™ on the lesser saphenous vein reported pre- and post-EVLT™ scores for oedema, pain and pruritus (an itching sensation). Patients were asked to categorise their symptoms as: not present (0), minor (1), moderate (2) or severe (3). The number of patients who reported no symptoms increased markedly for all three symptom categories after EVLT™. There was a corresponding clinically relevant (≥ 20%) decrease in the number of patients reporting severe symptoms after EVLT™. This study did not provide raw data for statistical analysis; therefore, the significance of these results could not be ascertained.

CEAP (clinical, etiology, anatomy, pathophysiology) is a stratified classification system developed to distinguish between morphological and functional aspects of varicose veins (Antignani 2001). The study by Chang and Chua (2002), which used ligation in addition to EVLT™ on the greater saphenous vein, reported a statistically significant improvement between pre- and post-EVLT™ in the CEAP severity score ($p<0.05$).

Table 30 Reduction of symptoms post-EVLT™

Study	Quality score	Length of follow-up	Population	Reduction of symptoms		
Proebstle et al (2003)	2.5/3	Median follow-up 6 months (range 3–12 months)	41 LSV[b] in 33 patients	Oedema		
				Score[c]	Pre	Post
				0	9.0%	59.0%
				1	16.0%	32.0%
				2	51.0%	3.0%
				3	24.0%	6.0%
				Pain		
				Score[c]	Pre	Post
				0	27.0%	91.0%
				1	11.0%	6.0%
				2	40.0%	0.0%
				3	22.0%	3.0%
				Pruritus		
				Score[c]	Pre	Post
				0	56.0%	91.0%
				1	8.0%	9.0%
				2	14.0%	0.0%
				3	22.0%	0.0%
Chang & Chua (2002)[d]	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[a] in 149 patients	CEAP severity score		
				6 months		
				Score[e]	Pre	Post
				0	0.0%	96.8%
				1	4.5%	0.8%
				2	43.3%	2.4%
				3	37.3%	0.0%
				4	14.9%	0.0%
				$p<0.05$ [f]		

[a] GSV = greater saphenous vein, [b] LSV = lesser saphenous vein, [c] scores: 0 = not present, 1 = minor, 2 = moderate, 3 = severe, [d] study by Chang & Chua (2002) used ligation in addition to laser treatment, [e] scores: 0 = no varices visible, 1 = varices in ankle, 2 = upper calf varices, 3 = mid-thigh varices, 4 = varices about the groin, [f] author's statistical analysis using a paired t-test, *p* value only, no statistics given, [g] calculated using McNemar's chi squared test, [h] df = degrees of freedom

Stripping

Only one of the 18 stripping studies, the good quality study by Rautio, Ohinmaa et al (2002), reported on the reduction of symptoms a mean of 50 days after knee to groin stripping surgery (Table 31). Venous clinical severity score (VCSS), venous segmental disease score (VSDS) and venous disability score (VDS) are adaptations of the CEAP severity scoring system. The VCSS combines nine clinical characteristics (eg pain) of venous disease, which are each graded from 0 to 3 (absent, mild, moderate, severe). The VSDS combines the anatomic and pathophysiological aspects of CEAP. The VDS is a modification of the existing CEAP disability score, which refers to the patient's ability to partake in normal activities. An improvement in all of these categories is indicated by a reduction in the score after stripping (Rutherford et al 2000).

Table 31 Reduction of symptoms after stripping

Study	Quality score	Length of follow-up	Population	Reduction of symptoms		
Groin to knee stripping						
Rautio, Ohinmaa et al (2002)	3/3	Mean follow-up of 50 days	13 GSV[a]	CEAP severity score		
				Score[e]	Pre	Post
				VCSS[b]	4 (4–6)[c]	4.4 ±1.1[f]
				VSDS[d]	1	12/13 = 0
						1/13 = 1
				VDS[e]	1	12/13 = 0
						1/13 = 1

[a] GSV = greater saphenous vein, [b] VCSS = venous clinical severity score, [c] median (range), [d] VSDS = venous segmental disease score, [e] VDS = venous disability score, [f] value = average decrease ± SD

Quality of life

EVLT™

None of the EVLT™ studies reported quality of life (QOL) as an outcome.

Stripping

Three of the 18 stripping studies reported on the quality of life of patients after knee to groin surgery (Table 32). The better quality study by Rautio, Ohinmaa et al (2002) reported pre- and post-surgery quality of life values using the RAND-36, a health survey used to assess the patient health-related quality of life. No within-group statistical analysis was performed on these data. The good quality study by Durkin at al (2001) used the Euro QOL, a single index health score, and the SF-36, a valid and reliable measure of health status. QOL values at 6-week follow-up were as poor or poorer than pre-surgery QOL values due to pain. All QOL categories demonstrated an improvement at 6 months although only the SF-36 score for physical functioning demonstrated a statistically significant difference between pre- and post-stripping scores. The good quality study by Lurie et al (2003) only provided the difference between the pre- and post-stripping scores, with a positive difference indicating a worsening of QOL. QOL values were poor immediately after stripping; however, by 4 months follow-up the differences between pre-and post-surgery were negligible.

Table 32 Quality of life after stripping

Study	Quality score	Length of follow-up	Population	Pre-operative quality of life	Post-operative quality of life
Groin to knee stripping					
Rautio, Ohinmaa et al (2002)	3/3	Mean follow-up of 50 days	13 GSV[a]	RAND-36[b] physical functioning 95 (85–100) role physical 100 (50–100) bodily pain 68 (68–90) health 75 (70–90) energy 70 (50–75) social function 100 (78–100) emotional functioning 100 (67–100) well-being 80 (64–84)	RAND-36[bc] physical functioning 5 (0–10) role physical 0 (-25–0) bodily pain -10 (-33–0) health -5 (-5–10) energy -10 (-25–10) social function 0 (0–0) emotional functioning 0 (0–0) well-being -8 (-8–0)
Durkin et al (2001) Follow-up study of patients from 1999 study	2.5/3	30/37 (81.1%) patients followed up for 6 months	37 GSV[a] in 37 patients	Euro QOL[bd] 0.8 (0.69–1.0) SF36[b] Physical summary 48 (33–55) Mental summary 51 (48–57)	Euro QOL[bd] 6 weeks 0.83 (0.69–1.1) $p = 0.163$[e] 6 months 1.0 (0.69–1.0) $p = 0.28$[e] SF36[b] Physical summary 6 weeks 48 (37–55) $p = 0.845$[e] 6 months 56 (46–58) $p = 0.003$[e] Mental summary 6 weeks 54 (45–58) $p = 0.766$[e] 6 months 56 (51–58) $p = 0.258$[e]

Lurie et al (2003)	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]		72 hours[f] Global score 13.3 ± 3.1 Pain score 2.9 ± 0.7 Physical score 4.85 ± 0.79 1 week Global score 3.7 ± 2.5 Pain score 1.2 ± 0.7 Physical score 2.02 ± 0.72 4 months Differences were negligible

[a] GSV = greater saphenous vein, [b] values shown are median (inter-quartile range), [c] mean difference from baseline score, [d] Euro QOL = Euro quality of life questionnaire, [e] authors' statistical analysis using Mann Whitney U test with Bonferroni correction, [f] only the differences between pre and post-stripping quality of life scores were presented, with a positive difference indicating a worsening of QOL

Time taken to resume normal activities

EVLT™

Only one of the nine full-text EVLT™ studies, by Gérard et al (2002), reported on the time taken for patients to return to normal activities (Table 33). All studies advised patients to resume normal activities as soon as possible after EVLT™ but this data was not recorded.

Table 33 Time taken to resume normal activities post-EVLT™

Study	Quality score	Length of follow-up	Population	Time taken to resume normal activities
Gérard et al (2002)	2/3	Follow-up of 30 days	20 GSV[a] in 20 patients	No work stoppage required for the 14 patients with occupational activities

[a] GSV = greater saphenous vein

Stripping

Only one of the 18 stripping studies, by Lurie et al (2003), reported on the time taken to resume normal activities after knee to groin stripping surgery (Table 34) and four studies reported on the time taken to return to work (Table 35). The better quality study by Rautio, Ohinmaa et al (2002) reported a mean of 11.6 days taken to return to work for patients who underwent groin to knee surgery. The longest period of time taken to return to work was reported by Neglén at al (1993), where patients who had undergone a mixture of both groin to knee and ankle to groin stripping required a mean of 20 days before returning to work.

Table 34 Time taken to resume normal activities after stripping

Study	Quality score	Length of follow-up	Population	Time taken to resume normal activities
Groin to knee stripping				
Lurie et al (2003)	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Mean 3.89 days 95%CI [2.67–5.12]

[a] GSV = greater saphenous vein

Table 35 Time taken to return to work after stripping

Study	Quality score	Length of follow-up	Population	Time taken to return to work
Groin to knee stripping				
Rautio, Ohinmaa et al (2002)	3/3	Mean follow-up of 50 days	13 GSV[a]	Mean 11.6 days[b]
Lurie et al (2003)	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Mean 12.4 days 95%CI [8.66–16.33]
Butler et al (2002)	2/3	Follow-up of 1 week	68 GSV[a]	Median 7 days (IQR[c] 4–11)
Both ankle to groin and groin to knee stripping				
Neglén et al (1993)	2.5/3	59/74 (80%) limbs followed up for 1 year 57/74 (77%) limbs followed up for 5 years	74 GSV[a]	Mean 20 days[b]

[a] GSV = greater saphenous vein, [b] range or SD not given, [c] IQR = inter-quartile range

Operating time for procedure

EVLT™

Two of the nine full-text EVLT™ studies reported the length of operating time for the EVLT™ procedure (Table 36). The procedure reported in Chang and Chua (2002) took a mean time of 122 minutes, which is double that of the operating time recorded by Gérard et al (2002), due to their technique of combining EVLT™ with ligation of the greater saphenous vein.

Table 36 Operating time for EVLT™ procedure

Study	Quality score	Length of follow-up	Population	Mean operating time
Chang & Chua (2002)[a]	2/3	Mean follow-up of 19 months (range 12–28 months)	252 GSV[b] in 149 patients	122 minutes (range 95–175 minutes)
Gérard et al (2002)	2/3	Follow-up of 30 days	20 GSV[b] in 20 patients	60 minutes[c]

[a] Study by Chang & Chua (2002) used ligation in addition to laser treatment, [b] GSV = greater saphenous vein, [c] range of SD not given

Stripping

Tributary vessels are treated during stripping and junction ligation, which impacts on the time taken to perform the procedure.

Four of the 18 stripping studies reported on the length of operating time for groin to knee stripping of the greater saphenous vein (Table 37). The better quality study by Rautio, Ohinmaa et al (2002) reported a mean operating time of 57 minutes for the groin to knee stripping procedure. The longest mean operating time of 89 minutes was reported by Lurie et al (2003). Butler et al (2002) reported a median of 25 minutes, which was the shortest time for the groin to knee stripping procedure.

Table 37 Operating time for stripping procedure

Study	Quality score	Length of follow-up	Population	Mean/median operating time for procedure
Groin to knee stripping				
Rautio, Ohinmaa et al (2002)	3/3	Mean follow-up of 50 days	13 GSV[a]	Mean 57 ± 11 minutes
Lurie et al (2003)	2.5/3	34/36 (94.4%) limbs followed up for 4 months	36 GSV[a]	Mean 89 ± 12 minutes
Butler et al (2002)	2/3	Follow-up 1 week	68 GSV[a]	Median 25 minutes (IQR[b] 20–30)
Sykes et al (2000)	1/3	Follow-up of 6 weeks	25 GSV[a] in 25 patients	Median 37 minutes (range 18–50)

[a] GSV = greater saphenous vein, [b] IQR= inter-quartile range

Summary of effectiveness outcomes

From the available literature, it would appear that the EVLT™ is effective in occluding the saphenous vein. It cannot be determined whether EVLT™ is as effective, or more effective, as the conventional stripping procedure.

What are the economic considerations?

The purpose of an economic evaluation is to assist decision-makers in ensuring that society's ultimately scarce resources are allocated to those activities from which we will get the most value. That is, it seeks to enhance economic efficiency. Economic evaluation under the MSAC process focuses on the scarce resources available within the Australian health system.

The aim of the present economic evaluation was to systematically review the evidence for the costs and effectiveness of EVLT™, compared to surgical stripping and ligation, of varicose veins under Australian conditions.

Due to the poor level of evidence, issues of clinical effectiveness remain unanswered; therefore, a cost effectiveness analysis was not possible. No evidence was available to ascertain the incremental cost effectiveness of EVLT™ as compared to stripping and ligation, with respect to the health care system or social costs. A formal cost analysis, were it to be undertaken, should include the total care of the condition, including any secondary follow-up treatment associated with the procedure. The EVLT™ procedure does not treat tributary varicosities, which will always require follow-up treatment with sclerotherapy (MBS item number 32500) approximately four weeks after the EVLT™ procedure. Tributary veins are ligated and avulsed during the stripping and junction ligation procedure therefore a smaller number of patients would require sclerotherapy post-treatment.

Table 2 on page seven reports the number of services on the MBS for conventional stripping and junction ligation in Australia for the period between July 2002 and June 2003. Approximately 10,000 claims were processed during this period, which may give some indication of the clinical need and subsequent costs should EVLT™ be introduced in the Australian setting.

Conclusions

An indirect comparison provides a simple presentation of the safety and effectiveness outcome rates for both procedures. It should not be used as a method of determining the comparative effectiveness of the two procedures. To make a sound comparison of EVLT™ and stripping, patients should be selected in the same way, operations should occur under similar conditions and in the same time period, and discharge and treatment protocols and clinical outcomes should be assessed and defined in the same manner. A new procedure may be evaluated initially without controls to determine safety and whether the procedure is potentially effective. Following these initial, uncontrolled pilot studies, randomised controlled trials should be conducted to assess effectiveness. Results from uncontrolled studies are affected by bias and confounding and are potentially misleading, and valid conclusions cannot be made (Sacks et al 1996). Naive (unadjusted) indirect comparisons, in which the results of individual arms between trials are compared as if from a single trial, are liable to bias and 'should be avoided wherever possible' (Song et al 2003). Even non-randomised concurrently controlled studies may give seriously misleading results (Deeks et al 2003).

It is understood that randomised controlled trials are difficult to conduct for rare medical conditions. However, the treatment of varicose veins represents one of the most common surgical procedures conducted in Australia, with an excess of 10,000 procedures conducted yearly, making a randomised controlled trial a viable option. A randomised controlled trial of EVLT™ versus conventional stripping surgery was scheduled to start in June 2003 at Leeds in the United Kingdom.

Safety

Good quality data are not available to assess the comparative safety of endovenous laser treatment for varicose veins. However, all of the EVLT™ studies assessed in this review reported fully on the outcomes of all enrolled EVLT™ patients. Pain, ecchymosis, induration, haematoma and phlebitis are common adverse events associated with EVLT™. In most cases these symptoms were self-limiting or required prescription of mild medication. Ecchymosis, or discolouration of the skin, was the most common adverse event and was reported in seven out of the eight full-text studies. The better quality studies report that ecchymosis was present in 100.0 per cent of limbs and symptoms persisted for 1 to 4 weeks. The most serious adverse events were deep vein thrombosis and incorrect positioning of the laser into the wrong vessel. Deep vein thrombosis occurred in only one patient and was an ongoing problem by the end of the study follow-up period, requiring long-term medication. This patient, who had a predisposition for thrombotic events, represented poor patient selection on behalf of the investigators. Despite ultrasound guidance, incorrect laser placement occurred in two patients (ie 0.3 per cent of total limbs) treated in the full studies. This represents serious operator error, and although no long-term harmful effects were noted, the potential for significant damage is real.

Infection, bruising, haematoma and paraesthesia are common adverse events associated with the 'gold standard' of surgical stripping of the saphenous vein. Paraesthesia, or damage to the saphenous nerve, was the most common and serious adverse event associated with stripping of the saphenous vein, and was reported in 10 of the 18 stripping studies. The highest rate of paraesthesia (30.3 per cent) was reported in a good quality study where ankle

to groin stripping was performed. The saphenous nerve runs parallel to the saphenous vein in the calf region, which increases the possibility of damage to the nerve when performing the full-length procedure. This rate was reduced to 4.5 per cent of limbs at the end of the 3-year follow-up. In studies that performed the groin to knee procedure, rates of paraesthesia were lower and ranged from 4.1 to 23.0 per cent. Due to the short-term follow-up of these studies, it is unclear if all symptoms resolved. Although infection was reported in 7 of the 18 studies, rates of infection were low and ranged from 2 to 8 per cent of limbs. Thrombotic events were rare. One study reported two incidents of superficial venous thrombosis and another study reported one patient who experienced a pulmonary embolism.

From the available literature, it would appear that the EVLT™ procedure is as safe as the conventional stripping procedure.

Effectiveness

There are no controlled studies available that assess the effectiveness of endovenous laser treatment for varicose veins in comparison with saphenous vein stripping and junction ligation. An indirect comparison was therefore undertaken.

The main treatment outcome of EVLT™ and stripping is the abolition of reflux. However, the two procedures differ in the assessment of reflux. Following EVLT™, reflux is assessed only in the saphenous vein, not in other veins in the limb. Following the stripping procedure, reflux cannot be assessed in the absent saphenous vein, but is assessed in vessels in the entire limb. The aim of the outcomes in the two studies, in respect to reflux, are so diverse that they are not comparable.

From the low-level case series evidence available for EVLT™, it would appear that endovenous laser treatment is of benefit to the majority of patients in the short term. Occlusion of the saphenous vein and the subsequent abolishment of reflux were achieved in 90.0 to 100.0 per cent of limbs in those studies that conducted EVLT™ on the greater saphenous vein. The study with the longest length of follow-up (24 months) reported an occlusion rate of 93.4 per cent. One study conducted EVLT™ on the lesser saphenous vein and reported an occlusion rate of 94.9 per cent of limbs. The combined treatment of EVLT™ and ligation of the greater saphenous vein resulted in 100.0 per cent occlusion at the end of the 19-month follow-up period. One full-text study reported re-treatment in 3.3 per cent of limbs. Similarly low rates for recanalisation were also noted. Clinically relevant reductions after EVLT™ in the symptoms associated with varicose veins, such as pain and oedema, were reported by two full-text studies.

Given the dynamic nature of the condition, and the difficulties involved in defining and distinguishing residual, recurrent or new incompetent veins, a follow-up of 6 to 12 months is adequate to determine the effectiveness of treatment in a particular area of the limb. Five out of the nine full-text studies provided sufficient follow-up (≥ 6 months) data on the treated limbs. The longest follow-up period in the full-text studies for EVLT™ on the greater saphenous vein, without junction ligation, was 24 months.

Many of the stripping studies were concerned with minor improvements in the stripping technique rather than reporting on long-term, functional outcomes. Abolition of reflux as an outcome was reported in only 6 out of the 18 studies. Of the four studies that described groin to knee stripping, one had a follow-up period greater than 6 months and reported reflux in 42.9 per cent of limbs. The two studies that described ankle to groin stripping

followed the same patient group and reported a reflux rate of 14.1 per cent after a long follow-up period of 5 years.

Recurrent varicose veins in the absence of reflux were reported in several stripping studies, all of which had long-term follow-up periods. For the groin to knee procedure, rates of recurrent varicose veins were reported between 22.2 and 30.6 per cent after a follow-up period of 21 to 48 months. The rate of recurrent varicose veins for the ankle to groin procedure was between 12.5 and 33.3 per cent with follow-up ranging from 31 months to 5 years.

From the available literature, EVLT™ appears to be effective in occluding the saphenous vein. However, the EVLT™ procedure does not treat tributary vessels, which require secondary, follow-up treatment. Whether EVLT™ is as effective as the stripping and ligation procedure, or more effective, cannot be determined. Tributary vessels are treated during the stripping and junction ligation procedure.

Cost-effectiveness

It is not possible to assess the cost-effectiveness of EVLT™ in comparison with vein stripping and junction ligation due to the lack of comparative evidence assessing clinical effectiveness. If a formal cost analysis was to be conducted, it should take into account the whole procedure, including follow-up treatment of tributary varicosities.

Recommendation

Endovenous laser treatment for varicose veins appears to be safe in comparison with stripping of varicose veins but there is insufficient evidence pertaining to effectiveness and cost-effectiveness, therefore MSAC recommended that public funding should not be supported for this procedure at this time.

The Minister for Health and Ageing accepted this recommendation on August 10th 2004.

Appendix A The MSAC terms of reference and membership

The MSAC's terms of reference are to:

- advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to AHMAC.

The membership of the MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumer health, and health administration and planning:

Member	**Expertise or affiliation**
Dr Stephen Blamey (Chair)	general surgery
Dr John Atherton	cardiology
Professor Bruce Barraclough	general surgery
Professor Syd Bell	pathology
Dr Michael Cleary	emergency medicine
Dr Paul Craft	clinical epidemiology and oncology
Professor Jane Hall	health economics
Dr Gerry Fitzgerald	Australian Health Minister's Advisory Council representative
Dr Kwun Fong	thoracic surgery
Dr Terri Jackson	health economics
Ms Rebecca James	consumer health issues
Professor Brendon Kearney	health administration and planning
Associate Professor Richard King	internal medicine
Dr Ray Kirk	health research
Dr Michael Kitchener	nuclear medicine
Mr Ian McRae	Assistant Secretary, Medicare Benefits Branch, Australian Government Department of Health and Ageing
Dr Ewa Piejko	general practice

Ms Sheila Rimmer	consumer health issues
Professor Jeffery Robinson	obstetrics and gynaecology
Professor John Simes	clinical epidemiology and clinical trials
Professor Bryant Stokes	neurological surgery, representing the Australian Health Ministers' Advisory Council
Professor Ken Thomson	radiology
Dr Douglas Travis	urology

Appendix B Advisory Panel

Advisory panel for the MSAC application 1059
Endovenous laser treatment (EVLT™) for varicose veins

Professor Ken Thomson (Chair) MD, FRANZCR, FRCR Director of Radiology The Alfred Hospital Melbourne, VIC	Member of the MSAC Radiologist
Mrs Margaret Charlton BEd Independent Consumer Representative Adelaide, SA	Nominated by the Consumers' Health Forum of Australia
Dr Brett Gooley MBBS, Dip (Obs.), DCH, FRACGP Blue Cross Medical Centre Sydney, NSW	Nominated by the Royal Australian College of General Practitioners
Mr Peter Milne MBBS, FRACS, FRCS (UK), FACS Vascular Surgeon Cabrini Medical Centre Melbourne, VIC	Co-opted member Vascular Surgeon
Dr Ewa Piejko MBBS, FRACGP, DRANZCOG The Circle Surgery Melbourne, VIC	Member of the MSAC General Practitioner
Associate Professor Philip Walker MBBS, FRACS Department of Surgery University of Queensland Queensland	Nominated by the Royal Australasian College of Surgeons Vascular Surgeon
Ms Linda Mundy G Dip PH Research Officer Health Technology Assessment Unit University of Adelaide Adelaide, SA	Evaluator
Ms Alex Lloyd Department of Health & Ageing	Project Manager

Appendix C Studies included in the review

Study profiles of included studies on prevalence

Study	Location	Study design	Study population	Assessment method	Prevalence of varicose veins
Abramson et al (1981)	Western Jerusalem, Israel	Population based cross-sectional survey Interview Response rate: 89%	4888 subjects (including 86 pregnant women) all residents of Jerusalem suburb Age: >20 years	Examination	Distended, tortuous veins only Men: 10.4% Women: 29.5%
Brand et al (1988)	Framingham, USA	Prospective cohort study	General population in Framingham 1,720 men 2,102 women Age: 40–89	Examination	Distended, tortuous veins only Men: 23% Women: 29.9%
Canonico et al (1998)	Campania region, Italy	Cross-sectional survey Response rate: NA[a]	Random sample from electoral rolls 560 men 759 women Age: 66–96	Questionnaire; Examination	Any visible reticular or truncal varicosities Men: 17% Women: 35.2%
Evans et al (1999)	Edinburgh, Scotland	Cross-sectional survey Response rate: 53.8%	Random sample from 12 general practices across Edinburgh 699 men 867 women Age: 18–64	Self-administered questionnaire; Clinical examination; Duplex scan	Dilated, tortuous veins only Men: 39.7% Women: 32.2% Hyphenweb and reticular varices only: 80%
Franks et al (1992)	West London, England	Cross-sectional survey Response rate: 64%	Quasi-random selection (every 3rd patient) from 3 general practices 634 men 704 women Age: 35–70	Questionnaire	Varicose veins not defined Men: 17% Women: 31%
Laurikka et al (1993)	Tampere, Finland	Cross-sectional survey Response rate: 81%	People born in 1929, 1939 and 1949 selected from general population on National Population Registry (171,000).	Questionnaire	Visible, dilated, tortuous veins only Men: 16% Women: 38%
Preziosi et al (1999)	Paris, France	Cross-sectional survey Response rate: NA[a]	1,318 men aged 45–60 1,747 women aged 35–60 were non-randomly selected from the SUVIMAX cohort[b]	Questionnaire; Examination	Varicose veins not defined Men: 18.3% Women: 30.6%

Prior et al (1970)	Carterton, New Zealand	Cross-sectional survey Response rate: 90.8%	Random selection of European households in Carterton 202 men and 230 women Age: 20–70+	Interview; Examination	Mild and moderate varicose veins Men: 20% Women: 39%
Sisto et al (1995)	Tampere, Finland	Cross-sectional survey Response rate: 90%	Subjects drawn from the national population registers from 40 geographical areas 3,322 men 3,895 women aged >30	Questionnaire	Varicose veins not defined Men: 6.8% Women 24.6%

[a] NA = not available, [b] Representative sample of the French population

Study profiles of included studies on safety and effectiveness of EVLT™

The assessment of the safety and effectiveness of EVLT™ for the treatment of varicose veins used studies that were case series and therefore level IV evidence.

Quality score	Study	Location	Study design	Study population	Outcome(s) assessed	Length of follow-up
2/3	Boné C & Navarro L (2001)	Palma de Mallorca, Spain	Case series	125 GSV[a] in 105 patients	Occlusion of the GSV and absence of reflux Ecchymosis, induration, recanalisation	Follow-up of 12 months
2/3	Chang C-J Chua J-J (2002)	Singapore	Case series	252 GSV[a] in 149 patients (122 female and 46 male)	Occlusion of the GSV and absence of reflux Laser-related adverse events, bleeding complications, ecchymosis, paraesthesia, recanalisation, phlebitis, reduction of symptoms, operating time for procedure	Mean follow-up of 19 months (range 12–28 months)
2/3	Gérard J-L Desgranges P Becquemin J-P Desse H Melliere D (2002)	Paris, France	Case series	20 GSV[a] in 20 patients	Occlusion of the GSV and absence of reflux Laser-related adverse events, pain, bleeding complications, time taken to resume normal activities, operating time for procedure	Follow-up of 30 days
3/3	Min RJ Zimmet SE Isaacs MN Forrestal MD (2001)	New York, USA	Case series, longitudinal study	90 GSV[a] in 84 patients (63 female and 21 male)	Occlusion of the GSV and absence of reflux Pain, ecchymosis, paraesthesia, re-treatment, reduction of symptoms	Mean follow-up of 6 months (range 1–9 months)

2.5/3	Min RJ Khilnani N Zimmet SE (2003)	New York & Texas, USA	Case series, longitudinal study	504 GSV[a] Results only presented for 499 limbs in 423 patients	Occlusion of the GSV and absence of reflux Phlebitis, bruising complications	Mean follow-up of 17 ± 11 months (range 1–39 months)
2/3	Navarro L Min RJ Boné C (2001)	New York, USA and Palma de Mallorca, Spain	Case series	40 GSV[a] in 33 patients	Occlusion of the GSV and absence of reflux Ecchymosis, induration, recanalisation	Mean follow-up of 4.2 months (range 7 days – 14 months)
2.5/3	Proebstle TM Gül D Kargl A Knop J (2003)	Mainz, Germany	Case series	41 LSV[b] in 33 patients	Occlusion of the LSV and absence of reflux Laser-related adverse events, DVT, pain, ecchymosis, paraesthesia, induration, phlebitis, recanalisation, reduction of symptoms	Median follow-up 6 months (range 3–12 months)
3/3	Proebstle TM (2002)	Mainz, Germany	Case series	95 GSV[a] in 77 patients (58 female and 19 male)	Occlusion of the GSV Ecchymosis, paraesthesia, induration, phlebitis	Does not state follow-up period
3/3	Proebstle TM Lehr HA Kargl A Espinola-Klein C Rother W Bethge S Knop J (2002)	Mainz and Germering, Germany	Case series	31 GSV[a] in 26 patients (19 female with 22 GSV and 7 male with 9 GSV)	Occlusion of the GSV and absence of reflux Pain, ecchymosis, induration, phlebitis	Follow-up of 28 days
Abstract from American Society for Laser Medicine and Surgery Conference	Goldman MP (2002)	San Diego, USA	Case series	20 consecutive patients	Occlusion of the GSV and absence of reflux Reduction in symptoms	Follow-up of 6 months
Abstract from 16th Annual Congress of the American College of Phlebology	Mackay E (2002)		Case series	25 LSV[b]	Occlusion of the LSV and absence of reflux Recanalisation	Follow-up of 12 months

Abstract from 15th Annual Congress of the American College of Phlebology	Min RJ (2001)		Case series	150 GSV[a] in 134 patients	Occlusion of the GSV and absence of reflux Rate of re-treatment	Follow-up of 3 to 22 months
Abstract from 28th Annual Scientific Meeting of the Society of Interventional Radiology[d]	Min RJ (2003a)	New York, USA	Case series	389 GSV[a] in 344 patients	Occlusion of the GSV and absence of reflux	389 limbs followed up for 1 to 36 months 88 limbs followed up for 24 months
Abstract from 28th Annual Scientific Meeting of the Society of Interventional Radiology[d]	Min RJ (2003b)	New York, USA	Case series	150 GSV[a] in 131 patients	Occlusion of the GSV and absence of reflux Pain, rate of bleeding complications	Follow-up of 12 months
Abstract from 28th Annual Scientific Meeting of the Society of Interventional Radiology[d]	Min RJ (2003c)	New York, USA	Case series	40 LSV[b] and 51 ALT[c]	Occlusion of LSV and ALT and absence of reflux	Follow-up of 24 months
Abstract from 15th Annual Congress of the American College of Phlebology	Navarro L & Boné C (2001)		Case series	150 GSV[a] in 128 patients	Occlusion of the GSV and absence of reflux Phlebitis, rate of re-treatment, recanalisation	Follow-up of 24 months (mean 12.09 months)
Abstract from 16th Annual Congress of the American College of Phlebology	Navarro L & Boné C (2002)		Case series	200 cases of GSV[a]	Occlusion of the GSV and absence of reflux Phlebitis, recanalisation	Follow-up of 36 months (mean 23.6 months

[a] GSV = greater saphenous vein, [b] LSV = lesser saphenous vein, [c] ALT = anterior-lateral tributary
[d] updated results of abstracts presented at the 16th Annual Congress of the American College of Phlebology

Study profiles of included studies on safety and effectiveness of stripping and/or junction ligation

The assessment of the safety and effectiveness of stripping and/or junction ligation of varicose veins used only the stripping arm of randomised controlled trials and were therefore considered case series, level IV evidence.

Quality score	Study	Location	Study design	Study population	Outcome(s) assessed	Length of follow-up
2/3	Butler CM Scurr JH Coleridge Smith PD (2002)	London, United Kingdom	Stripping + ligation arm of RCT	68 GSV[a] groin to knee	Blood loss, haematoma, duration of operation, time taken to resume normal activities	Follow-up of 1 week
3/3	Campanello M Hammarsten J Forsberg C Bernland P Henrikson O Jensen J (1996)	Varberg, Sweden	Stripping arm of RCT	18 GSV[a] in 18 patients with bilateral varicose veins groin to knee	VRT[b]	Mean follow-up of 48± 42 months (range 3–94 months)
1.5/3	Durkin M Turton EPL Scott DJA Berridge DC (1999)	Leeds, United Kingdom	Stripping + ligation arm of RCT	37 GSV[a] groin to knee	Bruising, infection, paraesthesia, cellulitis	Follow-up of 1 week
2.5/3	Durkin M Turton E Wijesinghe L Scott D Berridge D (2001) Follow-up study of patients from 1999 study	Leeds, United Kingdom	Stripping + ligation arm of RCT	37 GSV[a] groin to knee	QOL[d]	Follow-up of 6 months
2.5/3	Dwerryhouse S Davies B Harradine K Earnshaw JJ (1999) Follow-up to study by Jones et al (1996)	Gloucester, United Kingdom	Stripping + ligation arm of RCT	64 GSV[a] ankle to groin	Recurrent varicosities, neovascular-isation, patient satisfaction, venous insufficiency	Follow-up of 5 years

3/3	Fitridge R Dunlop C Raptis S Thompson M Leppard P Quigley F (1999)	Adelaide, Australia	Stripping + ligation arm of RCT	17 GSV[a] groin to knee	Venous volume, venous filling time, ejection fraction	Follow-up of 3 months
3/3	Hammarsten J Pedersen P Cederlund C-G Campanello M (1990)	Varberg, Sweden	Stripping arm of RCT	24 GSV[a] ankle to groin	Recurrent varicosities VRT[b]	Mean follow-up of 52 ± 5 months (range 43–60 months)
2.5/3	Jones L Braithwaite BD Selwyn D Cooke S Earnshaw JJ (1996)	Gloucester, United Kingdom	Stripping + ligation arm of RCT	64 GSV[a] ankle to groin	Recurrent varicosities, neovascular-isation, patient satisfaction, saphenous nerve damage	Mean follow-up of 31 months (range 28–33 months)
2/3	Lacroix H Nevelsteen A Suy R (1999)	Leuven, Belgium	Stripping arm of RCT	30 GSV[a] in 30 patients with bilateral varicose veins groin to knee	Haematoma, pain, saphenous nerve damage	Follow-up of 30 days
2.5/3	Lurie F Creton D Eklof B Kabnick Kistner RL Pichot O Schuller-Petrovic S Sessa C (2003)	Nancy & Grenoble, France New Jersey, USA Graz, Austria	Stripping arm of RCT	36 GSV[a] knee to groin	Total treatment time, time to return to normal activities, time to return to work, infection, venous thrombosis, ecchymosis, erythema, haematoma, paraesthesia, QOL[d]	Follow-up of 4 months
1.5/3	Munn SR Morton JB MacBeth WAAG McLeish AR (1981)	Christchurch, New Zealand	Stripping + ligation arm of RCT	100 GSV[a] in 100 patients with bilateral varicose veins ankle to groin	Varicose veins, paraesthesia, pain, infection, haematoma	Follow-up of 2.5–3.5 years
2.5/3	Neglén P Einarsson E Eklöf B (1993)	Lund, Sweden	Stripping + ligation arm of RCT	74 GSV[a]	Clinical assessment, PPG[c]	Follow-up of 5 years

3/3	Rautio T Ohinmaa A Perälä J Ohtonen P Heikkinen T Wiik H Karjalainen P Haukipuro K Juvonen T (2002)	Oulu, Finland Edmonton, Canada	Stripping arm of RCT	13 GSV[a] knee to groin	Pain, time to resume normal activities, QOL[d], CEAP scores, paraesthesia, haematoma, thrombophlebitis	Mean follow-up of 50 days
2.5/3	Rutgers P Kitslaar P (1994)	Maastrich, The Netherlands	Stripping arm of RCT	89 GSV[a] in 78 patients ankle to groin	Re-treatment, paraesthesia	Follow-up of 3 years
3/3	Sarin S Scurr JH Coleridge Smith PD (1992)	London, United Kingdom	Stripping + ligation arm of RCT	49 GSV[a] in 33 patients groin to knee	Reflux PPG[c] Paraesthesia, haematoma, infection	Follow-up of 3 months
2.5/3	Sarin S Scurr JH Coleridge Smith PD (1994) Follow-up study of patients from 1992 study	London, United Kingdom	Stripping + ligation arm of RCT	49 GSV[a] in 33 patients groin to knee	Reflux PPG[c]	Median follow-up of 21 months
1/3	Sykes TCF Brookes P Hickey NC (2000)	Worscester, United Kingdom	Stripping arm of RCT	25 GSV[a] in 25 patients groin to knee	Blood loss, operative time, bruising, pain, paraesthesia, infection, haematoma	Follow-up of 6 weeks
2/3	Wilson S Pryke S Scott R Walsh M Barker SGE (1997)	Kent, United Kingdom	Stripping arm of RCT	14 GSV[a] groin to knee	Infection, bleeding complications	Follow-up of 6 weeks

[a] GSV = greater saphenous vein, [b] VRT = venous return time, [c] PPG = photoplethysmography, [d] QOL = quality of life

Appendix D Search strategies

Searching on endovenous laser treatment

#1	Search venous insufficiency Field: MeSH Terms
#2	Search saphenous vein Field: MeSH Terms
#3	Search varicose veins Field: MeSH Terms
#4	Search #1 OR #2 OR #3
#5	Search saphenous near vein* Field: Text Word
#6	Search varicose near vein* Field: Text Word
#7	Search venous near (reflux or incomp* or insuff*) Field: Text Word
#8	Search #5 OR #6 OR #7
#9	Search #4 OR #8
#10	Search ultrasonography, doppler Field: MeSH Terms
#11	Search laser surgery Field: MeSH Terms
#12	Search vascular surgical procedures Field: MeSH Terms
#13	Search #10 OR #11 OR #12
#14	Search endovenous* Field: Text Word
#15	Search laser* Field: Text Word
#16	Search EVLT Field: Text Word
#17	Search endovasc* Field: Text Word
#18	Search #14 OR #15 OR #16 OR #17
#19	Search #13 OR #18
#20	Search #9 AND #19 Limits: Human

Searching on stripping and/or junction ligation

#1	Search venous insufficiency Field: MeSH Terms
#2	Search saphenous vein Field: MeSH Terms
#3	Search varicose veins Field: MeSH Terms
#4	Search #1 OR #2 OR #3
#5	Search saphenous near vein* Field: Text Word
#6	Search varicose near vein* Field: Text Word
#7	Search venous near (reflux or incomp* or insuff*) Field: Text Word
#8	Search #5 OR #6 OR #7
#9	Search #4 OR #8
#10	Search surgery Field: MeSH Terms
#11	Search vascular surgical procedures Field: MeSH Terms
#12	Search #10 OR #11
#13	Search strip* Field: Text Word
#14	Search junction lig* Field: Text Word
#15	Search junction near ligation Field: Text Word
#16	Search #13 OR #14 OR #15
#17	Search #12 OR #16
#18	Search #9 AND #17 Limits: Human, Randomized controlled trials, Meta-Analysis, English

Searching on prevalence of varicose veins

#1	Search risk* or epidemiol* or inciden* or natural histor* or cohort or population or registry or register Field: Text Word
#2	Search population characteristics Field: MeSH Terms
#3	Search risk Field: MeSH Terms
#4	Search natural history Field: MeSH Terms
#5	Search epidemiology Field: MeSH Terms
#6	Search cohort-studies Field: MeSH Terms
#7	Search incidence Field: MeSH Terms
#8	Search cross-sectional studies Field: MeSH Terms
#9	Search prevalence Field: MeSH Terms
#10	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11	Search venous insufficiency Field: MeSH Terms
#12	Search saphenous vein Field: MeSH Terms
#13	Search varicose veins Field: MeSH Terms
#14	Search #11 OR #12 OR #13
#15	Search saphenous near vein* Field: Text Word
#16	Search varicose near vein* Field: Text Word
#17	Search venous near (reflux or incomp* or insuff*) Field: Text Word
#18	Search #15 OR #16 OR #17
#19	Search #14 OR #18
#20	Search #10 AND #19 Limits: English, Human

Appendix E Health technology assessment internet sites

SPECIALIST VASCULAR WEB SITES

- American Venous Forum http://www.venous-info.com/
- Society of Interventional Radiology http://www.sirweb.org/
- Straub Foundation Fourth Pacific Vascular Symposium on Venous Disease http://www.straub-foundation.org/symposium/
- Union Internationale de Phlebologie http://www.sosflebite.com/riunioni/roma2001/programa.pdf
- Dermatologic Angiology & Phlebology http://members.aol.com/drgalle/webdoc2.htm

AUSTRALIA

- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) http://www.surgeons.org/open/asernip-s.htm
- Centre for Clinical Effectiveness, Monash University http://www.med.monash.edu.au/healthservices/cce/evidence/
- Health Economics Unit, Monash University http://chpe.buseco.monash.edu.au

AUSTRIA

- Institute of Technology Assessment / HTA unit http://www.oeaw.ac.at/ita/e1-3.htm

CANADA

- Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/en/index.htm
- Alberta Heritage Foundation for Medical Research (AHFMR) http://www.ahfmr.ab.ca/publications.html
- Canadian Coordinating Office for Health Technology Assessment (CCOHTA) http://www.ccohta.ca/newweb/pubapp/pubs.asp
- Canadian Health Economics Research Association (CHERA/ACRES) – Cabot database http://www.mycabot.ca
- Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org

- Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca
- Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm
- Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca

DENMARK

- Danish Institute for Health Technology Assessment (DIHTA) http://www.dihta.dk/publikationer/index_uk.asp

FINLAND

- FINOHTA http://www.stakes.fi/finohta/e/

FRANCE

- L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES) http://www.anaes.fr/

GERMANY

- German Institute for Medical Documentation and Information (DIMDI) / HTA http://www.dahta.dimdi.de/
- German Scientific Working Group of Technology Assessment http://www.epi.mh-hannover.de/(eng)/hta.html

THE NETHERLANDS

- Health Council of the Netherlands Gezondheidsraad http://www.gr.nl/engels/welcome/frameset.htm

NEW ZEALAND

- New Zealand Health Technology Assessment (NZHTA) http://nzhta.chmeds.ac.nz/

NORWAY

- Norwegian Centre for Health Technology Assessment (SMM) http://www.oslo.sintef.no/smm/Publications/Engsmdrag/FramesetPublications.htm

SPAIN

- Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III"I/Health Technology Assessment Agency (AETS) http://www.isciii.es/aets/cdoc.htm
- Catalan Agency for Health Technology Assessment (CAHTA) http://www.aatm.es/cgi-bin/frame.pl/ang/pu.html

SWEDEN

- Swedish Council on Technology Assessment in Health Care (SBU) http://www.sbu.se/admin/index.asp

SWITZERLAND

- Swiss Network on Health Technology Assessment (SNHTA) http://www.snhta.ch/

UNITED KINGDOM

- Health Technology Board for Scotland http://www.htbs.org.uk/
- National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA) http://www.hta.nhsweb.nhs.uk/
- University of York NHS Centre for Reviews and Dissemination (NHS CRD) http://www.york.ac.uk/inst/crd/
- National Institute for Clinical Excellence (NICE) http://www.nice.org.uk/index.htm

UNITED STATES

- Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov/clinic/techix.htm
- Harvard Center for Risk Analysis – Cost-Utility Analysis Database Project http://www.hcra.harvard.edu/tablesdata.html
- U.S. Blue Cross / Blue Shield Association Technology Evaluation Center (TEC) http://www.bcbs.com/consumertec/index.html
- U.S. Dept. of Veterans Affairs Technology Assessment Program (VATAP) http://www.va.gov/resdev/prt/pubs_individual.cfm?webpage=pubs_ta_reports.htm

Appendix F Studies excluded from the review

Studies excluded from the EVLT™ arm of the review

Radiofrequency or VNUS Closure system

Chandler, J. G., Pichot, O. et al (2000). 'Treatment of primary venous insufficiency by endovenous saphenous vein obliteration', *Vascular Surgery*, 34 (3), 201–214.

Dauplaise, T. L. & Weiss, R. A. (2001). 'Duplex-guided endovascular occlusion of refluxing saphenous veins', *Journal of Vascular Technology*, 25 (2), 79–82.

Fassiadis, N., Kianifard, B. et al (2001). 'No recurrence of reflux following endovascular radiofrequency ablation of the long saphenous vein (VNUS Closure) at one year', *British Journal of Surgery*, 88, 49–50.

Fassiadis, N., Kianifard, B. et al (2002b). 'A novel endoluminal technique for varicose vein management: The VNUS closure', *Phlebology*, 16 (4), 145–148.

Fassiadis, N., Kianifard, B. et al (2002a). 'A novel approach to the treatment of recurrent varicose veins', *International Angiology*, 21 (3), 275–276.

Goldman, M. P. (2000). 'Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of the vein wall in combination with ambulatory phlebectomy: preliminary 6-month follow-up', *Dermatologic Surgery*, 26 (5), 452–456.

Goldman, M. P. & Amiry, S. (2002). 'Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of the vein wall in combination with ambulatory phlebectomy: 50 patients with more than 6-month follow-up', *Dermatologic Surgery*, 28 (1), 29–31.

Harris, E. J. (2002). 'Endovascular obliteration of saphenous vein reflux: A perspective', *Journal of Vascular Surgery*, 35 (6), 1292–1294.

Manfrini, S., Gasbarro, V. et al (2000). 'Endovenous management of saphenous vein reflux', *Journal of Vascular Surgery*, 32 (2), 330–342.

Merchant, R. F., DePalma, R. G. & Kabnick, L. S. (2002). 'Endovascular obliteration of saphenous reflex: A multicenter study', *Journal of Vascular Surgery*, 35 (6), 1190–1196.

Mulkens, P. J. M. (2003). 'New results of endovenous radiofrequency therapy (VNUS) of varicose veins: A three year follow-up', *Vasomed*, 15 (1), 24–25.

Perrin, M. (2000). 'A new procedure in the treatment of varicose veins of the lower limbs: The closure (registered trademark) technique', *Angeiologie*, 52 (4), 23–28.

Pichot, O., Sessa, C. et al (2000). 'Role of duplex imaging in endovenous obliteration for primary venous insufficiency', *Journal of Endovascular Therapy*, 7 (6), 451–459.

Rautio, T., Ohinmaa, A. et al (2002). 'Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled trial with comparison of the costs', *Journal of Vascular Surgery*, 35 (5), 958–965.

Rautio, T. T., Perala, J. M. et al (2002). 'Endovenous obliteration with radiofrequency-resistive heating for greater saphenous vein insufficiency: A feasibility study', *Journal of Vascular and Interventional Radiology*, 13 (6), 569–575.

Sybrandy, J. E. M. & Wittens, C. H. A. (2002). 'Initial experiences in endovenous treatment of saphenous vein reflux', *Journal of Vascular Surgery*, 36 (6), 1207–1212.

Weiss, R. A. & Weiss, M. A. (2002). 'Controlled radiofrequency endovenous occlusion using a unique radiofrequency catheter under duplex guidance to eliminate saphenous varicose vein reflux: A 2-year follow-up', *Dermatologic Surgery*, 28 (1), 38–42.

Review or Editorial

Ahn, S. S., Wieslander, C. K. & Fleming, J. M. (2000). 'Minimally invasive vascular surgery', *Asian Journal of Surgery*, 23 (3), 218–232.

Bergan, J. J. (2002). 'Varicose veins: Hooks, clamps, and suction. Application of new techniques to enhance varicose vein surgery', *Seminars in Vascular Surgery*, 15 (1), 21–26.

Bergan, J. J., Kumins, N. H. et al (2002). 'Surgical and endovascular treatment of lower extremity venous insufficiency', *Journal of Vascular and Interventional Radiology*, 13 (6), 563–568.

Bergan, J. J., Sparks, S. R. et al (2001). 'Growing the vascular surgical practice: Venous disorders', *Cardiovascular Surgery*, 9 (5), 431–435.

Campbell, B. (2002). 'New treatments for varicose veins', *British Medical Journal*, 324 (7339), 689–690.

Coleridge Smith, P. (2002). 'End of an era', *Phlebology*, 17 (3–4), 87–88.

Goldman, M. P. (2001). 'Treatment of leg veins with lasers and intense pulsed light: Preliminary considerations and a review of present technology', *Dermatologic Clinics*, 19 (3), 467–473.

Khilnani, N. M. & Min, R. J. (2002*). Interventional radiology strategies treat venous insufficiency* /Internet]. CMP Healthcare. Available from: http://www.dimag.com/cme/articles/013.shtml [Accessed 2 September 2003].

Thorpe, P. E. & Osse, F. J. (2002), 'Chronic venous insufficiency: The role for endovascular therapy', In: Criado, F. (ed.), *Endovascular Intervention: New Tools and Techniques for the 21st Century,* Vol. 3, Futura Publ Co Inc, Armonk, pp. 155–182.

Weiss, R. A. (2001). 'Endovenous techniques for elimination of saphenous reflux: A valuable treatment modality', *Dermatologic Surgery*, 27 (10), 902–904.

Weiss, R. (2002). 'Vanquishing varicose veins. Less invasive techniques work well and slash recovery time', *Health News*, 8 (6), 4.

Weiss, R. A. & Dover, J. S. (2002a). 'Laser surgery of leg veins', *Dermatologic Clinics*, 20 (1), 19–36.

Weiss, R. A. & Dover, J. S. (2002b). 'Leg vein management: sclerotherapy, ambulatory phlebectomy, and laser surgery', *Seminars in Cutaneous Medicine and Surgery*, 21 (1), 76–103.

Letter

Bergan, J. J. (1996). 'New technology and recurrent varicose veins', *Lancet*, 348 (9022), 210–211.

Bush, R. G. & Proebstle, T. M. (2003). 'Regarding "Endovenous treatment of the greater saphenous vein with a 940-nm diode laser: Thrombolytic occlusion after endoluminal thermal damage by laser-generated steam bubbles" ', *Journal of Vascular Surgery*, 37 (1), 242.

Forrestal, M. D., Fronek, H. S. et al (2003). 'Endovenous laser treatment', *Dermatologic Surgery*, 29 (3), 312–313.

Goldman, M. P. & Eremia, S. (2002). 'Laser and sclerotherapy treatment of leg veins: My perspective on treatment outcomes', *Dermatologic Surgery*, 28 (10), 969–970.

Proebstle, T. M. (2002). 'Comment on R. A. Weiss: "Comparison of endovenous radiofrequency versus 810 nm diode laser occlusion of large veins in an animal model" ', *Dermatologic Surgery*, 28 (7), 648.

Proebstle, T. M. (2003). 'Regarding "Endovenous treatment of the greater saphenous vein with a 940-nm diode laser: Thrombolytic occlusion after endoluminal thermal damage by laser-generated steam bubbles" - Reply', *Journal of Vascular Surgery*, 37 (1), 242–242.

Weiss, R. (2001). 'Commentary on endovenous laser', *Dermatologic Surgery*, 27 (3), 326–327.

Weiss, R. (2003). 'Endovenous laser treatment - Reply', *Dermatologic Surgery*, 29 (3), 313–314.

Report or abstract from meeting

Corbett, C. R. R. (1997). Conference Proceeding: Annual General Meeting of the Venous Forum of the Royal Society of Medicine, London (1997), In: *Phlebology*, 12 (4), 151–155.

Corbett, C. R. R. (2002). 'Joint Symposium of the Venous Forum of the Royal Society of Medicine, with the Vascular Surgical Society of Great Britain and Ireland and Venous Papers', Conference Proceeding: Annual General Meeting of the Vascular Surgical Society of Great Britain and Ireland (2001), Brighton, England, In: *Phlebology*, 17 (1), 36–40.

Mueller, U., Philipp, C. M. et al (2002). 'Interstitial and intraluminal Nd : YAG-lasertherapy of superficial and deep varicose veins', Conference Proceeding: American Society for Laser Medicine and Surgery, In: *Lasers in Surgery and Medicine*, 40 (S14), Abstract Number: 133.

External use of lasers and telangiectasia

Dover, J. S., Sadick, N. S. et al (1999). 'The role of laser and light sources in the treatment of leg veins', *Dermatologic Surgery*, 25 (4), 328–336.

Eremia, S., Li, C. & Umar, S. H. (2002). 'A side-by-side comparative study of 1064 nm Nd:Yag, 810 nm diode and 755 nm alexandrite lasers for treatment of 0.3–3 mm leg veins', *Dermatologic Surgery*, 28 (3), 224–230.

Goldman, M. P. & Eckhouse, S. (1996). 'Photothermal sclerosis of leg veins. ESC Medical Systems, LTD Photoderm VL Cooperative Study Group', *Dermatologic Surgery*, 22 (4), 323–330.

Kaudewitz, P., Klovekorn, W. & Rother, W. (2001). 'Effective treatment of leg vein telangiectasia with a new 940 nm diode laser', *Dermatologic Surgery*, 27 (2), 101–106.

Kaudewitz, P., Klovekorn, W. & Rother, W. (2002). 'Treatment of leg vein telangiectases: 1-year results with a new 940 nm diode laser', *Dermatologic Surgery*, 28 (11), 1031–1034.

Sadick, N. S. (2001). 'Long-term results with a multiple synchronized-pulse 1064 nm Nd:YAG laser for the treatment of leg venulectasias and reticular veins', *Dermatologic Surgery*, 27 (4), 365–369.

Sadick, N. S. (2002). 'A dual wavelength approach for laser/intense pulsed light source treatment of lower extremity veins', *Journal of the American Academy of Dermatology*, 46 (1), 66–72.

Sadick, N. S., Weiss, R. A. & Goldman, M. P. (2002). 'Advances in laser surgery for leg veins: bimodal wavelength approach to lower extremity vessels, new cooling techniques, and longer pulse durations', *Dermatologic Surgery*, 28 (1), 16–20.

Vanscheidt, W. (1995). 'Laser therapy of varicosities', *Journal of the European Academy of Dermatology and Venereology*, 5, S48–S49.

Duplex imaging as a predictive tool

Pichot, O., Sessa, C. & Bosson, J.-L. (2002). 'Duplex imaging analysis of the long saphenous vein reflux: Basis for strategy of endovenous obliteration treatment', *International Angiology*, 21 (4), 333–336.

Animal study

Weiss, R. A. (2002). 'Comparison of endovenous radiofrequency versus 810 nm diode laser occlusion of large veins in an animal model', *Dermatologic Surgery*, 28 (1), 56–61.

Other

Proebstle, T. M., Sandhofer, M. et al (2002). 'Thermal damage of the inner vein wall during endovenous laser treatment: Key role of energy absorption by intravascular blood', *Dermatologic Surgery*, 28 (7), 596–600.

Schonholz, C., Onorati, D. et al (1999). 'Endovascular treatment of varicose veins of the lower extremities', *Journal of Endovascular Surgery,* 6 (1), 112–113.

Studies excluded from the stripping and junction ligation arm of the review

Descriptive studies or review of technique

Bearn, P. & Fox, J. A. (1993). 'A Modified Technique for Stripping of the Long Saphenous-Vein', *Phlebology,* 8 (1), 32–33.

Glass, G. M. (1998). 'Prevention of sapheno-femoral and sapheno-popliteal recurrence of varicose veins by forming a partition to contain neovascularization', *Phlebology,* 13 (1), 3–9.

Rigby, K. A., Palfreyman, S. J. et al Surgery for varicose veins: Use of tourniquet (Cochrane Review). In: *The Cochrane Library,* Issue 1, 2003. Oxford: Update Software.

Sommer, B. & Sattler, G. (2001). 'High ligation and stripping of the long saphenous vein', In: Hanke, C.W., Sommer, B. & Sattler, G. (eds), *Tumescent Local Anesthesia,* Springer-Verlag Inc, New York, pp. 160–170.

Method of randomisation unclear

Holme, J. B., Skajaa, K. & Holme, K. (1990). 'Incidence of lesions of the saphenous nerve after partial or complete stripping of the long saphenous vein', *Acta Chirurgica Scandinavica*, 156 (2), 145–148.

Jakobsen, B. H. (1979). 'The value of different forms of treatment for varicose veins', *British Journal of Surgery*, 66 (3), 182–184.

Melrose, D. G., Knight, M. T. & Simandl, E. (1979). 'The stripping of varicose veins: a clinical trial of intermittent compression dressings', *British Journal of Surgery*, 66 (1), 53–55.

Inappropriate outcomes reported or no objective assessment of outcomes

Fowler, A., Stechman, M. & Mitchell, D. (2002). 'A randomised controlled trial of the effect of Esmarch tourniquet use on blood loss, bruising and quality of life in elective varicose vein surgery', *Phlebology*, 17 (1), 10–12.

Kent, P. J., Maughan, J. et al (1999). 'Perforation-invagination (PIN) stripping of the long saphenous vein reduces thigh haematoma formation in varicose vein surgery', *Phlebology*, 14 (2), 43–47.

Recurrent varicose veins

Canonico, S., Campitiello, F. et al (1997). 'Diagnostic and surgical approaches to recurrent varicose veins of lower limbs', *Panminerva Medica,* 39 (4), 287–290.

Farrah, J. & Shami, S. K. (2001). 'Patterns of incompetence in patients with recurrent varicose veins: A duplex ultrasound study', *Phlebology,* 16 (1), 34–37.

Jiang, P., van Rij, A. M. et al (1999). 'Recurrent varicose veins: patterns of reflux and clinical severity', *Cardiovascular Surgery,* 7 (3), 332–339.

Labropoulos, N., Touloupakis, E. et al (1996). 'Recurrent varicose veins: Investigation of the pattern and extent of reflux with color flow duplex scanning', *Surgery,* 119 (4), 406–409.

Wright, D. D. I., Rose, K. G. et al (2002). 'Recurrence following varicose vein surgery', *Phlebology*, 16 (3), 101–105.

Duplicate study

Belcaro, G., Cesarone, M. et al (2003). 'Treatments for varicose veins: Surgery, sclerotherapy, foam-sclerotherapy and combined (surgery + sclerotherapy) options. A 10-year, prospective, randomised, controlled, follow-up study. The VEDICO* trial and EST (European Sclerotherapy Trial)', *Angeiologie,* 55 (1), 29–36.

Appendix G Critical appraisal checklists

Checklist for the critical appraisal of case series

Source: Young et al (1999). *Lung volume reduction surgery (LVRS) for chronic obstructive pulmonary disease (COPD) with underlying severe emphysema.* A West Midlands Development and Evaluation Committee Report, University of Birmingham, p51–53.

Title of review:
Title of study:
Author(s):
Year:
Comparators:
Score: /3

1. **Was the study conducted prospectively? /1**

- Were the key outcomes measured before and after the intervention, using clear criteria defined *a priori*?

2. **Was the method of selection of cases identified and appropriate? /1**

- Were patients selected consecutively or in an unbiased manner?
- Was there evidence that the characteristics of the included cases were not significantly different from those of the treated population?

3. **Was the duration and completeness of follow-up reported and was it adequate?**

- Are the number and characteristics of losses to follow-up presented? [#] **/0.5**
- Are losses to follow-up managed by performing sensitivity analysis and/or including them in the final analysis? **/0.5**

[#] Losses to follow-up >20% are unacceptable, particularly if unaccounted for.

Abbreviations

AIHW	Australian Institute of Health and Welfare
CEAP	Clinical, etiology, anatomy, pathophysiology
EVLT	endovenous laser treatment
GSV	greater or long saphenous vein
HIC	Health Insurance Commission
LSV	lesser or short saphenous vein
MSAC	Medical Services Advisory Committee
MBS	Medicare Benefits Schedule
NHMRC	National Health and Medical Research Council
RCT	randomised controlled trials
TGA	Therapeutic Goods Administration

References

Abramson, J. H., Hopp, C. & Epstein, L. M. (1981). 'The epidemiology of varicose veins. A survey in western Jerusalem', *Journal of Epidemiology and Community Health,* 35 (3), 213–217.

Adhikari, A., Criqui, M. H. et al (2000). 'The epidemiology of chronic venous diseases', *Phlebology,* 15 (1), 2–18.

Ahn, S. S., Wieslander, C. K. & Fleming, J. M. (2000). 'Minimally invasive vascular surgery', *Asian Journal of Surgery,* 23 (3), 218–232.

Allan, P. L., Bradbury, A. W. et al (2000). 'Patterns of reflux and severity of varicose veins in the general population - Edinburgh vein study', *European Journal of Vascular and Endovascular Surgery,* 20 (5), 470–477.

American College of Phlebology (1998). *Phlebology: The treatment of leg veins* [internet]. American College of Phlebology. Available from: http://www.phlebology.org/brochure.htm [Accessed 3 March 2003].

Antignani, P. L. (2001). 'Classification of chronic venous insufficiency: a review', *Angiology,* 52 (Suppl. 1), S17–26.

Bearn, P. & Fox, J. A. (1993). 'A Modified Technique for Stripping of the Long Saphenous-Vein', *Phlebology,* 8 (1), 32–33.

Belcaro, G., Cesarone, M. et al (2003). 'Treatments for varicose veins: Surgery, sclerotherapy, foam-sclerotherapy and combined (surgery + sclerotherapy) options. A 10-year, prospective, randomised, controlled, follow-up study. The VEDICO* trial and EST (European Sclerotherapy Trial)', *Angeiologie,* 55 (1), 29–36.

Bergan, J. J. (1996). 'New technology and recurrent varicose veins', *Lancet,* 348 (9022), 210–211.

Bergan, J. J. (2002). 'Varicose veins: Hooks, clamps, and suction. Application of new techniques to enhance varicose vein surgery', *Seminars in Vascular Surgery,* 15 (1), 21–26.

Bergan, J. J., Kumins, N. H. et al (2002). 'Surgical and endovascular treatment of lower extremity venous insufficiency', *Journal of Vascular and Interventional Radiology,* 13 (6), 563–568.

Bergan, J. J., Sparks, S. R. et al (2001). 'Growing the vascular surgical practice: Venous disorders', *Cardiovascular Surgery,* 9 (5), 431–435.

Boné, C. & Navarro, L. (2001). 'Endovenous laser: A new minimally invasive technique for the treatment of varicose veins. Endolaser', *Anales de Cirugia Cardiaca y Cirugia Vascular,* 7 (3), 184–188.

Bradbury, A., Evans, C. et al (1999). 'What are the symptoms of varicose veins? Edinburgh vein study cross sectional population survey', *British Medical Journal,* 318 (7180), 353–356.

Brand, F. N., Dannenberg, A. L. et al (1988). 'The epidemiology of varicose veins: The Framingham Study', *American Journal of Preventive Medicine,* 4 (2), 96–101.

Bush, R. G. & Proebstle, T. M. (2003). 'Regarding "Endovenous treatment of the greater saphenous vein with a 940-nm diode laser: Thrombolytic occlusion after endoluminal thermal damage by laser-generated steam bubbles" ', *Journal of Vascular Surgery,* 37 (1), 242.

Butler, C. M., Scurr, J. H. & Smith, P. D. C. (2002). 'Prospective randomised trial comparing conventional (Babcock) stripping with inverting (Pin) stripping of the long saphenous vein', *Phlebology,* 17 (2), 59–63.

Callam, M. J. (1994). 'Epidemiology of varicose veins', *British Journal of Surgery,* 81 (2), 167–173.

Campanello, M., Hammarsten, J. et al (1996). 'Standard stripping versus long saphenous vein-saving surgery for primary varicose veins: A prospective, randomized study with the patients as their own controls', *Phlebology,* 11 (2), 45–49.

Campbell, B. (2002). 'New treatments for varicose veins', *British Medical Journal,* 324 (7339), 689–690.

Canonico, S., Campitiello, F. et al (1997). 'Diagnostic and surgical approaches to recurrent varicose veins of lower limbs', *Panminerva Medica,* 39 (4), 287–290.

Canonico, S., Gallo, C. et al (1998). 'Prevalence of varicose veins in an Italian elderly population', *Angiology,* 49 (2), 129–135.

Chandler, J. G., Pichot, O. et al (2000a). 'Treatment of primary venous insufficiency by endovenous saphenous vein obliteration', *Vascular Surgery,* 34 (3), 201–214.

Chandler, J. G., Pichot, O. et al (2000b). 'Defining the role of extended saphenofemoral junction ligation: A prospective comparative study', *Journal of Vascular Surgery,* 32 (5), 941–952.

Chang, C.-J. & Chua, J.-J. (2002). 'Endovenous laser photocoagulation (EVLP) for varicose veins', *Lasers in Surgery and Medicine,* 31 (4), 257–262.

Coleridge Smith, P. (2002). 'End of an era', *Phlebology,* 17 (3–4), 87–88.

Corbett, C. R. R. (1997). Conference Proceeding: Annual General Meeting of the Venous Forum of the Royal Society of Medicine*,* London (1997), In: *Phlebology*, 12 (4), 151–155.

Corbett, C. R. R. (2002). 'Joint Symposium of the Venous Forum of the Royal Society of Medicine, with the Vascular Surgical Society of Great Britain and Ireland and Venous Papers', Conference Proceeding: Annual General Meeting of the Vascular Surgical Society of Great Britain and Ireland (2001)*,* Brighton, England, In: *Phlebology*, 17 (1), 36–40.

Cuzzilla, M. L. (2003). *Major superficial leg veins* [internet]. Imthage Pty Ltd. Available from: http://www.venocuff.com/patient/gen_data.htm#e [Accessed 25 August 2003].

Dauplaise, T. L. & Weiss, R. A. (2001). 'Duplex-guided endovascular occlusion of refluxing saphenous veins', *Journal of Vascular Technology,* 25 (2), 79–82.

De Backer, G. (1997). 'Epidemiology of chronic venous insufficiency', *Angiology,* 48 (7), 569–576.

Deeks, J. J., Dinnes, J. et al (2003). 'Evaluating non-randomised intervention studies', *Health Technology Assessment,* 7 (27).

Diomed Ltd (2001). *Endovenous laser treatment,* CD-ROM, Cambridge.

Dover, J. S., Sadick, N. S. et al (1999). 'The role of laser and light sources in the treatment of leg veins', *Dermatologic Surgery,* 25 (4), 328–336.

Downs, S. H. & Black, N. (1998). 'The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions', *Journal of Epidemiology and Community Health,* 52 (6), 377–384.

Durkin, M. T., Turton, E. P. L. et al (1999). 'A prospective randomised trial of PIN versus conventional stripping in varicose vein surgery', *Annals of the Royal College of Surgeons of England,* 81 (3), 171–174.

Durkin, M. T., Turton, E. P. L. et al (2001). 'Long saphenous vein stripping and quality of life - a randomised trial', *European Journal of Vascular and Endovascular Surgery,* 21 (6), 545–549.

Dwerryhouse, S., Davies, B. et al (1999). 'Stripping the long saphenous vein reduces the rate of reoperation for recurrent varicose veins: five-year results of a randomized trial', *Journal of Vascular Surgery,* 29 (4), 589–592.

Eremia, S., Li, C. & Umar, S. H. (2002). 'A side-by-side comparative study of 1064 nm Nd:Yag, 810 nm diode and 755 nm alexandrite lasers for treatment of 0.3-3 mm leg veins', *Dermatologic Surgery,* 28 (3), 224–230.

Evans, C. J., Allan, P. L. et al (1998). 'Prevalence of venous reflux in the general population on duplex scanning: The Edinburgh vein study', *Journal of Vascular Surgery,* 28 (5), 767–776.

Evans, C. J., Fowkes, F. G. R. et al (1997). 'Edinburgh Vein Study: Methods and response in a survey of venous disease in the general population', *Phlebology,* 12 (4), 127–135.

Evans, C. J., Fowkes, F. G. R. et al (1999). 'Prevalence of varicose veins and chronic venous insufficiency in men and women in the general population: Edinburgh Vein Study', *Journal of Epidemiology and Community Health,* 53 (3), 149–153.

Farrah, J. & Shami, S. K. (2001). 'Patterns of incompetence in patients with recurrent varicose veins: A duplex ultrasound study', *Phlebology,* 16 (1), 34–37.

Fassiadis, N., Kianifard, B. et al (2001). 'No recurrence of reflux following endovascular radiofrequency ablation of the long saphenous vein (VNUS Closure) at one year', *British Journal of Surgery,* 88, 49–50.

Fassiadis, N., Kianifard, B. et al (2002a). 'A novel approach to the treatment of recurrent varicose veins', *International Angiology,* 21 (3), 275–276.

Fassiadis, N., Kianifard, B. et al (2002b). 'A novel endoluminal technique for varicose vein management: The VNUS closure', *Phlebology,* 16 (4), 145–148.

Fitridge, R. A., Dunlop, C. et al (1999). 'A prospective randomized trial evaluating the haemodynamic role of incompetent calf perforating veins', *Australian and New Zealand Journal of Surgery,* 69 (3), 214–216.

Forrestal, M. D., Fronek, H. S. et al (2003). 'Endovenous laser treatment', *Dermatologic Surgery,* 29 (3), 312–313.

Fowkes, F. G., Evans, C. J. & Lee, A. J. (2001). 'Prevalence and risk factors of chronic venous insufficiency', *Angiology,* 52 (Suppl. 1), S5–15.

Fowler, A., Stechman, M. & Mitchell, D. (2002). 'A randomised controlled trial of the effect of Esmarch tourniquet use on blood loss, bruising and quality of life in elective varicose vein surgery', *Phlebology,* 17 (1), 10–12.

Franks, P. J., Wright, D. D. I. et al (1992). 'Prevalence of venous disease: A community study in West London', *European Journal of Surgery, Acta Chirurgica,* 158 (3), 143–147.

Gabella, G. (1995). 'Cardiovascular system', In: Williams, P. L., Bannister, L. H., Berry, M. M., Collins, P., Dyson, M., Dussek, J. E. & Ferguson, M. W. J. (eds), *Gray's Anatomy,* Churchill Livingstone, Edinburgh, pp. 1596.

Gérard, J.-L., Desgranges, P. et al (2002). 'Feasibility of ambulatory endovenous laser for the treatment of greater saphenous varicose veins: One-month outcome in a series of 20 outpatients', *Journal des Maladies Vasculaires,* 27 (4), 222–225.

Glass, G. M. (1998). 'Prevention of sapheno-femoral and sapheno-popliteal recurrence of varicose veins by forming a partition to contain neovascularization', *Phlebology,* 13 (1), 3–9.

Goldman, M. P. (2000). 'Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of the vein wall in combination with ambulatory phlebectomy: preliminary 6-month follow-up', *Dermatologic Surgery,* 26 (5), 452–456.

Goldman, M. P. (2001). 'Treatment of leg veins with lasers and intense pulsed light: Preliminary considerations and a review of present technology', *Dermatologic Clinics,* 19 (3), 467–473.

Goldman, M. P. (2002). 'Endoluminal laser treatment of the greater saphenous vein at 810 nm', Conference Proceeding: American Society for Laser Medicine and Surgery*,* In: *Lasers in Surgery and Medicine*, 30, (S14), 37, Abstract Number: 124,

Goldman, M. P. & Amiry, S. (2002). 'Closure of the greater saphenous vein with endoluminal radiofrequency thermal heating of the vein wall in combination with ambulatory phlebectomy: 50 patients with more than 6-month follow-up', *Dermatologic Surgery,* 28 (1), 29–31.

Goldman, M. P. & Eckhouse, S. (1996). 'Photothermal sclerosis of leg veins. ESC Medical Systems, LTD Photoderm VL Cooperative Study Group', *Dermatologic Surgery,* 22 (4), 323–330.

Goldman, M. P. & Eremia, S. (2002). 'Laser and sclerotherapy treatment of leg veins: My perspective on treatment outcomes', *Dermatologic Surgery,* 28 (10), 969–970.

Goldman, M. P., Weiss, R. A. & Bergan, J. J. (1994). 'Diagnosis and treatment of varicose veins: a review', *Journal of the American Academy of Dermatology,* 31 (3 Pt 1), 393–413.

Hammarsten, J., Pedersen, P. et al (1990). 'Long saphenous vein saving surgery for varicose veins. A long-term follow-up', *European Journal of Vascular Surgery,* 4 (4), 361–364.

Harris, E. J. (2002). 'Endovascular obliteration of saphenous vein reflux: A perspective', *Journal of Vascular Surgery,* 35 (6), 1292–1294.

Harrison, T. R. (2001). 'Vascular diseases of the extremities', In: Braunwald, E., Fauci, A. S., Kasper, D. L., Hauser, S. L., Longo, D. L. & Jameson, J. L. (eds), *Harrison's Principles of Internal Medicine,* 1 McGraw-Hill, Sydney, pp. 1441.

Holme, J. B., Skajaa, K. & Holme, K. (1990). 'Incidence of lesions of the saphenous nerve after partial or complete stripping of the long saphenous vein', *Acta Chirurgica Scandinavica,* 156 (2), 145–148.

Jakobsen, B. H. (1979). 'The value of different forms of treatment for varicose veins', *British Journal of Surgery,* 66 (3), 182–184.

Jiang, P., van Rij, A. M. et al (1999). 'Recurrent varicose veins: patterns of reflux and clinical severity', *Cardiovascular Surgery,* 7 (3), 332–339.

Jones, L., Braithwaite, B. D. et al (1996). 'Neovascularisation is the principal cause of varicose vein recurrence: results of a randomised trial of stripping the long saphenous vein', *European Journal of Vascular and Endovascular Surgery,* 12 (4), 442–445.

Kaudewitz, P., Klovekorn, W. & Rother, W. (2001). 'Effective treatment of leg vein telangiectasia with a new 940 nm diode laser', *Dermatologic Surgery,* 27 (2), 101–106.

Kaudewitz, P., Klovekorn, W. & Rother, W. (2002). 'Treatment of leg vein telangiectases: 1-year results with a new 940 nm diode laser', *Dermatologic Surgery,* 28 (11), 1031–1034.

Kent, P. J., Maughan, J. et al (1999). 'Perforation-invagination (PIN) stripping of the long saphenous vein reduces thigh haematoma formation in varicose vein surgery', *Phlebology,* 14 (2), 43–47.

Khilnani, N. M. & Min, R. J. (2002). *Interventional radiology strategies treat venous insufficiency* [internet]. CMP Healthcare. Available from: http://www.dimag.com/cme/articles/013.shtml [Accessed 2 September 2003].

Labropoulos, N., Touloupakis, E. et al (1996). 'Recurrent varicose veins: Investigation of the pattern and extent of reflux with color flow duplex scanning', *Surgery,* 119 (4), 406–409.

Lacroix, H., Nevelsteen, A. & Suy, R. (1999). 'Invaginating versus classic stripping of the long saphenous vein. A randomized prospective study', *Acta Chirurgica Belgica,* 99 (1), 22–25.

Laurikka, J., Sisto, T. et al (1993). 'Varicose veins in a Finnish population aged 40–60', *Journal of Epidemiology and Community Health,* 47 (5), 355–357.

Lofgren, E. P. (1985). 'Treatment of long saphenous varicosities and their recurrence: A long-term follow-up', In: Bergan, J. J. & Yao, J. S. T. (eds), *Surgery of the veins,* Grune and Stratton, Inc, Orlando, pp. 285–299.

Lurie, F., Creton, D. et al (2003). 'Prospective randomized study of endovenous radiofrequency obliteration (closure procedure) versus ligation and stripping in a selected patient population (EVOLVeS Study)', *Journal of Vascular Surgery,* 38 (2), 207–214.

Mackay, E. (2002). 'Transcatheter ablation of the lesser saphenous vein with endovenous laser', Conference Proceeding: 16th Annual Congress of the American College of Phlebology, Florida, USA, http://www.phlebology.org/AbstractsFTL.htm.

Madar, G., Widmer, L. K. et al (1986). 'Varicose veins and chronic venous insufficiency disorder or disease? A critical epidemiological review', *Vasa - Journal of Vascular Diseases,* 15 (2), 126–134.

Manfrini, S., Gasbarro, V. et al (2000). 'Endovenous management of saphenous vein reflux', *Journal of Vascular Surgery,* 32 (2), 330–342.

Melrose, D. G., Knight, M. T. & Simandl, E. (1979). 'The stripping of varicose veins: a clinical trial of intermittent compression dressings', *British Journal of Surgery,* 66 (1), 53–55.

Merchant, R. F., DePalma, R. G. & Kabnick, L. S. (2002). 'Endovascular obliteration of saphenous reflex: A multicenter study', *Journal of Vascular Surgery,* 35 (6), 1190–1196.

Min, R. J. (2001). 'Endovenous laser treatment of the incompetent greater saphenous vein: mid term results', Conference Proceeding: 15th Annual Congress of the American College of Phlebology, California, USA, http://www.phlebology.org/AbstractsLQ3.htm.

Min, R. J. (2003a). 'Endovenous laser treatment of saphenous vein reflux: Two year follow-up results', Conference Proceeding: 28th Annual Scientific Meeting of the Society of Interventional Radiology, Utah, USA, http://sir.attendeeinteractive.com/index.cfm?fuseaction=custom.sp_scisess_search_sub.

Min, R. J. (2003b). 'Endovenous laser treatment of saphenous vein reflux using continuous mode', Conference Proceeding: 28th Annual Scientific Meeting of the Society of Interventional Radiology, Utah, USA, http://sir.attendeeinteractive.com/index.cfm?fuseaction=custom.sp_scisess_search_sub.

Min, R. J. (2003c). 'Endovenous laser treatment of short saphenous vein and anterior-lateral tributary incompetence', Conference Proceeding: 28th Annual Scientific Meeting of the Society of Interventional Radiology, Utah, USA, http://sir.attendeeinteractive.com/index.cfm?fuseaction=custom.sp_scisess_search_sub.

Min, R. J., Khilnani, N. & Zimmet, S. E. (2003). 'Endovenous laser treatment of saphenous vein reflux: Long-term results', *Journal of Vascular and Interventional Radiology,* 14 (8), 991–996.

Min, R. J., Zimmet, S. E. et al (2001). 'Endovenous laser treatment of the incompetent greater saphenous vein', *Journal of Vascular and Interventional Radiology,* 12 (10), 1167–1171.

Mueller, U., Philipp, C. M. et al (2002). 'Interstitial and intraluminal Nd : YAG-lasertherapy of superficial and deep varicose veins', Conference Proceeding: American Society for Laser Medicine and Surgery, In: *Lasers in Surgery and Medicine*, 30, (S14), 40, Abstract Number: 133.

Mulkens, P. J. M. (2003). 'New results of endovenous radiofrequency therapy (VNUS) of varicose veins: A three year follow-up', *Vasomed,* 15 (1), 24–25.

Munn, S. R., Morton, J. B. et al (1981). 'To strip or not to strip the long saphenous vein? A varicose veins trial', *British Journal of Surgery,* 68 (6), 426–428.

Navarro, L. & Boné, C. (2001). 'Endovenous laser treatment of greater saphenous vein reflux: A two year report on a minimally invasive ultrasound guided technique', Conference Proceeding: 15th Annual Congress of the American College of Phlebology, California, USA, http://www.phlebology.org/AbstractsLQ3.htm.

Navarro, L. & Boné, C. (2002). 'Endolaser - a three year follow-up report: Implications on crossectomy and ligation and stripping', Conference Proceeding: 16th Annual Congress of the American College of Phlebology, Florida, USA, http://www.phlebology.org/AbstractsFTL.htm.

Navarro, L., Min, R. J. & Boné, C. (2001). 'Endovenous laser: A new minimally invasive method of treatment for varicose veins - Preliminary observations using an 810 nm diode laser', *Dermatologic Surgery,* 27 (2), 117–122.

Neglén, P., Einarsson, E. & Eklof, B. (1993). 'The functional long-term value of different types of treatment for saphenous vein incompetence', *Journal of Cardiovascular Surgery (Torino),* 34 (4), 295–301.

NHMRC (1999). *A guide to the development, implementation and evaluation of clinical practice guidelines,* National Health and Medical Research Council, Commonwealth of Australia, Canberra, ACT.

NHMRC (2000). *How to use the evidence: assessment and application of scientific evidence,* National Health and Medical Research Council, Canberra.

NICE (2000). *Varicose veins, Clinical guidelines* [internet]. National Institute for Clinical Excellence. Available from: http://www.nice.org.uk/article.asp?a=10631 [Accessed 27 February 2003].

Perrin, M. (2000). 'A new procedure in the treatment of varicose veins of the lower limbs: The closure (registered trademark) technique', *Angeiologie,* 52 (4), 23–28.

Pichot, O., Sessa, C. & Bosson, J.-L. (2002). 'Duplex imaging analysis of the long saphenous vein reflux: Basis for strategy of endovenous obliteration treatment', *International Angiology,* 21 (4), 333–336.

Pichot, O., Sessa, C. et al (2000). 'Role of duplex imaging in endovenous obliteration for primary venous insufficiency', *Journal of Endovascular Therapy,* 7 (6), 451–459.

Preziosi, P., Galan, P. et al (1999). 'Prevalence of venous insufficiency in French adults of the SUVIMAX cohort', *International Angiology,* 18 (2), 171–175.

Prior, I. A., Evans, J. G. et al (1970). 'The Carterton study. 6. Patterns of vascular, respiratory, rheumatic and related abnormalities in a sample of New Zealand European adults', *New Zealand Medical Journal,* 72 (460), 169–177.

Proebstle, T. M. (2002a). 'Comment on R. A. Weiss: "Comparison of endovenous radiofrequency versus 810 nm diode laser occlusion of large veins in an animal model" ', *Dermatologic Surgery,* 28 (7), 648.

Proebstle, T. M. (2002b). 'Endovenous laser therapy (EVLT) of the greater saphenous vein with a 940 nm diode laser', *Vasomed,* 14 (3), 98–104.

Proebstle, T. M. (2003). 'Regarding "Endovenous treatment of the greater saphenous vein with a 940-nm diode laser: Thrombolytic occlusion after endoluminal thermal damage by laser-generated steam bubbles" - Reply', *Journal of Vascular Surgery,* 37 (1), 242–242.

Proebstle, T. M., Gul, D. et al (2003). 'Endovenous laser treatment of the lesser saphenous vein with a 940-nm diode laser: Early results', *Dermatologic Surgery,* 29 (4), 357–361.

Proebstle, T. M., Lehr, H. A. et al (2002). 'Endovenous treatment of the greater saphenous vein with a 940-nm diode laser: Thrombotic occlusion after endoluminal thermal damage by laser-generated steam bubbles', *Journal of Vascular Surgery,* 35 (4), 729–736.

Proebstle, T. M., Sandhofer, M. et al (2002). 'Thermal damage of the inner vein wall during endovenous laser treatment: Key role of energy absorption by intravascular blood', *Dermatologic Surgery,* 28 (7), 596–600.

Rautio, T., Ohinmaa, A. et al (2002). 'Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled trial with comparison of the costs', *Journal of Vascular Surgery,* 35 (5), 958–965.

Rautio, T. T., Perala, J. M. et al (2002). 'Endovenous obliteration with radiofrequency-resistive heating for greater saphenous vein insufficiency: A feasibility study', *Journal of Vascular and Interventional Radiology,* 13 (6), 569–575.

Rigby, K. A., Palfreyman, S. J. et al (2003). Surgery for varicose veins: use of tourniquet (Cochrane Review). In: *The Cochrane Library,* Issue 2003. Oxford: Update Software.

Ruckley, C. V. (1983). *A colour atlas of surgery for varicose veins,* Wolfe Medical Publications, London.

Ruckley, C. V., Evans, C. J. et al (2002). 'Chronic venous insufficiency: Clinical and duplex correlations. The Edinburgh Vein Study of venous disorders in the general population', *Journal of Vascular Surgery,* 36 (3), 520–525.

Rutgers, P. H. & Kitslaar, P. J. (1994). 'Randomized trial of stripping versus high ligation combined with sclerotherapy in the treatment of the incompetent greater saphenous vein', *American Journal of Surgery,* 168 (4), 311–315.

Rutherford, R. B., Padberg, F. T. Jr. et al (2000). 'Venous severity scoring: An adjunct to venous outcome assessment', *Journal of Vascular Surgery,* 31 (6), 1307–1312.

Sacks, D., Marinelli, D. L. et al (1996). *General principles for evaluation of new interventional technologies and devices,* Society of Interventional Radiology, Pennsylvania, USA.

Sadick, N. S. (2001). 'Long-term results with a multiple synchronized-pulse 1064 nm Nd:YAG laser for the treatment of leg venulectasias and reticular veins', *Dermatologic Surgery,* 27 (4), 365–369.

Sadick, N. S. (2002). 'A dual wavelength approach for laser/intense pulsed light source treatment of lower extremity veins', *Journal of the American Academy of Dermatology,* 46 (1), 66–72.

Sadick, N. S., Weiss, R. A. & Goldman, M. P. (2002). 'Advances in laser surgery for leg veins: bimodal wavelength approach to lower extremity vessels, new cooling techniques, and longer pulse durations', *Dermatologic Surgery,* 28 (1), 16–20.

Sarin, S., Scurr, J. H. & Coleridge Smith, P. D. (1992). 'Assessment of stripping the long saphenous vein in the treatment of primary varicose veins', *British Journal of Surgery,* 79 (9), 889–893.

Sarin, S., Scurr, J. H. & Coleridge Smith, P. D. (1994). 'Stripping of the long saphenous vein in the treatment of primary varicose veins', *British Journal of Surgery,* 81 (10), 1455–1458.

Schonholz, C., Onorati, D. et al (1999). 'Endovascular treatment of varicose veins of the lower extremities', *Journal of Endovascular Surgery,* 6 (1), 112–113.

Sisto, T., Reunanen, A. et al (1995). 'Prevalence and risk factors of varicose veins in lower extremities: Mini-Finland health survey', *European Journal of Surgery, Acta Chirurgica,* 161 (6), 405–414.

Sommer, B. & Sattler, G. (2001). 'High ligation and stripping of the long saphenous vein', In: Hanke, C.W., Sommer, B. & Sattler, G. (eds), *Tumescent Local Anesthesia,* Springer-Verlag Inc, New York, pp. 160–170.

Song, R., Altman, D. G. et al (2003). 'Validity of indirect comparison for estimating efficiency of competing interventions: empirical evidence from published meta-analyses', *British Medical Journal,* 326 (7387), 472.

Stata Corporation. (2001). *Intercooled Stata 7.0 for Windows 98/95/NT* Stata Corporation, College City, Texas.

Sybrandy, J. E. M. & Wittens, C. H. A. (2002). 'Initial experiences in endovenous treatment of saphenous vein reflux', *Journal of Vascular Surgery,* 36 (6), 1207–1212.

Sykes, T. C. F., Brookes, P. & Hickey, N. C. (2000). 'A prospective randomised trial of tourniquet in varicose vein surgery', *Annals of the Royal College of Surgeons of England,* 82 (4), 280–282.

Thorpe, P. E. & Osse, F. J. (2002). 'Chronic venous insufficiency: The role for endovascular therapy', In: Criado, F. (ed), *Endovascular Intervention: New Tools and Techniques for the 21st Century,* Vol 3 Futura Publ Co Inc, Armonk, pp. 155–182.

Tisi, P. V. & Beverley, C. A. (2003). Injection sclerotherapy for varicose veins (Cochrane Review). In: *The Cochrane Library,* Issue 1, 2003. Oxford: Update Software.

Vanscheidt, W. (1995). 'Laser therapy of varicosities', *Journal of the European Academy of Dermatology and Venereology,* 5, S48–S49.

Weiss, R. (2001a). 'Commentary on endovenous laser', *Dermatologic Surgery,* 27 (3), 326–327.

Weiss, R. A. (2001b). 'Endovenous techniques for elimination of saphenous reflux: A valuable treatment modality', *Dermatologic Surgery,* 27 (10), 902–904.

Weiss, R. (2002a). 'Vanquishing varicose veins. Less invasive techniques work well and slash recovery time', *Health News,* 8 (6), 4.

Weiss, R. A. (2002b). 'Comparison of endovenous radiofrequency versus 810 nm diode laser occlusion of large veins in an animal model', *Dermatologic Surgery,* 28 (1), 56–61.

Weiss, R. (2003). 'Endovenous laser treatment - Reply', *Dermatologic Surgery,* 29 (3), 313–314.

Weiss, R. A. & Dover, J. S. (2002a). 'Laser surgery of leg veins', *Dermatologic Clinics,* 20 (1), 19–36.

Weiss, R. A. & Dover, J. S. (2002b). 'Leg vein management: sclerotherapy, ambulatory phlebectomy, and laser surgery', *Seminars in cutaneous medicine and surgery,* 21 (1), 76–103.

Weiss, R. A. & Weiss, M. A. (2002). 'Controlled radiofrequency endovenous occlusion using a unique radiofrequency catheter under duplex guidance to eliminate saphenous varicose vein reflux: A 2-year follow-up', *Dermatologic Surgery,* 28 (1), 38–42.

Wilson, S., Pryke, S. et al (1997). 'Inversion' stripping of the long saphenous vein', *Phlebology,* 12 (3), 91–95.

Wolf, B. & Brittenden, J. (2001). 'Surgical treatment of varicose veins', *Journal of the Royal College of Surgeons of Edinburgh,* 46 (3), 154–158.

Wright, D. D. I., Rose, K. G. et al (2002). 'Recurrence following varicose vein surgery', *Phlebology,* 16 (3), 101–105.

Young, J., Hyde, C. et al (1999). *Lung volume reduction surgery (LVRS) for chronic obstructive pulmonary disease (COPD) with underlying severe emphysema,* West Midlands Development and Evaluation Committee, Birmingham.