Ontario Health Technology Assessment Series 2010; Vol. 10, No. 6

Endovascular Laser Therapy for Varicose Veins

An Evidence-Based Analysis

Presented to the Ontario Health Technology Advisory Committee in November 2009

April 2010

Ontario

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

Suggested Citation

This report should be cited as follows:

Medical Advisory Secretariat. Endovascular laser therapy for varicose veins: an evidence-based analysis. Ont Health Technol Assess Ser [Internet]. 2010 April [cited YYYY MM DD]; 10(6) 1-92. Available from: http://www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_EVLT_20100422.pdf

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ISSN 1915-7398 (Online)
ISBN 978-1-4435-1588-7 (PDF)

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The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

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If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact the Medical Advisory Secretariat: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

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List of Abbreviations

AVVSS	Aberdeen varicose vein symptom score
CEAP	Clinical, etiological, anatomic, pathological classification
CIV	Chronic venous insufficiency
CIVIQ	Chronic venous insufficiency questionnaire
CCT	Controlled clinical trial
DUS	Duplex ultrasound
DVI	Deep venous insufficiency
DVT	Deep venous thrombosis
ELT	Endovascular laser therapy
EVLA	Endovascular laser ablation
GSV	Great saphenous vein
LEED	Linear endovascular energy density
MAS	Medical Advisory Secretariat
OHTAC	Ontario Health Technology Advisory Committee
OR	Odds ratio
PE	Pulmonary embolism
RCT	Randomized controlled trial
RF	Radiofrequency
RR	Relative risk
SD	Standard deviation
SFJ	Saphenofemoral junction
SF-36	Medical outcomes study short form
SPJ	Saphenopopliteal junction
SSV	Small saphenous vein
UGFS	Ultrasound guided foam sclerotherapy
VCSS	Venous clinical severity score

Executive Summary

Objective

The objective of the MAS evidence review was to conduct a systematic review of the available evidence on the safety, effectiveness, durability and cost–effectiveness of endovascular laser therapy (ELT) for the treatment of primary symptomatic varicose veins (VV).

Background

The Ontario Health Technology Advisory Committee (OHTAC) met on November 27, 2009 to review the safety, effectiveness, durability and cost-effectiveness of ELT for the treatment of primary VV based on an evidence-based review by the Medical Advisory Secretariat (MAS).

Clinical Condition

VV are tortuous, twisted, or elongated veins. This can be due to existing (inherited) valve dysfunction or decreased vein elasticity (primary venous reflux) or valve damage from prior thrombotic events (secondary venous reflux). The end result is pooling of blood in the veins, increased venous pressure and subsequent vein enlargement. As a result of high venous pressure, branch vessels balloon out leading to varicosities (varicose veins).

Symptoms typically affect the lower extremities and include (but are not limited to): aching, swelling, throbbing, night cramps, restless legs, leg fatigue, itching and burning. Left untreated, venous reflux tends to be progressive, often leading to chronic venous insufficiency (CVI).

A number of complications are associated with untreated venous reflux: including superficial thrombophlebitis as well as variceal rupture and haemorrhage. CVI often results in chronic skin changes referred to as stasis dermatitis. Stasis dermatitis is comprised of a spectrum of cutaneous abnormalities including edema, hyperpigmentation, eczema, lipodermatosclerosis and stasis ulceration. Ulceration represents the disease end point for severe CVI.

CVI is associated with a reduced quality of life particularly in relation to pain, physical function and mobility. In severe cases, VV with ulcers, QOL has been rated to be as bad or worse as other chronic diseases such as back pain and arthritis.

Lower limb VV is a common disease affecting adults and estimated to be the seventh most common reason for physician referral in the US. There is a strong familial predisposition to VV with the risk in offspring being 90% if both parents affected, 20% when neither is affected, and 45% (25% boys, 62% girls) if one parent is affected. Globally, the prevalence of VV ranges from 5% to 15% among men and 3% to 29% among women varying by the age, gender and ethnicity of the study population, survey methods and disease definition and measurement. The annual incidence of VV estimated from the Framingham Study was reported to be 2.6% among women and 1.9% among men and did not vary within the age range (40-89 years) studied.

Approximately 1% of the adult population has a stasis ulcer of venous origin at any one time with 4% at risk. The majority of leg ulcer patients are elderly with simple superficial vein reflux. Stasis ulcers are often lengthy medical problems and can last for several years and, despite effective compression therapy and multilayer bandaging are associated with high recurrence rates. Recent trials involving surgical treatment of superficial vein reflux have resulted in healing and significantly reduced recurrence rates.

Endovascular Laser Therapy for VV

ELT is an image-guided, minimally invasive treatment alternative to surgical stripping of superficial venous reflux. It does not require an operating room or general anesthesia and has been performed in outpatient settings by a variety of medical specialties including surgeons (vascular or general), interventional radiologists and phlebologists. Rather than surgically removing the vein, ELT works by destroying, cauterizing or ablating the refluxing vein segment using heat energy delivered via laser fibre.

Prior to ELT, colour-flow Doppler ultrasonography is used to confirm and map all areas of venous reflux to devise a safe and effective treatment plan. The ELT procedure involves the introduction of a guide wire into the target vein under ultrasound guidance followed by the insertion of an introducer sheath through which an optical fibre carrying the laser energy is advanced. A tumescent anesthetic solution is injected into the soft tissue surrounding the target vein along its entire length. This serves to anaesthetize the vein so that the patient feels no discomfort during the procedure. It also serves to insulate the heat from damaging adjacent structures, including nerves and skin. Once satisfactory positioning has been confirmed with ultrasound, the laser is activated. Both the laser fibre and the sheath are simultaneously, slowly and continuously pulled back along the length of the target vessel. At the end of the procedure, homeostasis is then achieved by applying pressure to the entry point.

Adequate and proper compression stockings and bandages are applied after the procedure to reduce the risk of venous thromboembolism, and to reduce postoperative bruising and tenderness. Patients are encouraged to walk immediately after the procedure and most patients return to work or usual activity within a few days. Follow-up protocols vary, with most patients returning 1-3 weeks later for an initial follow-up visit. At this point, the initial clinical result is assessed and occlusion of the treated vessels is confirmed with ultrasound. Patients often have a second follow-up visit 1-3 months following ELT at which time clinical evaluation and ultrasound are repeated. If required, sclerotherapy may be performed during the ELT procedure or at any follow-up visits.

Regulatory Status

Endovascular laser for the treatment of VV was approved by Health Canada as a class 3 device in 2002. The treatment has been an insured service in Saskatchewan since 2007 and is the only province to insure ELT. Although the treatment is not an insured service in Ontario, it has been provided by various medical specialties since 2002 in over 20 private clinics.

Methods

Literature Search

The MAS evidence–based review was performed as an update to the 2007 health technology review performed by the Australian Medical Services Committee (MSAC) to support public financing decisions. The literature search was performed on August 18, 2009 using standard bibliographic databases for studies published from January 1, 2007 to August 15, 2009. Search alerts were generated and reviewed for additional relevant literature up until October 1, 2009.

Inclusion Criteria

- English language full-reports and human studies
- Original reports with defined study methodology
- Reports including standardized measurements on outcome events such as technical success, safety, effectiveness, durability, quality of life or patient satisfaction

- Reports involving ELT for VV (great or small saphenous veins)
- Randomized controlled trials (RCTs), systematic reviews and meta-analyses
- Cohort and controlled clinical studies involving ≥ 1 month ultrasound imaging follow-up

Exclusion Criteria

- Non systematic reviews, letters, comments and editorials
- Reports not involving outcome events such as safety, effectiveness, durability, or patient satisfaction following an intervention with ELT
- Reports not involving interventions with ELT for VV
- Pilot studies or studies with small samples (< 50 subjects)

Summary of Findings

The MAS evidence search identified 14 systematic reviews, 29 cohort studies on safety and effectiveness, four cost studies and 12 randomized controlled trials involving ELT, six of these comparing endovascular laser with surgical ligation and saphenous vein stripping.

Since 2007, 22 cohort studies involving 10,883 patients undergoing ELT of the great saphenous vein (GSV) have been published. Imaging defined treatment effectiveness of mean vein closure rates were reported to be greater than 90% (range 93%- 99%) at short term follow-up. Longer than one year follow-up was reported in five studies with life table analysis performed in four but the follow up was still limited at three and four years. The overall pooled major adverse event rate, including DVT, PE, skin burns or nerve damage events extracted from these studies, was 0.63% (69/10,883).

The overall level of evidence of randomized trials comparing ELT with surgical ligation and vein stripping (n= 6) was graded as moderate to high. Recovery after treatment was significantly quicker after ELT (return to work median number of days, 4 vs. 17; $p = .005$). Major adverse events occurring after surgery were higher [(1.8% (n=4) vs. 0.4% (n = 1) 1 but not significantly. Treatment effectiveness as measured by imaging vein absence or closure, symptom relief or quality of life similar in the two treatment groups and both treatments resulted in statistically significantly improvements in these outcomes. Recurrence was low after both treatments at follow up but neovascularization (growth of new vessels, a key predictor of long term recurrence was significantly more common (18% vs. 1%; p = .001) after surgery. Although patient satisfaction was reported to be high (>80%) with both treatments, patient preferences evaluated through recruitment process, physician reports and consumer groups were strongly in favour of ELT. For patients minimal complications, quick recovery and dependability of outpatient scheduling were key considerations.

As clinical effectiveness of the two treatments was similar, a cost-analysis was performed to compare differences in resources and costs between the two procedures. A budget impact analysis for introducing ELT as an insured service was also performed. The average case cost (based on Ontario hospital costs and medical resources) for surgical vein stripping was estimated to be $1,799. Because of the uncertainties with resources associated with ELT, in addition to the device related costs, hospital costs were varied and assumed to be the same as or less than (40%) those for surgery resulting in an average ELT case cost of $2,025 or $1,602.

Based on the historical pattern of surgical vein stripping for varices a 5-year projection was made for annual volumes and costs. In Ontario in 2007/2008, 3481 surgical vein stripping procedures were performed, 28% for repeat procedures. Annual volumes of ELT currently being performed in the province in over 20 private clinics were estimated to be approximately 840. If ELT were publicly reimbursed, it

was assumed that it would capture 35% of the vein stripping market in the first year and increase to 55% in subsequent years. Based on these assumptions if ELT were not publicly reimbursed, the province would be paying approximately $5.9 million and if ELT were reimbursed the province would pay $8.2 million if the hospital costs for ELT were the same as surgery and $7.1 million if the hospital costs were less (40%) than surgery.

The conclusions on the comparative outcomes between laser ablation and surgical ligation and saphenous vein stripping are summarized in the table below (ES Table 1).

ES Table 1: Outcome comparisons of ELT vs. surgery for VV

Outcomes	Comparisons
Post procedural pain, minor complications	ELT < Surgery
Recovery	ELT < Surgery
Major adverse events	ELT < Surgery
Effectiveness - Imaging vein occlusion/ absence	ELT ~ Surgery
Effectiveness -Vein symptom improvement	ELT ~ Surgery
Effectiveness - Quality Of Life	ELT ~ Surgery
Recurrence	ELT ~ Surgery
Patient satisfaction	ELT ~ Surgery
Patient preference	ELT > Surgery
Procedure costs	ELT ~ < Surgery
Budget impact	ELT > Surgery

The outcomes of the evidence-based review on these treatments based on three different perspectives are summarized below:

Patient Outcomes – *ELT vs. Surgery*

- ELT has a quicker recovery attributable to the decreased pain, lower minor complications, use of local anesthesia with immediate ambulation.
- ELT is as effective as surgery in the short term as assessed by imaging anatomic outcomes, symptomatic relief and HRQOL outcomes.
- Recurrence is similar but neovascularization, a key predictor of long term recurrence, is significantly higher with surgery.
- Patient satisfaction is equally high after both treatments but patient preference is much more strongly for ELT. Surgeons performing ELT are satisfied with treatment outcomes and regularly offer ELT as a treatment alternative to surgery.

Clinical or Technical Advantages – *ELT Over Surgery*

- An endovascular approach can more easily and more precisely treat multilevel disease and difficult to treat areas
- ELT is an effective and a less invasive treatment for the elderly with VV and those with venous leg ulcers.

System Outcomes – *ELT Replacing Surgery*

- ELT may offer system advantages in that the treatment can be offered by several medical specialties in outpatient settings and because it does not require an operating theatre or general anesthesia.
- The treatment may result in ↓ pre-surgical investigations, decanting of patients from OR, ↓ demand on anesthetists time, ↓ hospital stay, ↓decrease wait time for VV treatment and provide more reliable outpatient scheduling.
- Depending on the reimbursement mechanism for the treatment, however, it may also result in closure of outpatient clinics with an increasingly centralization of procedures in selected hospitals with large capital budgets resulting in larger and longer waiting lists.
- Procedure costs may be similar for the two treatments but the budget impact may be greater with insurance of ELT because of the transfer of the cases from the private market to the public payer system.

Background

Objective of Analysis

The objective of this MAS report was to conduct a systematic review of the available evidence on the safety, effectiveness, durability, and cost–effectiveness of endovascular laser therapy (ELT) for the treatment of primary symptomatic varicose veins (VV).

Clinical Condition

VV are tortuous, twisted, or elongated veins. (1) The primary cause of the condition is poorly functioning valves and decreased elasticity in the vein walls, resulting in venous reflux (reversed blood flow in the vein); it may also be the result of prior thrombotic events. (2) The resultant blood pooling leads to an enlargement of the veins with smaller vessels developing telangiectasis (spider veins) and larger vessels such as the saphenous veins becoming elongated and tortuous. The symptoms of patients with VV can include: aching leg pain, leg swelling, throbbing, night cramps, restless legs, leg fatigue and heaviness, and/or itching and burning. (3;4) Untreated venous reflux has also been associated with various complications such as varices rupture with hemorrhage and superficial thrombophlebitis. (1) It may also lead to chronic venous insufficiency (CVI) with prevalence increasing with age. (5)

CVI itself is a pathological condition of the skin and subcutaneous tissues that is secondary to prolonged stasis of venous blood flow. (6) The clinical signs of CVI result from venous hypertension occurring over time causing chronic inflammation, which further leads to a spectrum of conditions including edema, hyperpigmentation, eczema, lipodermatosclerosis and ulcers. (7) Leg ulcers represent the disease end-point for severe CVI.

Prevalence and Incidence

Varices of the lower limbs is a very common adult disease and estimated to be the seventh most common reason for referral to a physician in the US. (8) A familial predisposition to VV is likely as the risk in offspring is 90% if both parents are affected, 45% (25% boys, 62% girls) if only one parent is affected, and 20% when neither affected. (9) The prevalence of VV worldwide ranges from 5% to 15% among men and 3% to 29% among women. (5) The variability in this prevalence is attributable to a range of factors and a function of the age of the population studied, gender distribution (higher in women), ethnicity of the study group (more common in Caucasians than Blacks or Asians), survey methods, and disease definition. The annual incidence of VV estimated from the Framingham Study was reported to be 2.6% among women and 1.9% among men and did not vary within the age range (40 to 89 years) studied. (10)

Leg ulcers of venous origin are also common in the adult population. Approximately 1% of the adult population has a leg ulcer of venous origin at any one time and 4% are at of risk of leg ulcer. (11) The majority of leg ulcer patients are elderly and have simple superficial venous reflux. Episodes of leg ulcers are lengthy, lasting in some cases for several years. In a UK population based study, the median duration of ulceration was nine months, while 20% of the ulcers had not healed within two years and 66% of the patients had episodes of ulceration lasting longer than five years. (8) Management of leg ulcers is also difficult. Although initial compression and multilayer bandaging have been shown to be effective, the recurrence is high. (12;13) Recent trials involving superficial vein surgery for treatment of vein reflux have resulted in initial healing and significantly reduced recurrence with leg ulcers. (14;15)

Disease Measurement

The internationally accepted classification system for chronic venous disease, the clinical status, etiology, anatomy and pathophysiology (CEAP) system was first developed in 1994 by a multidisciplinary committee convened by American Venous Forum. (16) The system recently underwent a revision and has been approved as part of the reporting standards for endovenous ablation treatment of venous insufficiency by the American Venous Forum and the Society of Interventional Radiology. (17)

The nomenclature of the lower limb venous system has also recently been revised by an international interdisciplinary panel to standardize and improve diagnosis, care and research into venous disorders. (18;19) The veins are divided into three systems: the superficial, deep and perforating. The superficial veins, consisting of the saphenous veins, their tributaries and accessory and communicating vessels, are located in the subcutaneous tissue and are the major causes of VV. The saphenous veins include the great saphenous vein (GSV) and the small saphenous veins (SSV). The junctions where these veins meet with the deep venous system are called the saphenofemoral junction (SFJ) and the saphenopopliteal junction (SPJ), which are also critical areas for occurrence of reflux.

Duplex ultrasonography is the recommended optimal approach for investigating diseases and disorders of the venous system. (20;21) It provides a map to document the extent of venous disease and presence of reflux. in the superficial venous system, deep venous systems, (19;22) This is essential to differentiate the relative involvement of the deep and superficial venous systems and the junctions and connectors between them in order to guide the selection of the appropriate treatment. Duplex ultrasound also has a role in surveillance after therapy to assess outcomes and detect recurrence.

A potential classification system for saphenous vein reflux was developed following a duplex ultrasound imaging survey of 2,275 limbs in 1,751 patients. The 5-point category system was based on the combination of varices, saphenous vein reflux, junction reflux, and malleus reflux present. (23) The most common source of saphenous insufficiency was the GSV in 82.7% (n=1,882) of cases and less commonly the SSV (10.9%; n=248) and non saphenous veins (6.4%; n=145). Varices without reflux, estimated to occur in 36.7% of cases, were thought to involve consultations mainly for aesthetic purposes. The overall proportion of limbs that were asymptomatic was 34.4%. Reflux affecting the entire saphenous system from the saphenous junction down to the ankle was reported to affect the oldest patients ($\geq$ 63 years).

Symptoms and HRQOL

A number of measures exist to evaluate symptoms and severity of vascular disease. The Venous Clinical Severity Scale (VCSS) has been a recommended instrument to report symptom severity. (17;24) It's based on physician assessment of nine common symptoms: pain, VV, venous edema, skin pigmentation, inflammation, induration, ulcers (number, state, size) of chronic venous disease, and the use of compression therapy. (24;25)

The impact of VV on health related quality of life (HRQOL) has also been evaluated in several clinical (26-28) and population (29) based surveys. Quality of life (QOL) was measured by SF-36 (a generic QOL instrument) and several disease-specific QOL instruments including the VEINES-QOL/Sym, CIVIQ-2, and the Aberdeen QOL. In general, chronic venous disease was found to be associated with significantly reduced HRQOL, particularly in relation to pain, physical function and mobility. There was also a strong linear trend of increasing impact on physical functioning and disability with increasing disease severity. In an international survey of patients presenting to general practitioners and vein disease specialists, 65% of VV patients had other disease processes such as oedema, skin changes or ulceration. (27) Physical and mental HRQOL scores were reported to decrease with the severity of symptoms and in the most severe cases, HRQOL rated by the SF-36 was worse than that of patients with chronic lung disease, back pain, or arthritis. VV alone without symptoms, however, was not found to alter HRQOL.

Management of VV

VV are initially managed with conservative therapy involving life style changes such as weight loss through diet and regular exercise, as well as elevation of the feet at the end of the day. (1) Compression therapies including the use of prescribed elastic or support stockings are also frequently recommended to decrease blood volume, edema, venous distension, and venous wall tension. (7) These therapies are also used to increase calf muscle pump function, which is one of the major sources of venous return. This can improve venous hemodynamics in patients with VV and reduce edema, but poor compliance attributable to the cost of the stockings, lack of patient education, and poor cosmesis, limits their effectiveness. Various pharmacological treatments and herbal supplements have also been used to treat symptoms, including dieuretics for edema, topical steroid creams for dermatitis, and antibiotics for infection involving stasis ulcers. (7)

For smaller veins such as telangiectasias and spider veins, sclerotherapy is the therapy of choice, having become one of the most common venous procedures performed in office settings. (30;31) The technique involves the injection of a chemical irritant into the veins to initiate chemical thrombophlebitis, occlusion, and subsequent vein fibrosis. Many different chemical materials are used as sclerosing agents. (31) The use of sclerosing foam has been on the rise because of advantages over liquid sclerosants in that it displaces blood rather than being diluted by it, has increased contact with endothelium, and is echogenic, which greatly increases treatment accuracy. (32) The major considerations for sclerotherapy have centered on maximizing treatment efficacy while minimizing risk through the proper selection of sclerosant for the vein to be treated. (2;31) Treatment efficacy can be reduced with too low a dose, while the risk of complications such as DVT or emboli increases at higher doses. (33) In practice, however, because of high rates of recanalization and recurrence, sclerotherapy is generally reserved for isolated varices without truncal reflux or for residual varices after surgery or intravascular ablation therapy. (34)

Ambulatory phlebectomy (PB) is another common procedure for VV that is usually performed in outpatient settings. (2) In the procedure, phlebectomy hooks are used to remove tributary veins of the saphenous veins through multiple skin incisions. Combination treatments involving PB with surgical or endovascular treatments such as radiofrequency or laser ablation may also be performed. Only local anesthesia is required and referred to as 'tumescent anesthesia,' which involves the injection of an anesthetic solution into the perivenous space along the length of the treated vein. This method eliminates multiple needle sticks and allows rapid anesthesia to extensive vein segments. It also produces local swelling and tissue firmness, reduces blood loss, decreases bruising, and increases patient comfort.

Surgery has been the mainstay treatment for superficial veins such as the great saphenous vein (GSV) and the small saphebous vein (SSV), which are the major cause of leg VV. (35) The surgery is performed in the operating room under general, spinal, or epidural anesthesia. The operative technique involves an initial ligation of the saphenofemoral junction (SFJ) followed by a stripping of the GSV. The stripping is usually only performed to the knee because of concerns over increased saphenous vein injury. (36) There is morbidity following surgery including a range of complications such as neurosensory loss, infection, hematomas lymph leaks, or deep vein thrombosis (DVT) reported to occur in approximately 18% to 20% of patients. (37;38) Patients also often require 2 to 3 weeks recovery time after surgery and, despite advances in techniques, high recurrence rates have continued. (39)

Endovascular techniques such as radiofrequency (RF) or endovascular laser ablation (ELT) are major treatment alternatives to surgery for VV. Both techniques involve ablation of the vein wall through thermochemical reactions. Most patients with superficial saphenous vein reflux are suitable for endovascular approaches. In a recent UK study, patient suitability for various endovascular treatment and surgery was assessed through duplex ultrasonography. (40) A total of 403 consecutive patients referred to a regional vascular center with five vascular surgeons for open surgery for VV underwent ultrasonographic assessments. Treatment eligibility was based on anatomic considerations including vein

diameter, tortuosity and the presence intraluminal thrombus. Patients were then categorized with: GSV diameters 3-12 mm suitable for radiofrequency (RF), diameters >3 mm suitable for ELT, diameters <1 cm suitable for foam sclerotherapy. Overall, 328 (73%) of the legs were suitable for at least one of the three endovascular approaches. The major reasons for exclusions included vein tortuosity or thrombosis.

Endovascular Laser Therapy

ELT is an image guided, minimally invasive treatment alternative to surgery for the treatment of incompetent VV. The treatment does not require an operating room or general anesthesia and has been performed in outpatient settings by various medical specialties including surgeons (vascular or general), interventional radiologists and phlebologists. It is generally considered after treatment with conservative therapy has failed. Although most patients with VV are eligible for the treatment, their anatomy must be amenable. Veins that are too tortuous for catheter access or too large to successfully ablate would not be amenable. Other contraindications include: pregnancy, inability to ambulate, poor general health, aneurysmal sources of venous reflux, and a compromised deep venous vascular system.

ELT works by ablating the endothelium of the vein wall, which is thought to be mediated by direct and indirect effects of the laser. (41) Direct heating effects may occur by direct absorption of photon energy (radiation) by the vein wall and indirectly by convection from steam bubbles and conduction from heated blood. (42;43) The steam produced by the blood's absorption of laser energy, however, is a small fraction of the energy necessary to damage the vein wall and not thought to be the primary mechanism of injury.

The lasers themselves come in two varieties, continuous wave and pulsed, with the latter generally being more powerful. Various laser wavelengths have been used for ablation including the 810-nm, 940-nm, 980-nm, 1064-nm and 1320- nm. (44) The primary target chromophore of the 810-nm and 940-nm lasers is haemoglobin, while the higher wavelength lasers primarily target water. During the procedure, the laser fibre is drawn down the vein in a stepped or continuous fashion with the laser firing continuously or in one-second pulses. The dose of energy delivered is reported as the linear endovenous energy density (LEED), in joules per cm of vein (J/cm), or as fluence, which is the energy delivered per surface area (J/cm^2). Controversy exists over the minimum energy needed to achieve optimal occlusion rates, but levels of 60 J/cm or higher are considered adequate. (41) The occurrence of treatment failures above these doses, however, suggests that other factors influence treatment success.

Treatment with ELT treatment begins with a color-flow doppler ultrasonography exam to confirm and map all areas of venous reflux. (45;46) The procedure then involves the introduction of a guide wire into the target vein under ultrasound guidance, followed by the insertion of an introducer sheath through which an optical fibre carrying the laser energy is advanced. A tumescent anesthetic solution is injected into the soft tissue surrounding the target vein along its entire length. In addition to providing anesthesia, this has a compression effect on the vein, which maximizes the laser's effect on the vein wall. When delivered in a sufficient volume to compress the vein and dissect it away from other structures, it then separates the vein from surrounding structures to protect other nerves and skin structures. It also acts as a thermal sink, which reduces peak temperatures in perivenous tissues. Once satisfactory positioning has been confirmed with ultrasound, the laser is activated. Both the laser fibre and the sheath are then slowly pulled back along the length of the target vessel. At the end of the procedure, homeostasis is achieved by applying pressure to the entry point. After the procedure, compression stockings and bandages are applied to reduce postoperative bruising, tenderness, and the risk of venous thromboembolism. (41)

Patients are encouraged to walk immediately and most return to usual activity within a few days. Follow-up protocols vary, with most patients returning 1 to 3 weeks later for a follow-up visit in which the occlusion of the treated vessels is evaluated by ultrasound. Patients often have a second follow-up visit in the 1 to 3 months following, at which time clinical evaluation and ultrasound are repeated. If required, sclerotherapy may be performed during the ELT procedure or at any follow-up visits.

Methods

Research Question(s)

The purpose of this evidence review was to determine the safety, effectiveness, durability, and cost-effectiveness of ELT in the management of primary symptomatic VV. The specific research questions addressed were:

1. What is the broader safety profile of ELT?
2. What is the treatment effectiveness of ELT for varicose vein reflux?
3. What is the treatment effectiveness of ELT for VV symptoms?
4. What is the impact of ELT on health related quality of life?
5. What is the durability of ELT treatment?
6. What is patient treatment satisfaction with ELT?
7. What is the comparative effectiveness of ELT with surgical ligation and vein stripping?

Literature Search

A literature search was performed on August 18, 2009 using OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cumulative Index to Nursing & Allied Health Literature (CINAHL), the Cochrane Library, and the International Agency for Health Technology Assessment (INAHTA) for studies published from January 1, 2007 to August 15, 2009 (Appendix 1). Search alerts were generated and reviewed for additional relevant literature up until October 1, 2009. Abstracts (n = 260) were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search. Additional Information Sources; Consultations with held with clinical experts (vascular surgeons and interventional radiologists) and industry representatives.

Inclusion Criteria

- English language full-reports and human studies
- Original reports with defined study methodology
- Reports including standardized measurements on outcome events such as technical success, safety, effectiveness, durability, quality of life or patient satisfaction
- Reports involving ELT for VV (great or small saphenous veins)
- Randomized controlled trials (RCTs), systematic reviews and meta-analyses
- Cohort and controlled clinical studies involving ≥ 1 month ultrasound imaging follow-up

Exclusion Criteria

- Non-systematic reviews, letters, comments and editorials
- Reports not involving outcome events such as safety, effectiveness, durability, or patient satisfaction following ELT
- Reports not involving interventions with ELT for varicose veins
- Pilot studies or studies with small samples (< 50 subjects)

Outcomes of Interest

The outcomes of interest included: technical outcomes, recovery, ultrasound defined absence of flow or

absence of vein, vein recanalization, neovascularization, vein reflux, complications, major adverse events, varicose vein symptoms and quality of life.

Quality of Evidence

The quality of evidence assigned to individual RCT studies was determined using a modified CONSORT Statement Checklist for Randomized Controlled Trials. (40;47) The CONSORT Statement was adapted to include three additional quality measures: the adequacy of control group description, significant differential loss to follow-up between groups, and study attrition.

The overall quality of the evidence was assessed as high, moderate, low, or very low according to the GRADE Working Group criteria (40;48) as presented below.

- Quality refers to the criteria such as the adequacy of allocation concealment, blinding and follow-up.
- Consistency refers to the similarity of estimates of effect across studies. If there are important and unexplained inconsistencies in the results, our confidence in the estimate of effect for that outcome decreases. Differences in the direction of effect, the magnitude of the difference in effect, and the significance of the differences guide the decision about whether important inconsistency exists.
- Directness refers to the extent to which the interventions and outcome measures are similar to those of interest.

As stated by the GRADE Working Group, the following definitions of quality were used in grading the quality of the evidence:

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain

Results of Evidence Based Analysis

Analysis - Literature Approach

The MAS systematic literature search identified 11 systematic reviews on treatments for VV, five reviews (41;49-52) focused only on endovascular treatment for VV and six (53-58) focused on all treatments including endovascular therapy (ELT) for VV (Table 1). Three HTA evidence reports (59-61) were also identified, two of which (59;60) were performed to support public healthcare financing decisions. The MSAC evidence review on ELT for VV published in 2008 (with search periods up until August 2007) was the most extensive review to date. The MAS evidence review was therefore performed to review available evidence on ELT published since 2007. In particular the literature was reviewed for the following: large studies (> 50) involving complications or adverse events reported in short or longer term cohort follow-up, large cohorts with longer term (> 1-year) follow up, randomization trials or controlled clinical trials comparing ELT with other approaches particularly surgery, which is considered the key comparator for endovascular approaches. The results of this search are outlined in Table 1 and include 13 randomized controlled trials, three controlled clinical trials and 28 cohort case series.

The results of the MAS evidence review are detailed below in two sections. The first section involves a summary of the evidence in the systematic reviews. The second section included the evidence from the MAS review that addresses three primary questions of ELT for VV; effectiveness of ELT, safety of ELT and comparative effectiveness of ELT with surgical ligation and vein stripping.

Table 1: Level of Evidence of Included Studies

Study Design	Level of Evidence†	Number of Eligible Studies
Large RCT (n> 100), systematic review of RCTs	1	6 RCTs 14 Systematic reviews
Large RCT unpublished but reported to an international scientific meeting	1(g)	1
Small RCT (n < 100)	2	6
Small RCT unpublished but reported to an international scientific meeting	2(g)	
Non-RCT with contemporaneous controls	3a	2
Non-RCT with historical controls	3b	1
Non-RCT presented at international conference	3(g)	
Surveillance (database or register)	4a	
Case series (multisite)	4b	5
Case series (single site)	4c	23
Retrospective review, modelling	4d	
Case series presented at international conference	4(g)	
	Total	59

* RCT refers to randomized controlled trial;

Section 1. Published Systematic Evidence Reviews

The summary details of the systematic evidence reviews identified in the literature on ELT of VV are listed below in Table 2. HTA evidence reports were performed in three countries, by NICE for the United Kingdom in 2003 (60), by MSAC for Australia in 2008 (59) and by CADTH for Canada in 2009 (61).

The NICE review performed in 2003 concluded that the five published case series on ELT were insufficient evidence to support the treatment at that time. The most recent evidence review by the MSAC in 2008 was based on 57 safety studies and five controlled clinical trials (two were RCTs) on the comparative effectiveness of ELT with surgical ligation and vein stripping. The conclusions of this report were that the short term clinical effectiveness of ELT are similar to surgery but with lower rates of adverse events and shorter recovery times. The recommendation to publicly fund ELT for VV was accepted by the Australian Ministry of Health and Ageing in May 2008. The HTA review by CADTH in 2009 was based on one HTA, four systematic reviews, four clinical trials (one being a RCT), two cost-effective studies, and two costing studies. The conclusions of the review were that the occurrence of serious adverse events was lower with ELT, the short term recovery was superior to surgery, and effectiveness was comparable but long term clinical effects need to be established. Of the other systematic reviews, six focused on all treatments (including ELT) and five were performed focusing only on ELT treatment.

Section 2. MAS Evidence Review

2A. Effectiveness of Endovascular Laser Ablation

A total of 22 large (n > 50) cohort studies published since 2007 were identified involving ELT for GSV the main superficial VV and seven cohort studies for the SSV. The details of these studies are summarized in Appendix 2 (Tables A2 and A3). The results on treatment effectiveness are discussed below for ELT separately for the GSV and the SSV.

Ablation of the Great Saphenous Vein

Twenty-two cohort studies concerning ELT ablation of the GSV were identified, collectively examining 10,883 patients. Each study involved interventions in outpatient clinics or angiography suites with procedures performed by various specialists including surgeons, interventional radiologists, or phlebologists. Although procedures were generally carried out under local anesthesia, some cohorts (64-69) used interventions in operating theatres using spinal or general anesthesia. The mean age of the patients in these trials, with the exception of the Barucchello et al. study (64) in which patients were elderly (between 70 to 85 years), ranged from 45 to 57 years of age and most were women (range 58% - 95%).

Several laser types were used including 810-nm (n=13 trials), 980-nm (n=7 trials), and 1470-nm (n=1 trial) wavelength units. Power mode and pullback rates of laser ablation were generally reported. The continuous mode of laser ablation (n=15 trials) was more commonly employed than the pulse mode (n=4 trials) and in a few instances (n=2 trials) the power mode varied from continuous to pulse. Secondary procedures used to treat other refluxing veins were generally performed concomitantly with ELT (usually phlebectomy or foam sclerotherapy) or in a staged fashion (usually foam sclerotherapy) if required. Two studies (67;70) also reported ligating superficial vein perforators concomitantly with ELT.

The details of the sixteen cohort studies reporting on imaging follow up outcomes on ablation of the GSV are outlined below in Table 3. The imaging defined anatomic measure of treatment success was generally defined as occlusion of the treated vessel with duplex ultrasound the imaging modality used in all reports. The short term (within 6 months) reported occlusion rates found in the studies were all greater than 90%

(range: 93.7% to 99%). In one trial (71), treatment success was defined as the absence of the treated vein on duplex ultrasound and in that study, 516 patients (685 ELT procedures) were followed over a 69 month period. Almost all treated veins (99.6%; 682/685) were completely absent on imaging follow-up with only three veins (0.4%) being closed but still visible on ultrasound beyond 12 months. The mean interval between treatment and ultrasound documented absence of vein was 6.4 months (minimum interval of 3 months). Longer term follow up was performed for most cohorts but generally for only up to 1 year, at which point the occlusion rates in those studies were still greater than 90% (range: 94% to 100%). Longer than one year follow-up was reported in five studies (64;72-75) with life table analysis performed in four of these (64;72;73;75), but the follow up was limited at three and four years. Vein occlusion rates of 97.8% (72) and 93.7% (74) were reported at 2 years.

Table 2: Systematic Reviews on Endovascular Laser Treatment of VV

Author	Year	Search Period	Review Objective	Evidence
HTA Reports - Endovascular Laser Treatment (ELT) of VV				
MAS - HTA	2009	2007 – Aug 2009	▪ Systematic review of evidence of the safety, effectiveness, durability and cost effectiveness of ELT for VV to support public financing decisions	Reports (3 HTA, 12 SR, 13 RCT, 3 CCT, 28 CS)
CADTH	2009	2004 – May 2009	▪ To review the clinical and cost effectiveness of ELT for VV	Reports (1 HTA, 4SR, 1RCT, 1 CCT, 2 CE, 2 costing)
MSAC	2008	Jan 1997 – Aug 2007 (surgery) Sep 2003 – Aug 2007 (laser)	▪ Systematic review of available evidence on ELT for VV to support public financing decisions	Safety [ELT 40 reports and surgery 22 reports (sample > 100)] Effectiveness: 1 SR, 2 RCT,3 CCT
NICE (Rapid Review)	2003	To Feb 2003	▪ Evaluate the safety and effectiveness of ELT of the long saphenous vein	5 case series
Systematic Reviews – Endovascular Laser Treatment of VV				
Darwood et al. (41)	2009	1950 – Dec 2008	▪ To identify original reports and RCT studies reporting outcomes for ELT	98 original studies (5 RCT)
Hoggan et al. (49)	2009	1997 – Aug 2007 (surgery) Sep 2003 – Aug 2007 (laser)	▪ To compare the safety and effectiveness of ELT and surgery for VV	59 studies: 4 RCT, 3 CCT, 37CS, 15 different comparators
Van Den Bus et al. (58)	2009	Not stated	▪ To inform clinicians about ELT and review the safety and effectiveness of ELT for varicose	237 reports (1 RCT)
Van Den Bus et al. (62)	2009	2007 - July 2008	▪ To review common and rare complications associated with ELT	34 studies
Mundy et al. (50)	2005	Jan 1966 – Sep 2004	▪ To assess the safety and effectiveness of ELT for VV	13 case series
Systematic Reviews – All Treatments for VV				
Bacho et al. (63)	2009	Not Stated	▪ To review the evidence regarding interventions (compression, sclerotherapy, surgery and endoluminal) for uncomplicated VV	ELT: 3 RCT, 1CCT, 3 case series
Leopardi et al. (55)	2009	Jan 1988 – Feb 2008	▪ To review the safety and effectiveness of varicose vein treatments (conservative therapy, sclerotherapy, phlebectomy, ELT, radiofrequency ablation and surgery involving saphenous vein ligation and stripping) for	ALL: 4 SR, 10 RCT, 3 CCT
Van Den Bus et al. (58)	2009	To Feb 2007	▪ Effectiveness of 4 therapies for lower extremity varicosities (foam sclerotherapy, ELT, radiofrequency, surgical ligation and stripping)	ELT: 30 case series
Badri et al. (54)	2008	Not stated	▪ To compare safety and effectiveness of ELT, radiofrequency and sclerotherapy to surgery (ligation and vein stripping) for VV	ELT: 3 RCT, 10 case series
Luebke et al. (56)	2008	1970 - 2007	▪ To assess the safety/effectiveness of endoluminal therapies (ELT, RF ablation, foam sclerotherapy) compared to conventional surgery	ELT: 3 RCT, 29 case series
Subramonia et al. (57)	2007	To 2005	▪ To review the evidence for new endoluminal interventions for lower limb varicoses	ELT: 11 case series

CADTH, refers to the Canadian Agency for Drugs and Technology in Health Care; MSAC, Medical Services Advisory Committee; NICE, National Institute for Clinical Excellence; CCT, Controlled clinical trial; CE, Cost effectiveness; CS, Cohort series; ELT, Endovascular laser treatment; HTA, Health technology assessment; SR, Systematic review

Table 3: Imaging Follow-Up and Outcomes of ELT Ablation of Great Saphenous Vein

Author, Year, Country	Sample	Treatment Success, Follow- UP	3 Months	6 Months	1 Year	2 Year	3 Year	4 Year
Barucchello 2009 (64) Italy	473 p (535 Legs) 330 GSV, 65 SSV, 140 other incompetent varices	▪ Recurrent varicosities on duplex ultrasound	-	-	1.7% 5/301 GSV recanalized	-	5.9% 7/117	-
Desmyttere 2007 (72) France	500 p (511 Legs)	▪ Vein closure with absence of flow on duplex ultrasound	-	95.7% (466)	96.8% (408)	97.8% (269)	99.3% (141)	97.1% (34)
Elmore 2008 (71) US	516 p (685 Legs) 475 GSV, 32 SSV, 9 other (anterior and posterior accessory GSV, posterior thigh circumflex veins)	▪ Absence of treated vein on duplex ultrasound	-	-	98.1% (510/516)	-	-	-
Fernandez 2008 (73) Venezuela	1559 p (1985 Legs) 1652 GSV, 285 SSV, 40 ALT, 8 PMT	▪ Primary ablation as absence of flow in treated vein on duplex ultrasound ▪ Secondary ablation rate absence of flow in treated vein after secondary sclerotherapy procedures ▪ Life table analysis	-	-	91.3% at 15 months	78.3% at 30 months	-	-
Hamel-Desmos 2008 (84) France/Switz.	1422 p (1703 Legs) 1394 GSV + 309 SSV	▪ Failure to occlude vessel on duplex ultrasound	-	3.6%	-	-	-	-
Jung 2008 (65) Korea	148 p (169 Legs) 135 GSV + 41 SSV	▪ Occluded vessel on duplex ultrasound, failure as treated vessel recanalization rate	94.3% (166/176)	-	-	-	-	-
Knipp 2008 (74) US	364 p (460 Legs)	▪ Occluded vessel on duplex ultrasound ▪ Life table analysis	-	98.7% VAR 214	95.9% VAR 105	91.4% VAR 11	-	-
Lu 2008 (70) China	1060 p (1186 Legs)	▪ Totally and partially occluded treated vessel on duplex ultrasound	-	98.6% (1169/1186)	-	-	-	-
Mackenzie, 2008 (66) UK	640 P (713 Legs) 579 GSV + 119 SSV + 60? AAGSV	▪ Absence of flow on color doppler or absence of visible vein	96.1% (610/635)	-	-	-	-	-

Author, Year, Country	Sample	Treatment Success, Follow- UP	3 Months	6 Months	1 Year	2 Year	3 Year	4 Year
Myers 2009 (75) Australia	361 p (509 Legs) 509 GSV	▪ Primary success to occlude lumen of the treated vein on duplex ultrasound, secondary success after secondary treatment with sclerotherapy ▪ Life table analysis	-	-	VAR 198	VAR 67	VAR 26	VAR 8 75.5%, 97.2%
Pannier 2009 (85) Latvia	100 p (117 Legs) 108 GSV + 26 SSV	▪ Occlusion of the treated vein on duplex ultrasound	100% (134/134)	-	100% (99/99)	-	-	-
Park 2009 (86) Korea	312 p (438 Legs) 331 GSV, 106 SSV	▪ Absence of blood flow in entire ablated vein on duplex ultrasound	99.7% (373/374)	100% (274/274)	-	-	-	-
Sadik 2007 (87) US	90 p (94 Legs) 94 GSV	▪ Recurrence on duplex ultrasound	-	-	5.9% (2/34)	3.6% (1/28)	3.4% (1/29)	-
Tan 2009 (67) Singapore	169 p (270 Legs) 270 GSV	▪ Recurrence varicosities on duplex ultrasound	-	-	2.4% (4/169)	-	-	-
van den Bremer 2009 (68) Netherlands	323 p (403 Legs)	▪ Complete or partial occlusion of treated vein on duplex ultrasound	6 weeks 93.7% (282/301)	-	-	-	-	-
Vuylsteke 2008 (88) Belgium	97 p (129 Legs) 129 GSV	▪ Absence of flow in occluded vein on duplex ultrasound	1 month 94.6% (122/129)	90.7% (107/118)	-	-	-	-

GSV refers to the great saphenous vein; SSV, small saphenous vein; VAR, veins at risk

Table 4: Imaging Follow-Up and Outcomes of ELT Ablation of the Small Saphenous Vein

Author, Year, Country	Sample	Treatment Success, Follow- UP	≤ 3 Months	6 Months	1 Year	2 Year	3 Year
Gibson 2007 (76) US	187 p (210 legs) 210 SSV	▪ Occlusion of treated vein on duplex ultrasound at 3 month ▪ Mean follow-up of 4 months (range: 2 - 11 months)	At 2-4 days 100% SSV occluded	Final scans available 2 -11 months post for 126 legs 60% Recanalization in 4% (5/126 legs) and without symptoms	-	-	-
Huisman 2009 (77) Netherlands	150 p (169 legs) 169 SSV	▪ Occlusion of treated vein on duplex ultrasound	At 3 months ultrasound available in 150/169 (89%) 148/150 (98.7%) were completely occluded.	-	-	-	-
Kontothanassis 2009 (78) Italy	204 p (229 legs) 229 SSV	▪ Occlusion of treated vein on duplex ultrasound ▪ Mean follow-up of 16 months (range: 2 - 39 months) ▪ Life table analysis	UP to 4 months all but 4 patients had a follow-up exam 1.3% recanalization (2 after 1 week and 1 after 2 months)	VAR 225 After 8 or 12 months ablated veins were generally not distinguishable on duplex ultrasound Reflux in 7 limbs (3.1%)	VAR 154 After I year reflux in new areas from treated areas developed in 8 limbs (5.2%) and 4 underwent treatment for symptoms	VAR 66	VAR 53
Nwaejike 2009 (82) UK	61 p (66 legs) 66 SSV	▪ Vein closure on duplex ultrasound at 6 week and 3 month review ▪ Median follow-up of14 months	All attended 6 week and 3 month follow-up, 100% veins occluded on duplex ultrasound	At 6 months post no recurrence was detected	-	-	-
Park S.J. 2008 (83) Korea	344 p (390 legs) 390 SSV (45 bilateral and 113 also ELT GSV reflux)	▪ Vein closure on duplex ultrasound at 1, 2 years ▪ Mean follow-up of 9 months (SD: 7 months)	At week 1 389/390 (99.7%) treated veins were closed no detectable flow US 3 months – (21 limbs lost to follow-up) Vein closure 355/369 (96.2%)	38 limbs lost to FUP Vein closure 260/272 (95.6%) 17 veins recanalized by 6 months (1 at week, 14 by 3 months, 2 by 6 months)	37 limbs lost to follow-up Vein occluded in 102/108 (94.4%)	23 patients were followed up after 2 years and no recurrences were seen	-

Author, Year, Country	Sample	Treatment Success, Follow- UP	≤ 3 Months	6 Months	1 Year	2 Year	3 Year
Park S.W. 2008 (80) Korea	84 p (96 legs)	▪ Vein closure on duplex ultrasound ▪ Mean F-up 4 months	Follow-up at 1 week in 83 patients (95 Legs) At 1 month closure in 89/93 veins (96%) Within 1 month 4/95 (4.2%) veins recanalized with reflux recurrence At 3 months, 82/82 (100%) veins closed	82/82 (100%) closed	VAR All of the 77 veins closed	VAR All of the 71 veins closed	VAR All of the 55 veins closed
Theivacumar 2007 (81) UK	65 p (68 legs) 68 SSV	▪ Duplex ultrasound exam for vein visibility, patency and if patent compressibility and visible color flow following calf squeeze. ▪ Venous reflux assessed by Doppler waveform and color flow imaging ▪ 6 month follow-up	At 6 and 12 weeks US confirmed complete occlusion in 68/68 (100%) SSV to the level of SPJ	46 patients(48 Legs) completed 6 month follow-up. SSV not visible in 42 legs (88%), isoechoic in 4 for simple occlusion and hyperechoic (obliteration/fibrosis) in 2	-	-	-

DU refers to Duplex ultrasound: SSV, small saphenous vein; VAR, veins at risk

Ablation of the Small Saphenous Vein

Seven cohort studies (76-81) involving ablation of the less common cause of superficial vein reflux, the small saphenous vein, were identified (summarized in Appendix 2, Table A3). As with ablation of the GSV, laser operators included surgeons, phlebologists and interventional radiologists. Procedures were all performed in outpatient settings with local, tumescent anesthesia. The laser wavelength used involved either the 980-nm (n=4 trials) or the 810-nm (n=3 trials). Secondary procedures were performed either concomitantly (phlebectomy or sclerotherapy) (76;78;82) or staged at 6 weeks post-op (sclerotherapy) (77;80;81). In one trial (83) concomitant phlebectomy was performed only for the most severe cases and followed by a staged secondary intervention with sclerotherapy if required. In another trial (78), concomitant phlebotomy or sclerotherapy was performed in addition to vein ligation for incompetent tributaries and perforate veins. These studies tended to involve fewer subjects (the largest involved 344 patients) as SSV reflux is a much less common cause of reflux than the GSV. (83) The mean age in the cohorts ranged from 47 to 57 years of age and, as with the trials of GSV ablation, most patients were female with representation as high as 82% (77) and 88% (76)

The imaging follow up outcomes reported for the seven cohort studies are outlined below in Table 4. The imaging defined anatomic measures of treatment success for the SSV were also defined as occlusion of the treated vessel on duplex ultrasound (duplex ultrasound follow-up was employed in all studies). All studies reported high (> 90%) SSV occlusion rates at 3 and 6 months follow-up. Only three studies (78;80;83) reported 1-year follow-up, but the high vein occlusion rate (>90%) was maintained. Continuing high occlusion rates were reported at 2-year (100%) and 3-year (100%) follow-up. (80)

2B. Safety of Endovascular Laser Therapy

The reporting standards for adverse events after ELT recommended by both the Society Interventional Radiology and the Society Vascular Surgery were adopted for this report. (17) Complications or adverse events following laser ablation in the GSV and SSV cohort studies are listed in Appendix 2, Tables A4 and A5. For this evidence review, major adverse events after ELT included vascular events such as deep venous thrombosis (DVT), pulmonary embolism (PE), infection, nerve damage, or skin burns. Other events requiring additional care or hospitalization were also considered major adverse events. Minor complications such as pain and bruising frequently occur following ELT but are generally of short duration and self limiting without clinical sequelae. Other complications such as hematoma were often cited as complications more likely related to secondary or concomitantly performed procedures (e.g. phlebectomy) than to the primary laser treatment. Such minor complications are not generally included as major events unless they result in additional care or hospitalization.

Major adverse events were reported in 10 of the 22 cohort studies (summarized in Table 5). The overall major adverse event rate for ELT was 0.63% (69/10,883), while DVT and skin burns occurred at rates of less than 0.5% and 0.2%. Nerve damage, PE, and infection were also rarely reported, each occurring in less than 1 in a 1000 patients.

The complications and major adverse events occurring after ELT ablation of the SSV are listed in Appendix 2, Table A5. The seven cohort studies with primarily ablation of the SSV involved 1,095 patients (1,228 legs). The overall major adverse event rate after SSV ablation was 0.46% (5/1095). All of these events were nerve injury related, either the sural nerve or in one case the lateral cutaneous nerve (83). There were no reported events of infection, skin burns, pulmonary embolism or DVT. Superficial thrombophlebitis was reported in several studies, but it resolved spontaneously within three months and without clinical sequelae. DVT was conservatively defined in one study (76) as any protrusion of any thrombus into the popliteal vein from the saphenopopliteal junction. Although thrombus extension was often observed post-operatively, none persisted at short-term follow-up. An overall superficial thrombophlebitis rate of 2.8% (34/1,226 legs) was reported in the studies with rates ranging from 1.3% (78) to 5.7% (76).

Table 5: Major Adverse Events After Endovascular Laser Ablation in Great Saphenous Vein

Event	Number of Occurrences	Percent	Rate of Occurrence
DVT	39/10,883	0.36%	< 5 in 1,000
Skin Burns	14/10,883	0.13%	< 2 in 1,000
PE	4/10,883	0.04%	< 1 in 1,000
Nerve Damage	2/10,883	0.02%	< 1 in 1,000
Infection	10/10,883	0.09%	< 1 in 1,000
Overall Major AE	69/10,883	0.63%	< 1 in 100

AE refers to adverse events; DVT, deep venous thrombosis; PE, pulmonary embolism

2C. Randomized Controlled Studies Involving Endovascular Laser Therapy

Fifteen RCT and CCT studies involving ELT for VV were identified in the MAS evidence review. The RCT studies identified in earlier published systematic reviews were included in the MAS review to ensure a comprehensive evaluation of ELT compared to surgery. The clinical trials were divided into three groups based on varying comparators to ELT:

Group A: ELT vs. surgery,

Group B: ELT vs. other endovascular interventions, and

Group C: comparisons of alternative technical ELT approaches.

The methodological details of the studies including design, conduct and evaluation are outlined in Appendix 2, Table A6. The primary and secondary outcomes for the clinical trials are summarized in Appendix 2, Table A7. The outcome measures included validated measures for symptom and HRQOL improvement with both generic and vein disease specific instruments. The outcomes reported in the clinical trials were grouped as being either technical, functional, clinical or patient related (see Table 6).

Group A: ELT vs. Surgery

Six RCT studies (89-95), one with partial randomization (95), compared ELT to surgical ligation and stripping of the GSV (as outlined in Appendix 2, Table A8 and summarized below in Table 7). All but one trial (89) involved two treatment arms. The Darwood et al. trial involved three treatment groups: Group 1 underwent ELT at low laser power (12W intermittent power); Group 2 underwent ELT at high laser power (14W continuous power); and Group 3 underwent surgical ligation and vein stripping. Patient median ages in the clinical trials ranged from 46 to 54 years and again involved a high proportion of females, ranging from 57% to 95%. (90) Vascular surgeons performed both the surgery and endovascular laser ablations in all the clinical trials. The anesthesia approach used in the trials was the same for both treatment groups, except in the case of Darwood et al. trial (89) in which ELT was performed with local tumescent anesthesia and surgery was performed with general anesthesia.

The trials varied in the conduct of interventions in both arms, particularly for ELT. ELT without surgical ligation was performed in four trials and in two trials (90;93) a surgical high ligation of the GSV was included before the endovascular laser ablation. Stripping techniques included forward stripping, although additional procedures involving cryostripping were performed in one study. (96) All studies documented extensive secondary interventions for both arms, either in a concomitant or staged fashion. The concomitant interventions (usually phlebectomy or ligation of tributary varices) reflected the desire to avoid under treating patients and requiring them to return for subsequent additional interventions. The other approach taken, particularly for ELT treatment arms, was to avoid overtreatment and provide additional interventions such as sclerotherapy in a staged manner.

Table 6: Clinical Trial Reported Outcomes and Endpoints

Study	Technical				Functional			Clinical		Patient Satisfaction	Vein Disease specific QOL	Generic QOL	Costs
	Procedure	Pain	Recovery	Complications	Vein Reflux	Recan / Neovasc*	Varicosities Needing treatment	Vein Symptoms	Cosmesis				
ELT vs. Surgery													
Darwood, 2006	✓	✓	✓	✓	✓			✓	✓	✓	✓		
DeMedeiros, 2005		✓		✓		✓			✓	✓			
Disselhoff, 2008	✓	✓	✓	✓	✓	✓		✓			✓	✓	✓
Kalteis, 2008		✓	✓	✓					✓	✓	✓		
Rasmussen, 2007,2009	✓	✓	✓	✓		✓		✓			✓	✓	✓
Theivacumar, 2009						✓				✓			
ELT vs. Radiofrequency or Sclerotherapy													
Almeida, 2009		✓		✓	✓	✓		✓			✓		
Morrison, 2005				✓		✓							
Almeida, 2006				✓		✓							
Gonzales, 2008		✓		✓	✓	✓		✓					
ELT Technical Issues													
Carradice, 2008	✓	✓	✓	✓	✓		✓	✓		✓	✓	✓	
Disselhoff, 2008				✓	✓			✓					
Kim, 2009				✓	✓	✓							
Lugli, 2009		✓		✓									
Theivacumar, 2008		✓		✓			✓	✓		✓	✓		

*Recanalization Neovascularization

Table 7: RCT of Endovascular Laser Ablation vs. Surgical Ligation and Stripping of Great Saphenous Vein

Study	Trial Type, Subjects	Main Intervention ELT vs. Surgery	Co-Interventions ELT vs. Surgery	Anesthesia ELT vs. Surgery	Follow-Up
Darwood 2006, UK	3-arm RCT 118 p	ELT1 vs. ELT2 vs. Ligation and Stripping	Staged vs. concurrent	Local vs. general anesthesia	3 months 1 year
DeMedeiros 2005, Brazil	2-arm RCT (Within person) 20 p	ELT + Ligation vs. Ligation and Stripping	Concurrent vs. concurrent	Epidural block and subarachnoid	1 month 2 months
Disselhoff 2008, 2009 Netherlands	2-arm RCT (CE) 120 p	ELT vs. Ligation and Stripping	Staged vs. concurrent and staged	Patient choice anesthesia	6 months 1, 2 years
Kalteis 2008, Austria	2-arm RCT 100 p	ELT + Ligation vs. Ligation and Stripping	Concurrent vs. concurrent	General or regional anesthesia	4 months
Rasmussen 2007, 2008 Denmark	2-arm RCT (CS) 121 p	ELT vs. Ligation and Stripping	Concurrent vs. concurrent	All office based, local anesthesia	6 months 2 years
Theivacumar 2009, UK	2-arm RCT 127 p (68 randomized)	ELT vs. Ligation and Stripping	Staged vs. concurrent	All general anesthesia	2 years

ELT refers to endovascular laser therapy; RCT, randomized clinical trial

Recovery and Post Procedural Complications

Recovery after ELT or surgery was reported as 'time to usual activity' or 'time to return to work' in four trials (89;91;93;94) (Table 8). Recovery after treatment was not the study objective in one trial (95) and in another the trial (90) randomization was within-person and recovery could not be compared. Only one trial (89) compared assigned local tumescent anesthesia for ELT with general anesthesia for surgery. In that study, the median time to recovery to usual activity was significantly (p = .001) shorter for patients undergoing ELT than surgery (2 days vs. 7 days).

Recovery time was also significantly (p = .001) shorter in the Disselhoff et al. trial (91), 75% vs. 45% returned to normal activity by 10 days. In that trial, however, the assignment of anesthesia had been by patient choice and more patients undergoing surgery had general anesthesia (82% vs. 63% respectively).

In the Kalteis et al. trial (93), recovery was reported as the median return to work time and was higher, but not significantly so, for ELT (20 days vs. 14 days; p =.054). The comparison in this trial, however involved ELT combined with surgical ligation and anesthesia in both treatment groups was general or regional.

The Rasmussen et al. trial (94) was unusual in that it was the only one in which office based local tumescent anesthesia was used for both ELT and surgery. In the study, recovery was reported as both the mean number of days to usual activity (7.7 vs. 6.9; $p > .05$) and the mean number of days to return to work (7.6 vs. 7.0; $p > .05$), which were higher, but not significantly so, for ELT than for surgery. Individual recovery times were, however, highly variable in the study, with a range of about a month in both treatment groups.

Table 8: Recovery After Endovascular Laser Ablation or Surgical Stripping for VV

Author	Anesthesia for ELT	Anesthesia for Surgery	Recovery for ELT	Recovery for Surgery	Recovery Difference
Darwood (89)	Local tumescent anesthesia	Day case general anesthesia	85.3% (29/34) for ELT 1 and 83.3% (20/24) for ELT 2 returned to normal activity within a week and the median time to normal activity 2days for ELT1 and 2 days for ELT2	56% (14/25) to normal activity within a week and median time to normal activity 7 days	ELT < Surgery p = .001
DeMedeiros (90)	Subarachnoid or epidural anesthesia	Subarachnoid or epidural anesthesia			NA (within-person RCT)
Disselhoff (92)	38 general anesthesia and 22 local tumescent anesthesia	patient choice of anesthesia (49 general anesthesia and 11 local tumescent anesthesia)	75% return to normal activity by 10 days	45% return to normal activity by 10 days	ELT < Surgery p = .001
Kalteis (93)	General anesthesia 48%, regional 51% [n= 47]	General anesthesia 34%, regional anesthesia 66% [n=48]	Median return to work time 20 days (range: 14.0 - 25.5)	Median return to work time 14.0 days (range: 12.8 - 25)	ELT ~ Surgery p = .054
Rasmussen (94)	Office based local tumescent anesthesia and conscious sedation (midazolam)	Office based local tumescent anesthesia and conscious sedation (midazolam)	Return to normal activity time mean days 7.7 ± 6.1 (range: 0 - 29)	Return to normal activity mean time days 6.9 ± 7.0 (range: 0 - 29)	ELT ~ Surgery p > .05
			Return to work time mean of 7.6 ± 4.9 days (range: 1 - 28)	Return to work mean time 7.0 ± 6.0 days (range: 1 - 31)	
Theivacumar (95)	Local tumescent anesthesia	General anesthesia	NR	NR	

ELT refers to endovascular laser therapy; NA, not applicable; NR, not reported

Safety

The major adverse events reported in the RCTs for ELT and surgery are outlined in Table 9. The overall major adverse event rate was 0.4% (1/269) in the ELT groups and 1.8% (4/221) in the surgery groups and rates were not significantly different (p = .26). There were no DVT or PE in the 479 cases reported in the trials. The four adverse events in the surgical groups involved mainly infections (n=3) related to the surgical cut down and access in the groin. In the ELT group, one case involved a two week hospitalization due to excessive pain and post-operative inflammation. (93) The complication was attributed to over-treatment with the laser.

The DeMedeiros et al. (90) trial was a within-person randomization trial of 20 patients with bilateral disease, in which each received ELT on one leg and ligation and surgical vein stripping on the other. No major adverse events were reported in the trial but a detailed comparison was made of minor complications such as pain, bruising, oedema and swelling. Subarachnoid blocking or epidural anesthesia was used for the procedure and the majority of patients in both groups (85% ELT and 80% surgery) reported pain to be absent or of slight intensity. Bruising was significantly greater in the surgery group with 60% exhibiting large bruises compared to 20% in the ELT group (p = .025). Edema and swelling was also more common in the surgery group at 40% and 15% respectively (p = .025). Post-operative persistent oedema was thought to be related to potential injury of lymphatic vessels under the knee, particularly due to the pulling on nearby tissues with surgical stripping.

Table 9: Major adverse events in RCT of ELT vs. surgery

Author, Study Size (ELT, Surgery)	ELT	Surgery
Darwood et al. . N = 118 (47,33,34)	0	2 groin infections 1 acute respiratory distress syndrome, ICU admit with 2 days ventilation
Disselhoff et al. N = 120 (60,60)	0	0
Kalteis et al. N = 100 (47,48)	1 hospitalized two weeks post op due to excessive pain and inflammation over treated GSV, resolved in 4 days	
Medeiros et al. . 20 pairs (20,20)	0	0
Rasmussen et al. . N = 121 (62,59)	0	1 groin infection requiring antibiotics
Total = 479 (269, 221)	**1 (0.4%)**	**4 (1.8%)**

Imaging Defined Outcome after Ablation of Great Saphenous Vein

Four RCT studies (89;91;94;95) reported duplex ultrasound defined measures of treatment effectiveness, usually as closure or absence of the treated vein. The surgical approach was similar in all the studies except in the Disselhoff et al. trial (91) in which cryosurgery was used to strip the GSV. In the ELT treatment groups, two lasers, the 810-nm diode laser (in three studies) and the 980-nm diode laser (in one study) were used variable energy density levels were reported. Co-interventions such as ligation of side tributaries and stab avulsions or phlebectomies were generally performed for additional varices in the surgical groups. In the ELT treatment groups, secondary interventions involving phlebectomy or schlerotherapy were usually performed in a staged fashion (if required) 6 or 12 weeks post operatively.

In the Rasmussen et al. trial (94), the primary outcome measure was duplex defined closed or absent GSV at 6 months. Six month follow-up was available for 76% (47/62) of the ELT patients and 74% (51/69) of the surgery patients. In the surgical group, two operations failed (2/59; 3%) and in the ELT group, three GSVs (3/62; 4.8%) had recanalized. At 2 years follow-up, the development of new varices occurred in 33% and 26% of the surgical and laser groups, respectively. A total of 11% of the patients had been re-operated.

In the Darwood et al. trial (89), the primary outcome was defined as reflux in the treated vein on duplex imaging (color flow sonography and Doppler spectral trace) at 3 months and 1 year. At 3 months, the majority of the patients in the two groups undergoing ELT remained free of reflux in the treated vein [97.6% (41/42) and 89.7% (26/29) respectively]. Patients in the surgical group also remained free of reflux (87%) (28/32) and differences between the groups were not significant (p = .227). At 1-year follow-up, recurrence was low and the majority of patients remained free of vein reflux. The difference between the groups was not significant (85.7% for the laser groups vs. 90.5% for the surgery group). Causes for recurrence, however, varied in the treatment groups. Recurrences in the ELT group were due to recanalization of the treated vessel whereas recurrence in surgical group was due to neovascularization.

Longer term imaging outcomes of up to 2 years were reported in two trials. (91;95) In the Disselhoff et al. trial (91), the primary outcome measure was recurrent vein reflux on duplex imaging assessed by life-table analysis at 6, 12, and 24 months follow-up. At six months GSV reflux was successfully ablated in 95% (57/60) and 100% (60/60) of the patients undergoing laser ablation and surgical ligation and stripping. At 2 years, follow-up was available for 92.5% (111/120) of the treated patients and it was found that 77% (95% CI: 72 - 78) of those who underwent laser treatment and 66% (95% CI: 60 - 67) of those who underwent surgery were free from recurrence. The difference between the groups was not statistically significant (p = .253), however, the pattern, time, and type of recurrences were. Recurrences in the ELT group occurred six months earlier in follow-up and tended to be due to recanalization, whereas recurrence in the surgical group occurring at one year tended to be due to neovascularisation. Approximately 20% (11/56), of the surgical group also exhibited recurrence at 2 years. There were no cases of neovascularization in the ELT group.

Theivacumar et al. (95) used recurrence and neovasularization at 2 years as the primary outcome measure. Only patients recruited early in the trial (53%; 68/127) had been randomized. Follow-up was reported at 1 and 2 years for 97.8% (134/137) and 94.2% (129/137) of treated legs. The clinical recurrence at 2 years was 6.6% (4/60) in the surgery group and 7.0% (5/69) in the ELT group; this was not a statistically significant difference. The four cases of clinical recurrence in the surgical group were due to mid thigh perforator (n=2) and residual GSV with neovascularization (n=2). The five cases of clinical recurrence in the laser group were attributable to GSV recanalization (n=3), mid thigh perforator (n=1), and development of new anterior saphenous vein reflux (n=1). Neovascularization, however, was significantly higher (p = .001) in the surgical group than the laser group [18% (11/60) and 1% (1/69), respectively].

Vein Symptom Improvement

Three trials (89;91;94) compared the impact of ELT and surgery on venous clinical symptoms using a validated instrument the Venous Clinical Severity Score (VCSS). In all three trials, venous clinical symptoms were significantly improved over baseline at 3 months, 6 months, and at 2 years (see Table 10). In the Darwood et al. trial (89) the VCSS scores were reported as group median values and the baseline median (inter quartile ranges) scores of 4 (3-5) improved to 0 (0-1) in both groups at 3 months ($p < .001$). The Disselhoff et al. (91) and Rasmussen et al. (94) trials reported mean VCSS scores at multiple follow-up points. In the Disselhoff et al. trial, the VCSS scores were significantly improved after treatment and continued to improve over time. Differences between the treatment groups were not statistically significant at any follow-up point (p = 0.561). The biggest improvements were noted to be improvements in pain and varicosity in both groups at 6 months follow-up.

Table 10: Venous Clinical Severity Scores at Baseline and at Follow-up

Author	Treatment arms	VCSS Baseline Mean (range)	3-Month Mean (range)	6-Month Mean (range)	1-Year Mean (range)	2-Year Mean (range)
Disselhoff et al.	ELT	3.2 (0-6)	ND	1.0 (0-3)	0.7 (0-4)	0.6 (0-4)
	Surgery	3.4 (0-6)	ND	1.0 (0-3)	0.9 (0-2)	0.8 (0-2)
Rasmussen et al.	ELT	2.8 (1-8)	0.1 (0-2)	0.4 (0-7)	ND	ND
	Surgery	2.4 (2-12)	0.2 (0-2)	0.2 (0-2)	ND	ND
		VCSS Baseline Median (IQR)	3-month Median (IQR)			
Darwood et al.	ELT1 – 12 W ELT2 – 14 W	4 (3-5)	0 (0-1)			
	Surgery	4 (3-5)	0 (0-1)			

ELT refers to endovascular laser therapy; ND, not done; IQR, inter quartile range; VCSS, venous clinical severity score

In the Rasmussen et al. trial (94), mean VCSS scores significantly improved from baseline at 3 months and scores were not significantly different between groups at any time point. Scores for individual patients undergoing surgical treatment were reported to improve in 57 patients, worsen in one, and remain unchanged in one. The scores for individual patients undergoing endovascular laser ablation were reported to improve in all cases. Although the VCSS scores were not reported in the Theivacumar et al. study (95), improvements in patients with ulcers were reported. At baseline, two patients in the ELT group had active ulcers prior to treatment and a further two (one from each group) had healed ulcers. The active ulcers in the ELT group were reported to be healed by 12 weeks and 6 months and all remained healed at 2-years follow-up.

Health Related Quality of Life

A vein disease specific Health Related Quality of Life (HRQOL) instrument, the Aberdeen Varicose Vein Symptom Score (AVVSS), was reported in three clinical trials (89;91;94) comparing ELT to surgery for various follow-up time points (see Table 11). The AVVSS is based on 15 questions with scores ranging from 1 (worst) to 100 (best) QOL ratings. In the Darwood et al. study (89) AVVSS, scores significantly improved at 3-month follow-up over baseline in all groups ($p < .001$). Differences in improvements between the groups were not significant ($p = .694$). The improvements in HRQOL were maintained in all groups at 1-year follow-up. Significant improvements in HRQOL scores over baseline were also reported in the Disselhoff et al. study (91) at 1 and 2-years of follow-up and there were no difference between the treatment groups over time ($p = .064$). The QOL scores were similarly and significantly improved in the two treatment groups at the 3 and 6-months follow-up in the Rasmussen et al. study. (94)

Table 11: Varicose Vein Disease Specific Health Related Quality of Life Scores at Baseline and at Follow-up

Author	Treatment arms	AVVSS Baseline Median (IQR)	3-Month Median (IQR)	6-Month Median (IQR)	1-Year Median (IQR)	2-Year Median (IQR)
Darwood et al.	ELT – 12W low power	11.8 (9.81 – 9.44)	5.60 (1.45-8.20)	ND	1.82 (0.13-5.86)	ND
	ELT – 14W high power	14.3 (8.88 - 19.60)	4.19 (1.70 -7.85)	ND	2.53 (0—5.64)	ND
	Surgery	14.0 (9.49 - 19.16)	5.32 (1.03 – 7.66)	ND	3.89 (0-10.29)	ND
		AVVSS Baseline Mean (Range)	**3-Month Mean (Range)**	**6-Month Mean (Range)**	**1-Year Mean (Range)**	**2-Year Mean (Range)**
Disselhoff et al.	ELT	15.8 (1.9 - 42.9)	ND	5.6 (0-20.3)	5.4 (0-27.1)	5.2 (0-25.6)
	Surgery	13.6 (0.8 - 37.2)	ND	6.2 (0-29.3)	7.0 (0-31.6)	4.5 (0.2-19.0)
Rasmussen et al.	ELT	18.6 (3.6 - 40.2)	6.9 (0-43.8)	7.1 (0-38.7)	ND	ND
	Surgery	16.1 (4.4 - 34.3)	8.2 (0-31.2)	5.3 (0-33.1)	ND	ND

AVVSS refers to Aberdeen Varicose Vein Symptom Score; ELT, endovascular laser therapy; IQR, inter quartile range; ND, not done

Patient Satisfaction

Four clinical trials (41;89;93;95) reported patients' satisfaction with treatment either by endovascular laser ablation or surgical ligation and stripping. In the Darwood et al. trial (89), patient satisfaction was rated on a 100-mm linear visual analogue scale and reported as median values with interquartile ranges at 3 month follow-up. Satisfaction in all three treatment groups was high: 95 (range: 89 - 98) in the low laser ELT group, 91 (range: 84 - 97) in the high laser level ELT group and 91 (range: 81 - 95) in the surgical group. Between group differences were not statistically significant ($p = .267$).

In the Kalteis et al. trial (93), patients in the ELT group also underwent surgical high ligation, limiting the comparison of the endovascular and surgical approaches. At 4 months, 91% of the ELT patients and 81% of the surgery patients were content or very content with their cosmetic results. Patients in both groups were also satisfied with their treatment and the majority would undergo the same treatment again if it was required (96% of the ELT group and 89% of the surgical group).

In the Theivacumar et al. trial (95), patient satisfaction with treatment was reported at the 2-year follow-up. Satisfaction with treatment was high in the two study groups at 88% and 90% in the ELT and surgical groups, respectively ($p = .37$).

In the DeMedeiros et al. trial (90), patient satisfaction was evaluated indirectly in a within person comparison. Patients with bilateral VV disease had one leg treated with ELT and one with surgery and were unaware of their leg assignments. When patients were asked which leg was felt to have benefitted the most from the treatment, 70% reported that the leg undergoing the laser had benefitted the most. No significant differences were noted by 10% of the patients.

Patient Preference

Patient preference for treatment was evaluated in several reports. Recruitment information reported by Darwood et al. (41) showed that 47% (136 of 331) of eligible patients agreed to randomization, while 177 declined to participate, primarily because of a declared preference for ELT.

In the Disselhoff et al. trial (91) patient preference for anesthesia was evaluated. The setting and method of anesthesia were assigned based on patient preference for treatment as a day case with general or regional anesthesia or in an outpatient setting with tumescent local anesthesia. In the surgical group, 82% of patients preferred day case treatment under regional (spinal) or general anesthesia and in the ELT group, the majority of patients (66%
) also preferred the day case setting under regional or general anesthesia.

Treatment preference was also reported in a large prospective cohort of patients in which 1,559 patients including 102 (6.5%) with open leg ulcers presenting to a vein clinic, were offered ELT or surgery for their VV. (73) Nearly all reported a preference for ELT over surgery and only 0.2% experienced a technically-related treatment failure. Of the 500 patients completing the patient satisfaction questionnaire, 93% claimed that symptoms had resolved, 87% were highly satisfied with the cosmetic result and 91% were willing to undergo the procedure again if required.

Additional information on patient preference is available from a small consumer panel composed mainly , mostly female and currently in the work force organized by MSAC for their evidence review on ELT for varices. (59) The information and opinions from this panel group favoured ELT over surgery for a number of reasons. Among them were the less invasive nature of ELT with minimal scarring and decreased pain following the procedure and the ability to maintain physical activity and return top work quickly after the procedure. ELT, because it can be performed on an outpatient basis, avoids waiting lists and uncertainties of inpatient booking, instead enabling a scheduled and planned approach that allows for budgeting.

Vascular surgeons in Ontario treating patients with VV confirm that in their consultations on treatment options, patients expressed an overwhelming preference for ELT over surgery (Personal Communication, November 2009). In most cases it was a cost barrier that prevented patients from choosing ELT. The quick recovery, limited time off work, and reliable outpatient scheduling for the treatment were major issues for patients with VV. The surgeons also commented that the shortage of operating room time and greater priority of arteriole over venous disease conditions resulted in longer wait times for VV surgery.

Group B: ELT vs. Other Endovascular Approaches

Four trials compared ELT with other endovascular treatment approaches. (97-100) Three of these trials (97;98;100), two being RCT (98;100) compared ELT with radiofrequency (RF) and one (99) with foam sclerotherapy for treatment of great saphenous vein reflux (see Appendix 2, Table A9).

ELT vs. Radiofrequency

In the Almeida et al. trial (98), all procedures were performed by interventional radiologists in outpatient clinics and with local tumescent anesthesia. Patients were not informed of their treatment assignments, which were either ELT (980-nm, continuous energy mode targets of 80 J/cm) or the ClosureFast® radiofrequency catheter. Primary endpoints for the study involved procedurally related complications, short term recovery, and technical success at one month follow-up. Post-operative pain levels ($p < .0001$ at 2 weeks), tenderness ($p < .0005$ at 2 weeks) and ecchymosis or bruising ($p = .005$ at 1 month) were significantly less in the RF group than the ELT group, although differences for pain and tenderness were no longer significant at one month follow-up. Overall complications were less frequent ($p = .021$) among those treated with RF at 4.4% (2/46), vs. 22% (9/41) in the ELT group. Complications in the ELT group

included phlebitis (n=6), erythema (n=4) and paresthesia (n = 1), while in the RF group, hyperpigmentation (n = 10) and parasthesia (n = 1) were reported. A DVT in a patient who underwent ELT was the only major adverse event to occur. Symptom improvements and QOL measures were not significantly different between the groups at 1 month follow-up. Vein occlusion and elimination of treated vein reflux was reported for cases in both treatment groups.

The Morrison et al. trial (100) was a within-person RCT that involved 50 patients with bilateral disease. The GSVs were randomly treated in one leg with RF using an early RF device design, while the other leg was treated with ELT (810-nm). The primary endpoint was ablation of the treated vein at 1 year follow-up, which occurred significantly more often ($p < .05$) in the RF than the ELT treated veins at 80% (40/50) and 66% (33/50) respectively. The overall DVT rate was 0.8%. The occurrences of paresthesia (< 1%), leg edema (< 1%), and superficial thrombophlebitis (2.3%) were similar in the two groups.

In the third study (97), 819 cases (483 GSV) of EVL treatment was compared to 128 cases (95 GSV) of treatment with RF. Four different laser wavelengths (810-nm, 940-nm, 980-nm and 1320-nm were used. The RF device was not identified. A life-table analysis was performed to evaluate treated vein ablation rates. The primary closure rates at 500 days for RF and ELT were 85% and 92%, respectively, and differences were significant ($p < .0001$). Adverse events were reported to be minimal. Transient paresthesia developed in two legs in RF group and two legs in the ELT group. Thrombus extension into the common femoral vein requiring anticoagulation occurred in two cases after ELT.

ELT vs. Foam Sclerotherapy

In the Gonzalez et al. trial (99), patients choose between ultrasound guided foam sclerotherapy and ELT for treatment of their primary GSV reflux. Ninety-eight patients were treated, 53 by foam sclerotherapy and 45 by ELT. Ultrasound imaging within one month demonstrated incomplete closure in 7.6% (4/53) of the foam sclerotherapy group and in none of the ELT group. The cumulative ultrasound documented vein closure rates at 1-year follow-up were 93.4% (95% CI: 81.5% - 98.4%) for the ELT group and 77.4% (95% CI: 64.3 – 86.7) for the foam sclerotherapy group.

A subgroup analysis of GSV vein diameter showed an increase in failure rate from 7% in the < 8 mm subgroup to 67% in the > 12 mm subgroup treated with sclerotherapy ($p < .001$). All of the patients who failed in the ELT group also had large veins (> 12mm). Vein diameter was the strongest predictor of treatment success. A 90% success rate was predicted for veins < 6.5 mm in the sclerotherapy group and for veins < 12 mm in the ELT group. Minor complications were common after both treatments. Pain ($p = .008$) and induration ($p = .005$) occurred more frequently after ELT. Phlebitis, although occurring more frequently after sclerotherapy, was not significantly higher ($p = .053$). Of the major adverse vascular events two episodes of DVT occurred, both in the sclerotherapy group.

Group C: Alternative Technical Approaches with Endovascular Laser Ablation

Five clinical trials (101-105), including four RCTs (101;102;104;105), were identified of comparisons of different technical approaches with ELT. The comparisons involved the clinical utility of ELT performed with and without concomitant phlebectomy (101;103), surgical ligation (102), and eccentric leg compression (104). The optimal method of treating below-knee varices reflux was also evaluated. (105) The details of these trials are outlined in Appendix 2, Table 10.

The first technical matter examined was the necessity of concomitant procedures to treat other sites of venous reflux in addition to GSV reflux. In the Carradice et al. trial (101), 50 patients were randomized to receive either ELT for GSV reflux and concomitant phlebectomy (EVLTAP) for varicose tributaries, or to ELT with sequential phlebectomy, performed at 6 weeks if necessary. At one week all treated veins were occluded in both groups and at 1-year follow-up, recanalization had occurred in three patients (two with reflux) in the EVLTAP group and one in the ELT group. Improvements in vein symptoms and quality of

life occurred in both groups. Although improvements were initially higher in the EVLTAP group, differences were not maintained at 1-year follow-up. Secondary interventions, however, were significantly reduced ($p < .001$) in the EVLTAP group. In the ELT group, 67% (16/24) required subsequent phlebectomy whereas in the EVLTAP group, 4% (1/25) required a secondary intervention.

In the Kim et al. study (103), another approach to treating initial tributary varicosities was evaluated. In this study, ELT for GSV reflux with concomitant phlebectomy in a sequential group of patients was compared with a later group of patients who received ELT and the concomitant treatment of superficial tributary varicosities with a smaller needle laser instead of phlebectomy. Minor complications occurred at equal rates in the two groups. There were, however, seven cases of skin burns (five in the ELT only group and two in the ELT and phlebectomy combination group). Three of the skin burns, all in the ELT only group, did not resolve spontaneously and required a lengthy period of wound care. Duplex ultrasound did not identify any recanalization in the treated veins over 25.6 ±12.8 months of follow-up in the combination treatment group or in 11.8 ± 8.2 months of follow up in the ELT only group. Recurrent varicosities were noted in 9.1% (n=12) of the combination group and in 8.3% (n=11) of the ELT only group.

The second technical issue examined was whether or not ligation of the saphenofemoral junction (SFJ) improved two year treatment outcomes for ELT. In the Disselhoff et al. trial (102), 43 patients with bilateral disease were treated by random assignment with ELT only in one leg and ELT with SFJ ligation in the other leg. Two-year life table analysis showed that freedom from recurrence was similarly ($p = .47$) high in both groups: 83% in the ELT only group and 87% in the ELT with ligation group. Groin vein recurrence due to neovascularization was noted in five cases, all from the ELT plus ligation group. The 2-year life table analysis of freedom from overall varicose vain recurrence was 71% (95% CI: 51-87) in the ELT group and 73% (95% CI: 53-87) in the ELT with ligation group. Complications involving superficial thrombophlebitis, bruising, pain, and tightness did not differ between the two groups. There were four wound complications (though none required surgical treatment) in the ELT with ligation group. Overall, short term follow-up showed no differences in outcomes between the two groups.

The third technical consideration involved the utility of compression techniques on the limbs following ELT intended to minimize treatment related complications, particularly post-operative pain. In the Lugli et al. trial (104), 200 patients were randomized to receive eccentric cylindrical compression along the GSV from the knee to the groin. Elastic stockings were applied to the treated limbs of patients in both groups. Patients were ambulatory immediately after the procedure and discharged within three hours. No major complications were detected in either group. Both self reported pain levels on numerical rating scales (1.4 ± 1.6 vs. 4.9 ±1.6; $p < .0001$) and analgesic usage (18% vs. 58%; $p < .001$) were significantly lower in the group undergoing the compression technique.

The final technical issue related to the appropriate treatment for below-knee saphenous vein reflux. In the Theivacumar et al. trial (105), 65 patients with below–knee varicosities associated with both above and below-knee GSV reflux were randomized to one of three treatment groups: Group A, ELT performed only for above-knee GSV reflux; Group B, ELT performed for above and below-knee GSV reflux; and Group C, ELT performed for above-knee GSV reflux and foam sclerotherapy for below-knee reflux. Sclerotherapy was thought to provide potential advantages in patients in whom below-knee tortuosity prevented ELT or to further minimize the risk of saphenous nerve injury. The primary study endpoints were the presence of residual varicosities requiring sclerotherapy and improvement in QOL.

At 1 and 6-week follow-up, duplex ultrasound confirmed that above-knee GSV was ablated in all limbs in all groups. The untreated below-knee GSV in Group A, however, was patent in all legs with 65% (15/23) showing persistent reflux at 1week and 52% (12/23) at 6 weeks. The ablation rate was higher in those treated with ELT (100%) than in those who had received foam sclerotherapy for below-knee GSV (86%). Three of the patients with patent below-knee GSV in the sclerotherapy treated group had persistent reflux,

which was retreated with foam sclerotherapy. Sequential ultrasound also showed that ELT (for both above-knee GSV in all groups and below-knee GSV in Group B) resulted in progressive and significant reductions in vein diameter. These reductions were not observed for the below-knee GSV treated by sclerotherapy.

The retreatment rates, reported as the overall requirements for sclerotherapy at 12 weeks (both for below-knee GSV and superficial varicosities), for the three groups were 61% (14/23) for Group A, 17% (4/23) for Group B, and 36% (8/22) for Group C. Differences among the groups were significant ($p = .01$) largely due to the difference between groups A and B. Pain scores were not significantly different in the groups, although some tenderness was recorded in all limbs at 1 week. Skin staining over the below–knee GSV however, was noticeable at 6 weeks in 9% (2/220) of limbs in Group C. None were detected in the ELT group.

GRADE Level of Evidence

The levels of evidence, as rated according to GRADE criteria (48), for the primary review research question on the comparative effectiveness of ELT with surgical stripping for VV are outlined below in Table 12.

Table 12: GRADE Evidence Level for Endovascular Laser Ablation vs. Surgical Ligation and Stripping for VV

Outcome	Study Design	Quality (Consort)	Consistency Effects	Directness and generalizability	Summary Study Findings	Overall Quality
Recovery	4 RCT	Moderate	Variable reporting but consistent outcomes	Appropriate range of patients with recovery to both usual activity and return to work	ELT significantly quicker than surgery – return to work 4 vs. 17 days (p = .005)	Moderate
Vein occlusion or obliteration	4 RCT	High	High degree consistency	Appropriate range of patients with ultrasound defined occlusion or reflux obliteration	ELT comparable to surgery with occlusion rates > 95%	High
Vein Symptom Relief	3 RCT	Moderate	High degree consistency	Appropriate range patients with reliable and valid assessment	Significant improvement in vein symptoms in both groups with no between group differences	Moderate
HRQOL	3 RCT	Moderate	High degree consistency	Appropriate range patients with reliable and valid assessment	Significant improvement in vein specific QOL in both groups with no between group differences	Moderate
Recurrence	4 RCT	Low to moderate	Limited and variable reporting	Appropriate range of patients with ultrasound defined varices reflux	Low recurrence rates in both groups but with limited long term follow-up, although neovascularization a significant predictor long term recurrence occurred more commonly after surgery	Low to moderate
Patient satisfaction	3 RCT	Low to moderate	Limited and variable reporting	Appropriate range of patients	Patient satisfaction is similar and very high in both groups	Low to moderate

HRQOL; health related quality of life, RCT; randomized controlled trial

Discussion

Since the earlier systematic evidence reviews on ELT treatment of VV performed by MSAC in 2007, there have been numerous reports with extensive evidence of its effectiveness and safety, based on over 10,000 patient experiences. All of the trials reported duplex ultrasound imaging follow-up with successful vein ablation rates in > 90% cases. Major adverse events were also uncommon or rarely reported. Minor complications such as swelling, inflammation, hematoma and leg pain were common after ELT, although it was not always certain to what extent these complications were attributable to primary ELT treatment or concomitant procedures. Although the majority of subjects in these reports were in their forties and fifties, there was also a large cohort trial of elderly patients, which demonstrated similarly high successful vein ablation rates, low complication rates, and quick recovery. (64) This is particularly important because of the increasing prevalence of both VV and leg ulcers with age.

In contrast, the evidence comparing ELT with surgical ligation and vein stripping was limited. The reported outcomes, although largely short term, were generally similar for both treatments. For both surgery and ELT, technical success, defined as duplex ultrasound confirmed vein ablation or vein absence, occurred in almost all cases leading to significant improvements in symptoms and quality of life. As expected, there were also few major adverse events reported in the RCTs. The few that did occur after surgery (infection and admittance to intensive care after post intubation inhalation) were related to the open surgical ligation and stripping procedure and general anesthesia. The skin burns that occurred following ELT were related to over treatment, which can be corrected by adjusting energy levels.

The clinical trials comparing ELT to surgery for symptomatic primary VV were similar in several respects. Interventions in all the trials, both ELT and surgery, were performed by vascular surgeons. Patients in the trials were also similar with respect to their age, gender, and disease stage and severity. Follow-up in all the trials was performed with clinical exams and duplex ultrasound imaging. There were, however, notable differences between the trials. In particular, the method of anesthesia for ELT varied in the trials and involved various combinations of general anesthesia, epidural, or local anesthesia and was often based on patient preference. Endovascular minimally invasive treatments such as ELT do not usually require general anesthesia and can be adequately performed in outpatient settings with only local tumescent anesthesia. The advantages of local anesthesia, immediate ambulation, and the reduced risk of adverse events were, therefore, not fully evaluated in these studies. The use of co-interventions and their timing, whether concomitantly or in a staged manner, also varied by trial and between treatment arms. Concomitant procedures such as phlebectomy were employed more often in the surgical arm and tended to be performed in a staged manner in the ELT arm. Additional surgical treatments, such as ligation of the GSV and of all tributaries in the groin, were performed concomitantly with ELT in two trials limiting conclusions on effectiveness of ELT as a primary treatment. (90;93) Despite all these differences, outcomes on treatment effectiveness in the trials were similar, at least in the short term.

The recurrence rate, a key measure of treatment success, has been reported to be extremely variable with surgery, ranging from 20% to 80% depending on various patient, physician and technical factors. It has thus become a well known limitation of surgical ligation and vein stripping. (39;106;107) The duration of follow-up in the ELT clinical trials was limited mainly to 1 and 2 years; it's still too early to evaluate longer term recurrence. Although recurrences in the RCT studies were similarly low between the two treatments at 2-year follow-up, when they did occur, the causes differed between the two. In the ELT group, the most common cause of recurrence was vein recanalization due to under treatment, whereas recurrence in the surgical group was more often due to neovascularization or the growth of new vessels. Neovascularization, has been reported to be a major predictor of long term recurrence after surgery. (108-110) It has been suggested to be a natural response to injury related to the surgical ligation and stripping and an inherent limitation to a surgical approach for venous reflux. (107)

Several technical issues related to the treatment of VV were also investigated in the RCTs. For some patients and physicians, treatment decisions are about a comprehensive approach for all possible sources of vein reflux in one session. The technical issue has thus been whether or not the use of concomitant procedures such as phlebectomy or sclerotherapy to manage tributary varices represents over-treatment if these sources of reflux would have responded to ELT alone. One RCT (101) addressed this issue with ELT performed with and without phlebectomy. Although the combined procedure took longer, it greatly reduced the number of patients who returned for subsequent treatments in the short term. Patient recovery, however, was faster without concomitant procedures. Phlebectomy itself is also associated with multiple stab wounds and is not without morbidity from a range of complications including dysesthesia, hematomas, wound infection, keloids and superficial thromboplebitis. (111) Other less invasive approaches to concomitant treatment were investigated with the use of smaller laser needles to treat superficial tributaries reflux. (103) Although the procedure was reported to be technically possible, the duration of the procedure increased and there were more skin burns, some requiring long term wound care. The impact of this treatment on the need for subsequent repeat interventions was not reported.

The other approach evaluated for managing the side tributaries of GSV was surgical ligation. This has often been part of the protocol to a complete surgical approach but it has not been generally employed with ELT. Given that ELT performed without ligation of side tributaries resulted in high levels of treatment success for many cohort studies, the need for this was questionable. This issue was specifically addressed in one RCT in which patients with bilateral disease received ELT in addition to ligation of the SFJ in one leg and not in the other. (112) Follow-up and 2- year life-table analysis confirmed similar low recurrence rates in both groups. Groin neovascularization was again noted to occur only in the leg receiving ligation. This trial provides further support against the routine ligation of tributaries. Longer term follow-up to evaluate recurrence due to neovascularization, however, is still not available.

Venous reflux can have a broader involvement than just the above-knee GSV reflux that is commonly targeted for surgical approach. The below-knee areas of reflux are often not treated because of the increased nerve injury risk in the area arising from the closer proximity of nerves and veins. An evaluation was made of various treatment approaches to below-knee GSV vein reflux in a three-arm RCT. (113) The study protocol involved standard ELT ablation performed for above-knee GSV reflux in all groups and below-knee GSV reflux was assigned to one of three treatments: no treatment, ELT or foam sclerotherapy. The GSV below-knee remained patent in all the untreated limbs and ELT of below-knee GSV was ablated in all cases treated by ELT and by almost all the cases treated by foam sclerotherapy. The need for secondary sclerotherapy of superficial varicosities at 12 week follow- up was significantly reduced in the below-knee treated groups either by ELT or sclerotherapy compared to the untreated groups. The ELT below-knee treated group had fewer secondary treatment requirements (though not significantly) than the sclerotherapy treated group. Follow-up in this trial was limited to 12 weeks so the implications for these approaches to longer term effectiveness are uncertain.

Although the key comparator for ELT of venous reflux in the MAS review was surgery, other endovascular approaches including radiofrequency and ultrasound guided foam sclerotherapy are also potential comparators to ELT. Sclerotherapy, however, has been generally restricted to treatment for smaller diameter surface veins and residual varices after surgery or ELT. (44;114) A single trial compared sclerotherapy with ELT and that trial involved a patient choice design. (99) In the trial, vein closure was higher after ELT at early follow-up and remained so 1-year follow-up. The significance of vein diameter for successful vein ablation, however, was detailed for both sclerotherapy and ELT. ELT was estimated to be more successful than sclerotherapy with larger vein diameters but treatment success was reduced even for ELT in very large diameter veins >12 mm.

Radiofrequency, on the other hand, is based on similar principles of endovascular vein ablation as ELT and is emerging as a treatment alternative for venous reflux. The clinical trials comparing these treatments are still limited and their reported comparative effectiveness has been inconsistent. In trials comparing

ELT with RF, vein closure rates were not reported in one trial (98) and reported to be significantly higher for RF than ELT at one year in a within-person RCT (100) and significantly lower than ELT in an observational study cohort with a 500 day life table analysis. (97) At this point, there is still limited evidence comparing different endovascular approaches, particularly RF and ELT, which are generally considered to be the major competing endovascular treatment alternatives to surgery for varices.

Conclusion

The comparisons between ELT and surgery for primary venous reflux involved a broad range of outcomes from several perspectives (results summarized in Table 13). In comparisons, patient outcomes were generally more favourable for ELT. Patients undergoing ELT require local rather than general anesthesia, exhibit faster recovery attributable to the decreased pain, immediate ambulation, and lower rates of minor complications. ELT was as effective as surgery in the short term as assessed by imaging anatomic outcomes, symptomatic relief, and HRQOL outcomes. Recurrence rates after were similar but neovascularization, a key predictor of long term recurrence, was significantly higher with surgery. Patient satisfaction was equally high after both treatments but patient preference was much greater for ELT.

The additional clinical or technical advantages of ELT are also a consideration. As an image guided intervention, it can more easily and precisely treat multilevel disease and difficult to treat areas, particularly those that present nerve damage risks. For elderly patients with venous reflux and for those with venous leg ulcers, it's also a less invasive option. Further investigations in patients with leg ulcers may well identify those with superficial saphenous vein reflux who could be more appropriately treated.

Replacing surgery with ELT may also offer system-related advantages. As the treatment can be provided by several medical specialties, service delivery could be improved. As the treatment does not require an operating room it could efficiently decant patients from the operating room to a more appropriate setting. This would also provide related decreases in pre-operative works ups, demands on anaesthetist time, and hospital stay. Outpatient procedures might also decrease the treatment wait times and enable more reliable scheduling. Depending on the reimbursement mechanism, however, insuring ELT may also result in closure of outpatient clinics with an increasing centralization of procedures in selected hospitals with large capital budgets resulting in larger waiting lists. A cost exercise suggests that the average case cost of ELT may be similar to surgery or slightly less, but the overall budget impact may be greater with insurance of ELT because of the transfer of the cases from the private market to the public payer system.

Table 13: Outcome Comparisons Between ELT and Surgery for VV

Outcomes	Comparisons
Post procedural pain, minor complications	ELT < Surgery
Recovery	ELT < Surgery
Major adverse events	ELT < Surgery
Effectiveness - Imaging vein occlusion/ absence	ELT ~ Surgery
Effectiveness -Vein symptom improvement	ELT ~ Surgery
Effectiveness - Quality Of Life	ELT ~ Surgery
Recurrence	ELT ~ Surgery
Patient satisfaction	ELT ~ Surgery
Patient preference	ELT > Surgery
Procedure costs	ELT ~ < Surgery
Budget impact	ELT > Surgery

Ontario Health System

VV are managed by various medical specialties including general practitioners, dermatologists, phlebologists (physicians who are vein specialists), surgeons (both general and vascular) and interventional radiologists (radiologists who provide image guided interventions). In Ontario, ELT is not an insured medical service, although it has as been provided in Ontario since 2002 in over 20 private clinics. In contrast, surgical ligation and stripping of saphenous veins is the standard treatment for symptomatic VV and an insured service. Phlebectomy, performed either as a co-intervention with surgery or as a stand-alone therapy in outpatient settings, is also an insured service. The wait time for these surgeries has been estimated to be over a year (Personal Communication, clinical experts, October 2008).

The volumes of surgeries and phlebectomies performed for VV treatment in Ontario over a 5-year period are listed Table 14. Surgical volumes were extracted from MOHLTC physician billing databases (codes R837, R844, R868, R869). The majority of the surgeries were for the more common cause of varicose vein reflux, the GSV. Repeat surgical procedures, ranging from 25% in 2002/2003 to 28% in 2007/2008, also represented a significant proportion of the annual volumes. Overall, volumes have been declining at an average annual rate of 7%, for a total decline of 28% over the past 5 years. The rate of repeat surgeries, however, has remained relatively constant.

The volumes of surgeries performed for the GSV, SSV and repeat procedures, are outlined in Table 15 by gender and by age. Women are more likely (67.6%) to undergo surgical treatment, exceed men by almost two-to-one in every age group. The peak demand for vein surgery occurs in the 45 to 54 year age range, but it remains high over the broader 35 to 60 year age range. The decline in volume after 65 years of age is inconsistent with the increasing prevalence of varices and leg ulcers with age.

Table 14: Surgical Ligation and Saphenous Vein Stripping in Ontario from (2002 - 2008)

	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008
Great saphenous vein	3,467	3,228	3,046	3,029	2,766	2,403
Small saphenous vein	178	163	107	110	118	104
Repeat surgeries	1,197	1,081	997	1,163	1,045	974
Total Surgeries	4,842	4,472	4,150	4,302	3,929	3,481
Phlebectomy	3,643	3,156	3,074	3,157	2,785	2,623

Table 15: Combined Number of Claims for Surgical Ligation and Saphenous Vein Stripping (2007-2008)

Age Range	Female	Male	Total
15-24	22	18	40
25-34	290	108	398
35- 44	639	229	868
45-54	726	336	1,962
55-64	334	262	596
65-74	223	115	338
75-84	43	23	66
≥ 85	1	1	2
Total	**2,278**	**1,092**	**3,370**

Claims include GSV, SSV and repeat procedures

Economic Analysis

Study Question

The objective of this project was to assess the economic impact of endovascular laser treatment (ELT) in the province of Ontario.

Analysis Method

ELT and surgical vein stripping, the main comparator reimbursed by the public system, are comparable in clinical benefits. Hence a cost-analysis was conducted to identify the differences in resources and costs between both procedures and a budgetary impact analysis (BIA) was conducted to project costs over a 5 year period in the province of Ontario.

Literature Review

A literature search was conducted and is described in Appendix 1. We reviewed published articles that fit the following inclusion criteria:

- full economic evaluations (cost-effectiveness analysis [CEA], cost-utility analysis [CUA], cost-benefit analysis [CBA])
- economic evaluations reporting Incremental Cost-Effectiveness Ratios (ICER) i.e. cost per quality adjusted life year (QALY)/life years gained (LYG) or cost per event avoided
- studies in patients with VV
- studies reporting on EVL and vein stripping to manage VV
- studies in English

Four cost studies, one within a HTA report (59) were identified. The cost studies are shortly described below.

Disselhoff et al. (92) described a comparison of costs and cost-effectiveness based on a randomized controlled trial comparing 2-year results of cryostripping and endovenous laser ablation (ELT) in 120 patients. The authors reported that mean SF-6D scores improved slightly from baseline. QALYs were comparable between both treatments 1.59 vs. 1.60 for EVLA 2 years after treatment. The costs of both procedures were comparable and cryostripping was associated with an ICER of €32 per QALY gained. The authors concluded that outpatient cryostripping was less costly and more effective 2 years after treatment.

Rasmussen et al. (94) compared endovascular laser (ELT) ablation of the great saphenous vein (GSV) with high ligation and stripping (HL/S). The groups were randomized to each group and were matched for patient and GSV characteristics. The authors reported that quality of life scores at 3 months were similar between both groups. The groups did not different in mean time to resume to normal physical activity and work. Post-operative pain and bruising was higher in the stripping group. The total cost of the procedures was higher in the ELT group but the difference was reduced by the lower loss of productivity among the ELT patients. The authors concluded that the short-term efficacy and safety of ELT and HL/S were similar.

Vuylsteke et al. (69) compared endovenous laser treatment (ELT) for VV with conventional surgical stripping in terms of short-term recovery and costs. Eighty-four patients were treated by ligation, stripping and phlebectomy if required and eighty patients were assigned to the laser arm of the study.

There were no significant differences in baseline characteristics between both groups. The authors reported that there were less post-operative complications and sick leave was significantly shorter in the laser group. They reported that the operative costs of ELT were slightly higher due to those cost of the catheter and the diode laser fibre. The cost of the stripping operation and the ELT procedure were equivalent. The total cost from a societal perspective was significantly higher in the stripping arm than the laser arm because of the indirect costs. The authors reported a greater productivity loss by patients in the stripping arm vs. the laser arm. The authors concluded that ELT may offer advantages over vein stripping in terms of reduced post-operative pain, shorter sick leave and faster return to usual occupational activities and it appears to be cost-saving for saving.

The Medical Services Advisory Committee (MSAC) in Australia issued a HTA report in March 2008. (59) They reported an incremental cost ELT per patient of -$170.75 due mostly to the large difference in hospital care between both procedures. Hospital stay because of vein stripping surgery was costed at $2,500 and ELT was costed at $1,500. They concluded that ELT could have a potential cost saving in the healthcare system.

Target Population

The target population of this economic analysis was patients with primary VV.

Perspective

The primary analytic perspective was that of the Ministry of Health and Long-Term Care.

Resource Use and Costs

A standard resource utilization questionnaire (described in Appendix 3) was filled out by two clinical experts in the field of VV treatment. One expert was a vascular surgeon and the other was an interventional radiologist. Both consultants were situated in Toronto.

The questionnaire addressed questions about direct costs incurred with treatment of VV with either conventional surgical vein stripping or ELT. Direct costs include resources that are required for the provision of patient care and are absorbed by the public system such as hospital day-stay, pharmacotherapy, laboratory tests, medical procedures and medical visits. ELT is currently being performed in the private setting and patients are paying out of pocket. However resources incurred pre-procedure preparing patients for the procedure and resources incurred post-procedure following up on patient status are absorbed by the public system and were also captured with the questionnaire. A detailed description of the resources and costs associated with both surgical vein stripping and ELT are shown in Appendices Table A11- A14.

Private clinics are charging on average $2,950-$3,000 per leg to perform ELT (Personal Communication, clinical expert, October 2009). Currently the average weighted cost absorbed by hospitals for the surgical vein stripping procedure coded as 1KR87 is approximately $1,059 per case.(115) The code 1KR87 is defined as:

Excision partial, veins of leg NEC (not else classified);

- Includes: stripping and ligation, VV of leg, stripping, VV of lower limbs, that with hook avulsions;
- Excludes: harvesting, lower limb vein (see 1KR58), sclerotherapy (see 1KR59);
- Omit code: when performed with subfascial endoscopic perforator vein surgery (see 1KR51).

A weighted average cost was obtained by summing the products of the number of cases performed each year by the average direct cost of that year and then dividing it by the total number of cases for all years for the past six fiscal years. The direct costs and number of cases for this procedure was obtained from the Ontario Case Costing Initiative (OCCI). (115) CCI provides an average cost per case derived from the hospitals in Ontario participating in the initiative. The data are limited because they are not capturing all the procedures performed in Ontario but it can provide an estimate of the cost being absorbed by the hospital setting.

Table 16 describes the direct costs and number of cases associated with procedure 1KR87 within the hospital setting for the past six fiscal years (FY).

Table 16: Direct costs and number of vein stripping cases from 2002 - 2008 in Ontario

Outpatient	# Cases	Average Direct Cost per Case	Std Dev	Min	Max
2002-2003	958	$1,438	$720	$198	$3,489
2003-2004	759	$911	$327	$129	$2,383
2004-2005	853	$869	$433	$62	$6,197
2005-2206	978	$1,133	$426	$6	$2,768
2006-2007	932	$796	$455	$83	$3,043
2007-2008	713	$1,077	$569	$112	$4,493
Weighted Averages:	5,193	$1,045	$492	$97	$3,694
Inpatient	**# Cases**	**Average Direct Cost per Case**	**Std Dev**	**Min**	**Max**
2002-2003	33	$1,717	$962	$307	$5,111
2003-2004	12	$1,908	$1,367	$892	$5,883
2004-2005	18	$1,453	$514	$799	$3,140
2005-2006	6	$3,182	$4,402	$625	$12,098
2006-2007	13	$2,500	$1,500	$1,097	$7,117
2007-2008	FOI	FOI	FOI	FOI	FOI
Weighted Averages:	82	$1,918	$1,260	$649	$5,621
All Cases	**# Cases**	**Average Direct Cost per Case**	**Std Dev**	**Min**	**Max**
2002-2008	5,275	$1,059	$504	$106	$3,724

OCCI data capture all direct costs associated with the procedure within the hospital context excluding fees associated with physician labour. Those fees are reported in the Ontario Schedule of Benefits (OSB) under the following codes: (116)

R868 – high ligation and stripping of long saphenous vein with groin dissection
R 869 – stripping of short saphenous vein with popliteal dissection
R837- multiple ligation and avulsion
R844 – recurrent VV – multiple ligation and/or stripping

Table 17 describes the fees associated with each code and the assumptions made to cost out a cost for anesthesia and surgical assistance since these tasks are costed on a per unit basis in the OSB.

Table 17: Physician billing codes for vein stripping procedures in Ontario

Resource	Cost/unit	Assumption	Reference
Great saphenous vein surgery	$148.60		OSB R868
Phlebectomy	$148.60	R837 is always performed with R868	OSB R837
Short saphenous vein surgery	$107.50		OSB R869
Recurrent vein surgery	$353.80		OSB R844
Anesthesia	$119.16	assumed 2 hour surgery therefore 6 base units plus 1 unit in the first hour and 2 units after the first hour up to and including the first 1.5 hours	vascular surgeon in Toronto; OSB R868
	$119.16	assumed 2 hour surgery therefore 6 base units plus 1 unit in the first hour and 2 units after the first hour up to and including the first 1.5 hours	vascular surgeon in Toronto; OSB R837
	$119.16	assumed 2 hour surgery and adjust cost based on proportion quoted above = $14.90	vascular surgeon in Toronto; OSB R869
	$119.16	assumed 2 hour surgery and adjust cost based on proportion quoted above = $41.71	vascular surgeon in Toronto; OSB R844
Surgical assistance	$102.60	assumed 2 hour surgery therefore 6 base units plus 1 unit in the first hour and 2 units after the first hour	vascular surgeon in Toronto; OSB R868
	$102.60	assumed 2 hour surgery therefore 6 base units plus 1 unit in the first hour and 2 units after the first hour	vascular surgeon in Toronto; OSB R837
	$102.60	assumed 2 hour surgery and adjust cost based on proportion quoted above = $12.83	vascular surgeon in Toronto; OSB R869
	$102.60	assumed 2 hour surgery and adjust cost based on proportion quoted above = $35.91	vascular surgeon in Toronto; OSB R844

Vein stripping surgeries have been declining in the province by an average of 7% a year. ELT was introduced into the market in 2002 and may be a plausible explanation for the decline in surgical procedures. The following table (Table 18) describes physician billings for vein stripping surgeries in the past six fiscal years obtained from a Ministry of Health and Long-Term Care database.(117) These numbers were then used to project surgeries in a linear fashion up to five years into the future described in Table 19.

Table 18: Number of physician billings for vein stripping procedures from 2002 - 2008 in Ontario

Surgery	2002-2003	2003-2004	2004-2005	2005-2206	2006-2007	2007-2008
R868 Great saphenous vein strip	3,467	3,228	3,046	3,029	2,766	2,403
R837 Phlebectomy	3,643	3,156	3,074	3,157	2,785	2,623
R869 Short saphenous vein strip	178	163	107	110	118	104
R844 Recurrent vein strip	1,197	1,081	997	1,163	1,045	974

Table 19: Vein stripping surgeries projected over 5 years in Ontario

Surgery	Year 1	Year 2	Year 3	Year 4	Year 5
R868 Great saphenous vein strip	2,318	2,125	1,933	1,741	1,549
R837 Phlebectomy	2,460	2,285	2,110	1,935	1,759
R869 Short saphenous vein strip	80	65	51	37	22
R844 Recurrent vein strip	970	940	910	880	850

In order to calculate a procedural cost for ELT, equipment costs were included in the calculations. It was assumed that the hospital cost and physician labour fees (excluding anesthesia and surgical assistance) were the same for both procedures. Table 20 describes the extra equipment related costs associated with ELT. The manufacturer provided details on a D30 laser machine with a lifespan of 5 years (Personal Communication, manufacturer, October 2009). Two expert opinions commented on their experience with treating patients with ELT in their private practices and an average number of patients per machine per year was calculated to be 77 (Personal Communication, clinical experts, October 2009).

As a publicly reimbursed procedure, vein stripping surgery data is available from physician billing records. ELT data, however, was not available and assumptions had to be made in order to calculate future projections. According to private data, an average of 70 EVLT procedures was performed per month last year in the province of Ontario, for an annual average of 840 procedures. There is no data to project an average increase in ELT procedures a year, thus it was assumed that this market would increase by 10% a year. This is a reasonable estimate considering that the vein stripping market has been decreasing on average by 7% a year. It was also assumed that ELT would capture 35% of the vein stripping surgery market if it were publicly reimbursed followed by 55% market capture in subsequent years. Table 21 describes the projections and assumptions associated with the calculations.

Table 20: Unit costs associated with vein stripping surgery and endovenous laser treatment

Resource	Unit	Vein Stripping	Endovascular Laser Treatment	References
Hospital				
Procedure	per case	$1,059	$1,059	(115)
Medical Visits				
Great saphenous veins - surgeon	per case	$148.60	$148.60	(116)
Phlebectomy - surgeon	per case	$148.60	$148.60	(116)
Anaesthetist	per case	$238.32		(116) (2 components: vein stripping and phlebectomy)
Surgical assistant	per case	$205.20		(116) (2 components: vein stripping and phlebectomy)
Equipment				
Laser machine	per case		$179	manufacturer reported D30 laser = $69,000 over 5 year lifetime for an average of 77 patients per machine, per year
Laser kit	per case		$490	manufacturer
TOTAL		**$1,799**	**$2,025**	

Table 21: Endovascular laser treatment procedures projected over 5 years in Ontario

	Year 1	Year 2	Year 3	Year 4	Year 5	Assumptions	Reference
Total number of ELTs in ON	840	924	1,016	1,118	1,230	Assumed 70 procedures per month in year 1 and a 10% increase every year.	Private data from industry
Number of ELTs captured from VS market	1,861	2,175	2,025	1,874	1,724	Assumed EVT will capture VS market by 35% in the first year and then 55% in subsequent years.	Clinical expert opinion
Total ELTs	**2,701**	**3,099**	**3,041**	**2,992**	**2,954**		

ELT refers to endovascular laser treatment; VS, vein stripping

Ontario Perspective

Burden of vein stripping surgeries to the province was calculated by multiplying the number of cases for that year by the cost of the procedure which included the physician fee associated with that procedure and the hospital cost for the surgery. Table 22 displays the average burden to the province from vein stripping surgeries in previous years.

Table 22: Burden of vein stripping surgeries in Ontario from 2002 - 2007

Procedure	2002-2003	2003-2004	2004-2005	2005-2206	2006-2007	2007-2008
Great saphenous vein stripping	5.0M	4.6M	4.4M	4.3M	4.0M	3.4M
Phlebectomy	1.3M	1.2M	1.1M	1.2M	1.0M	971K
Short vein stripping	247K	226K	149K	153K	164K	144K
Recurrent vein stripping	2.0M	1.8M	1.6M	1.9M	1.7M	1.6M
Total	8.5M	7.8M	7.3M	7.6M	6.9M	6.1M

M refers to millions; K, thousands

If ELT continues to be performed at private clinics and not publicly reimbursed vein stripping surgeries would continue to minimally decline in a linear fashion based on previous years. Table 23 displays the decline in burden. If ELT is publicly reimbursed it was assumed that it would capture the vein stripping market by 35% in the first year and 55% in subsequent years along with new cases every year based on experience of what is currently happening in the province from two private clinics (Personal Communication, clinical experts, October 2009). Table 24 describes the change in burden from vein stripping surgeries and Table 25 describes the burden from ELT projections up to five years.

Table 23: Burden of vein stripping surgeries in Ontario projected over 5 years without reimbursement for endovascular laser treatment

Procedure	Year 1	Year 2	Year 3	Year 4	Year 5
Great saphenous vein stripping	3.3M	3.0M	2.8M	2.5M	2.2M
Phlebectomy	911K	846K	781K	716K	652K
Short vein stripping	111K	91K	71K	51K	31K
Recurrent vein stripping	1.6M	1.5M	1.5M	1.4M	1.4M
Total	5.9M	5.5M	5.1M	4.7M	4.3M

M refers to millions; K, thousands

Table 24: Burden of vein stripping surgeries in Ontario projected over 5 years with reimbursement for endovascular laser treatment

Procedure	Year 1	Year 2	Year 3	Year 4	Year 5
Great saphenous vein stripping after introduction of ELT	2.2M	1.4M	1.2M	1.1M	996K
Phlebectomies after introduction of ELT	592K	381K	352K	322K	293K
Total	2.7M	1.7M	1.6M	1.4M	1.3M

EVLT refers to endovascular laser treatment; M, millions; K, thousands

Table 25: Burden of endovascular laser treatment procedures in Ontario projected over 5 years

2007 - 2008	Year 1	Year 2	Year 3	Year 4	Year 5
ELTs	1.7M	1.9M	2.1M	2.3M	2.5M
ELTs - capture from vein stripping market	3.8M	4.4M	4.1M	3.8M	3.5M
Total	5.5M	6.3M	6.2M	6.1M	6.0M

EVLT refers to endovascular laser treatment; M, millions; K, thousands

If ELT is reimbursed it will capture a good portion of the vein stripping market however the existing ELT market will likely amplify as well. This will of course depend on various factors, such as prevalence of disease, health systems capacity and physician willingness to perform the procedure given that this may not be as profitable under the public system. But simply looking at increase in numbers of procedures a year, it can be shown that the budget for this procedure will have an impact. In the base case scenario we assumed that the hospital cost will remain the same for ELT as for vein stripping. The projected impact is shown in Table 26. MSAC reported that the estimated ELT hospital cost to be 40% less than vein stripping. Therefore we varied the ELT hospital cost by 40% and projected the impact in Table 27.

Table 26: Budget impact of vein stripping surgery and endovascular laser treatment in Ontario – base case analysis

Base Case Analysis	Year 1	Year 2	Year 3	Year 4	Year 5
Vein stripping					
No ELT reimbursement (status quo)	5.9M	5.5M	5.1M	4.7M	4.3M
With ELT reimbursement	2.7M	1.7M	1.6M	1.4M	1.3M
Endovascular laser treatment					
ELT	1.7M	1.9M	2.1M	2.3M	2.5M
ELT capture	3.8M	4.4M	4.1M	3.8M	3.5M
Total	8.2M	8.0M	7.8M	7.5M	7.3M

Table 27: Budget impact of vein stripping surgery and endovascular laser treatment in Ontario – sensitivity analysis

Sensitivity Analysis	Year 1	Year 2	Year 3	Year 4	Year 5
Vein stripping					
No ELT reimbursement (status quo)	5.9M	5.5M	5.1M	4.7M	4.3M
With ELT reimbursement	2.7M	1.7M	1.6M	1.4M	1.3M
Endovascular laser treatment					
ELT	1.3M	1.5M	1.6M	1.8M	2.0M
ELT capture	3.0M	3.5M	3.2M	3.0M	2.8M
Total	7.1M	6.7M	6.5M	6.2M	6.0M

EVLT refers to endovascular laser treatment; M, millions; K, thousands

Conclusion

ELT is comparable in clinical benefits to vein stripping surgery. It has the extra cost of the laser machine and disposables including laser fibre and catheters that need to be factored into the total cost per procedure but it does not require an operating room, anaesthetist and surgical assistant fees.

Appendices

Appendix 1: Literature Search Strategies

Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, Wiley Cochrane, CINAHL, Centre for Reviews and Dissemination/International Agency for Health Technology Assessment

Database: Ovid MEDLINE(R)
1950 to August Week 2 2009

Search Strategy:

1 exp Laser Therapy/ (40892)
2 (evlt or laser*).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (124916)
3 1 or 2 (124925)
4 exp Varicose Veins/ (13069)
5 ((varicose adj2 vein*) or varices or varicosis).ti,ab. (14074)
6 exp Venous Insufficiency/ (4774)
7 ((venous or vein* or saphenous) adj2 (reflux or incomp* or insuff*)).ti,ab. (4332)
8 exp Saphenous Vein/ (11815)
9 saphenous vein*.ti,ab. (10058)
10 or/4-9 (39156)
11 3 and 10 (768)
12 limit 11 to (english language and humans and yr="2007 -Current") (176)

Database: EMBASE
1980 to 2009 Week 33

Search Strategy:

1 exp low level laser therapy/ (3906)
2 (evlt or laser*).ti,ab. (88747)
3 1 or 2 (90163)
4 exp varicosis/ (17802)
5 ((varicose adj2 vein*) or varices or varicosis).ti,ab. (10479)
6 exp vein insufficiency/ (4199)
7 ((venous or vein* or saphenous) adj2 (reflux or incomp* or insuff*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (5918)
8 exp saphenous vein/ (5233)
9 saphenous vein*.ti,ab. (8436)
10 or/4-9 (31900)
11 10 and 3 (797)
12 limit 11 to (human and english language and yr="2007 -Current") (167)

Table A1: CINAHL literature search queries (publish dates: Jan. 2007 – Dec 2009)

#	Query	Results
S12	S11	21
S11	S3 and S10	64
S10	S4 or S5 or S6 or S7 or S8 or S9	2,802
S9	saphenous vein*	452
S8	(MH "Saphenous Vein")	325
S7	((venous or vein* or saphenous) and (reflux or incomp* or insuff*)).	845
S6	(MH "Venous Insufficiency")	368
S5	varicose NEAR2 vein* or varices or varicosis	408
S4	(MH "Varicose Veins+")	1,389
S3	S1 or S2	6,404
S2	evlt or laser*	6,312
S1	(MH "Lasers+")	1,932

Economics Literature Search Strategies

Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, OVID EMBASE, Wiley Cochrane, CINAHL, EconLit, Centre for Reviews and Dissemination/International Agency for HTA

Database: Ovid MEDLINE(R) <1950 to September Week 4 2009>

Search Strategy:

1 exp Laser Therapy/ (41133)
2 (evlt or laser).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (121231)
3 1 or 2 (121915)
4 exp Varicose Veins/ (13119)
5 ((varicose adj2 vein*) or varices or varicosis).ti,ab. (14141)
6 exp Venous Insufficiency/ (4803)
7 ((venous or vein* or saphenous) adj2 (reflux or incomp* or insuff*)).ti,ab. (4363)
8 exp Saphenous Vein/ (11886)
9 saphenous vein*.ti,ab. (10132)
10 or/4-9 (39347)
11 3 and 10 (770)
12 limit 11 to (english language and humans and yr="2007 -Current") (183)
13 exp Economics/ (414933)
14 exp Models, Economic/ (6833)
15 exp Resource Allocation/ (13084)
16 exp "Value of Life"/ or exp "Quality of Life"/ (83190)
17 (econom$ or cost$ or budget$ or pharmacoeconomic$ or pharmaco-economic$ or valu$).ti. (185467)
18 ec.fs. (262398)
19 ((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay").ti,ab. (61385)
20 or/13-19 (703238)
21 12 and 20 (11)

Database: EMBASE <1980 to 2009 Week 40>

Search Strategy:

1 exp low level laser therapy/ (4026)
2 (evlt or laser*).ti,ab. (89594)
3 1 or 2 (91049)
4 exp varicosis/ (17975)
5 ((varicose adj2 vein*) or varices or varicosis).ti,ab. (10558)
6 exp vein insufficiency/ (4223)
7 ((venous or vein* or saphenous) adj2 (reflux or incomp* or insuff*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (5959)
8 exp saphenous vein/ (5277)
9 saphenous vein*.ti,ab. (8490)
10 or/4-9 (32153)
11 10 and 3 (813)
12 limit 11 to (human and english language and yr="2007 -Current") (179)
13 exp "Health Care Cost"/ (110057)
14 exp Health Economics/ (241148)
15 exp Resource Management/ (15102)
16 exp Economic Aspect/ or exp Economics/ or exp Quality Adjusted Life Year/ or exp Socioeconomics/ or exp Statistical Model/ or exp "Quality of Life"/ (505320)
17 (econom$ or cost$ or budget$ or pharmacoeconomic$ or pharmaco-economic$ or valu$).ti. (111985)
18 ((cost$ adj benefit$) or costbenefit$ or (cost adj effective$) or costeffective$ or econometric$ or life value or quality-adjusted life year$ or quality adjusted life year$ or quality-adjusted life expectanc$ or quality adjusted life expectanc$ or sensitivity analys$ or "value of life" or "willingness to pay").ti,ab. (55047)
19 or/13-18 (580041)
20 19 and 12 (29)

Appendix 2: Additional Tables & Study Data

Table A2: Clinical Cohort Trials of Endovascular Laser Treatment for VV – Ablation of the Great Saphenous Vein

Author, Year, Country	Sites, Operators, Anesthesia	Laser Wavelength (λ), Mode, Energy (J/cm)	Sample (% Female)	Concomitant or Staged Procedures	Objective	Follow-Up
Barucchello 2009 (64) Italy	▪ Multi-center ▪ general surgeons ▪ local or spinal anesthesia, tumescent anesthesia rarely used	▪ 808nm ▪ 6-12W power continuous mode ▪ variable retraction rate <1 to 3 mm/sec	▪ 473 p (% F NR) ▪ age range: 70-85 yrs ▪ 535 Legs ▪ 330 GSV, 65 SSV, 140 other incompetent varices	Concomitantly peripheral incompetent varices treated with ELA (n=210) or with foam sclerotherapy and stab avulsions (n=250) or stab avulsions only (n=75), incompetent perforators subject to ELT (n=243) surgical interruption or foam sclerotherapy (n=243)	Short and mid term safety and effectiveness	3 year
Desmyttere 2007 (72) France	▪ 1 outpatient site ▪ phlebologists ▪ tumescent anesthesia	▪ 980nm ▪ 10 W power continuous mode ▪ Min 50 J/mm for 2-4.5 vein diameter to 120 J/mm > 10 mm diameter	▪ 500 p (87% F) ▪ Mean age 52.6 yrs ▪ 511 Legs	Concomitant ambulatory phlebectomy in 98%	Mid term effectiveness and safety	4 year
D'Othee 2008 (118) United States	▪ 1 site ▪ interventional radiologists ▪ tumescent anesthesia	▪ 980nm ▪ 13 W power continuous mode, ▪ 93 J/cm	▪ 112 p (74% F) ▪ 112 Legs ▪ 41 B-GSV, 1B-SSV, 66 U-GSV, 6 U-SSV)	NR	Feasibility of bilateral ELT with low lidocaine tumescent anesthesia	1 year
Elmore 2008 (71) United States	▪ 1 site ▪ Outpatient vein clinic ▪ Tumescent anesthesia	▪ 810nm ▪ 12-10 W power at pulsed mode	▪ 516 p (74% F) ▪ 685 Legs ▪ 475 GSV, 32 SSV, 9 other (anterior and posterior accessory GSV, posterior thigh circumflex veins)	Staged, branch varicosities treated several weeks post op with foam sclerotherapy	Safety and effectiveness	1 year Mean 15.2 months (range: 3-65)
Fernandez 2008 (73) Venezuela	▪ 1 site angiography suite ▪ 3 interventional radiologists ▪ tumescent anesthesia	▪ 810nm ▪ 14 W power continuous mode ▪ 140 J/cm or 70 J/cm	▪ 1559 p (81% F) ▪ 1985 Legs ▪ 1652 GSV, 285 SSV, 40 ALT, 8 PMT	Concomitant Mueller micro phlebectomy for all refluxing truncal veins	Safety and clinical effectiveness	15, 30 months

Author, Year, Country	Sites, Operators, Anesthesia	Laser Wavelength (λ), Mode, Energy (J/cm)	Sample (% Female)	Concomitant or Staged Procedures	Objective	Follow-Up
Hamel-Desnos 2008 (84) France / Switzerland	▪ 22 outpatient centers ▪ vascular surgeons ▪ local tumescent anesthesia	▪ 980nm ▪ pulse or continuous ▪ mean energy density 64 J/cm (GSV) and 65 (SSV)	▪ 1422 p (74% F) ▪ Median age 57 years (range: 15 – 92) ▪ 1703 Legs ▪ 1394 GSV + 309 SSV	Concomitantly associated tributaries treated with phlebectomy and/or sclerotherapy	Immediate (1 month) and short term (3 months) outcomes on feasibility, safety, side effects, effectiveness	6 month
Jung 2008 (65) Korea	▪ 1 outpatient site ▪ surgeon ▪ local tumescent anesthesia and spinal for more extensive cases	▪ 810nm ▪ 12-14 W power continuous mode withdraw rate 1.2 – 2 mm/sec	▪ 148 p (59% F) ▪ Mean age 51.7 yrs, (range: 18-74) ▪ 169 Legs ▪ 135 GSV + 41 SSV	Concomitantly ambulatory phlebectomy	Safety and effectiveness	3 month (mean 5.6 months (range 3 – 13 months)
Knipp 2008 (74) United States	▪ 1 site – 3 settings ▪ outpatient surgery center (n=231 L), interventional radiology suite (n=48 L), operating room (n=181) – general anesthesia in most cases ▪ tumescent anesthesia	▪ 810nm ▪ 14 W power continuous mode with 1mm/sec pullback for first 100 seconds followed by 2.5 mm/second until 1 cm from skin surface ▪ energy density 80.7 J/cm	▪ 364 p (95% F) ▪ Mean age 50.6 yrs and 51.1 yrs ▪ 460 Legs	Concomitant phlebectomy with stab avulsions	Evaluate the mid-term experience of ELT GSV and compare outcomes in those with and without deep venous insufficiency	1 and 2 years
Lu 2008 (70) China	▪ 1 site ▪ vascular surgeons ▪ tumescent anesthesia	▪ 810nm ▪ 12W power pulsed or continuous mode with pullback rate 1-2 mm/sec	▪ 1060 p (60% F) ▪ Mean age 56 yrs (range: 23-79) ▪ 1186 Legs	Concomitant ligation GSV and all tributary varices and stab avulsions	Effectiveness of ELT for GSV reflux and tributary varices	12 months mean 27 (range: 12-48)
Mackenzie 2008 (66) United Kingdom	▪ 1 site ▪ vascular surgeons ▪ Day case operating suite under general anesthesia (n=119) and later tumescent saline anesthesia only with conscious sedation (n=275)	▪ 810nm ▪ 12 W pulsed mode with pullback rate 1.4-1.7 mm/sec or 14W continuous mode with pullback rate 1.6–2.0 mm/sec ▪ energy density 70-85 J/cm	▪ 640 P (66% F) ▪ Median age 51 yrs (IQR 39-61) ▪ 713 Legs ▪ 579 GSV + 119 SSV + 60? AAGSV	Refluxing truncal veins treated concomitantly or staged with foam sclerotherapy at 3 months	Trends, issues and early outcomes in delivering the new service	3 months

Author, Year, Country	Sites, Operators, Anesthesia	Laser Wavelength (λ), Mode, Energy (J/cm)	Sample (% Female)	Concomitant or Staged Procedures	Objective	Follow-Up
Marston 2008 (119) United States	▪ 1 site ▪ vascular surgeons ▪ tumescent anesthesia	▪ 810nm ▪ 14 W power with pullback rate 5-6 seconds per cm to ▪ energy density 70-80 J/cm	▪ 75 p (71% F) ▪ Average age 57 yrs ▪ 75 Legs	No incompetent perforator veins were treated	Evaluate outcomes in patients with and without deep venous reflux	Median: 13.1 months
Myers 2009 (75) Australia	▪ 1 site outpatient center ▪ surgeon ▪ tumescent anesthesia	▪ 810nm ▪ 14 W power on continuous mode with pullback rate 1.3-8.8 mm/sec	▪ 361 p (64% F) ▪ Median age 52 yrs (range: 24-76) ▪ 509 Legs ▪ 509 GCV	Staged 1 -3 weeks ultrasound guided sclerotherapy for residual varices (for 80%)	Medium term results	4 year
Pannier 2009 (85;120) Latvia	▪ 1 outpatient phlebology center ▪ NR ▪ tumescent anesthesia	▪ 1470nm ▪ 15 W power continuous mode ▪ energy density 129 J/cm	▪ 100 p (82% F) ▪ Mean age 45 yrs (range: 17-77, SD 12.6) ▪ 117 Legs ▪ 108 GSV + 26 SSV	Concomitant phlebectomies (97.4% cases)	Immediate results and short term complications and effectiveness of 1430nm laser	1 year
Park 2009 (86) Korea	▪ 1 site angiography suite ▪ interventional radiologists (referrals from vascular, thoracic and cardiovascular surgery outpatient clinics) ▪ NR	▪ 980nm ▪ 8-12 W power on SSV and 10-14W power on GSV ▪ energy density 107 J/cm (GSV)	▪ 312 p (55% F) ▪ Mean age 45.8 yrs (range: 21-71) ▪ 438 Legs ▪ 331 GSV, 106 SSV	Foam sclerotherapy of tributaries prior to ELT	Technical feasibility and early results	6 months
Prince 2008 (121) United States	▪ 1 outpatient clinic ▪ 5 interventional radiologists ▪ tumescent anesthesia	▪ 980nm ▪ 12 W power continuous mode variable pullback rate ▪ Mean energy density 83.8 J/cm ± 34.4	▪ 474 p (79% F) ▪ Average age 49 yrs (range: 21-85) ▪ 586 Legs ▪ 365 GSV, 49 SSV, 60 other V	Concomitant foam sclerotherapy in 71 patients (46%). 57 patients with bilateral disease had staged treatment - second leg treated at least one month after first	Compare failure rates with delivered laser energy density level	Mean 5 months (range: 0.2 – 26.3)

Author, Year, Country	Sites, Operators, Anesthesia	Laser Wavelength (λ), Mode, Energy (J/cm)	Sample (% Female)	Concomitant or Staged Procedures	Objective	Follow-Up
Sadik 2007 (87) United States	▪ 1 site ▪ NR ▪ local anesthesia tumescent anesthesia	▪ 810nm ▪ 14 W power continuous mode with 1-2 second pullback rates ▪ Energy density 28J/cm	▪ 90 p (76% F) ▪ Mean age 40 yrs (range: 24-79) ▪ 94 Legs ▪ 94 GSV	Concomitant ambulatory phlebectomy of associated truncal varices	Outcomes and recurrence at long term follow up	4 year
Tan 2009 (67) Singapore	▪ 1 site operating theatre ▪ 2 vascular surgeons ▪ general anesthesia	▪ 940nm	▪ 169 p (66% F) ▪ Mean age 54 yrs (range: 19-78) ▪ 270 Veins	ELT was with and without ligation of perforators	Short term outcomes	1 year
Theivacumar 2008 (122) United Kingdom	▪ 2 sites (venous clinics) ▪ NR ▪ tumescent anesthesia	▪ 810nm ▪ 12W power pulse mode	▪ 582 p (65% F) ▪ Median age 50 yrs (range: 16-86) ▪ 644 Legs	Staged foam sclerotherapy offered at 6 weeks for residual varicosities	Assess factors including energy density that influence effectiveness	Minimum 3 month
Theivacumar 2008 United Kingdom	▪ 1 site (venous clinic) ▪ NR ▪ Tumescent anesthesia	▪ 810nm ▪ 12 W power pulse mode	▪ 73 p (58% F) ▪ 84 Legs ▪ 84 GSV	NR	Determine association of vessel recanalization with loss of clinical benefit	1 year
Timperman 2007 United States	▪ 1 site (angiogr. suite) ▪ interventional radiologist ▪ tumescent anesthesia	▪ 810nm ▪ 14 W power continuous mode with pullback rate 6-9 mm/sec mean ▪ Energy density 82 J/cm (range 56-114)	▪ 44 p (68% F) from 576 consecutive patients ▪ Mean age 53 (range: 26-82, SD 15) ▪ 50 Legs	NR	Evaluate clinical failure and untreated incompetent below the knee GSV	1 year
van den Bremer 2009 (68) Netherlands	▪ 1 site (community hospital) ▪ 3 surgeons ▪ general or spinal anesthesia with tumescent anesthesia	▪ 980nm ▪ 15W power continuous mode with pullback speed ▪ Energy density 50 J/cm.	▪ 323 p (91% F) ▪ Mean age 45.1 yrs (range: 16-74) ▪ 403 Legs	Concomitant hook phlebectomy (Mueller's method) for varices and saphenous tributaries	Results following the start of a new service	6 weeks
Vuylsteke 2008 (88) Belgium	▪ 1 site ▪ vascular surgeon ▪ general or spinal anesthesia with tumescent anesthesia	▪ 980nm ▪ 10 W pulse mode (7 W below the knee) ▪ mean energy density 51 J/cm ± 17	▪ 97 p (74% F) ▪ Mean age 50 yrs (range: 23-79) ▪ 129 Legs ▪ 129 GSV	Concomitant foam sclerotherapy and limited phlebectomy	Measure relationship between energy fluence and recanalization	6 months

Table A3: Clinical Cohort Series Undergoing Endovascular Laser Treatment for VV – Ablation of the Small Saphenous Vein

Author, Year, Country	Sites Operators Anesthesia	Laser Wavelength (λ), Mode, Energy (J/cm)	Sample (% Female)	Concomitant or Staged Procedures	Objective	Follow-Up
Gibson 2007 (76) United States	▪ 1 outpatient site ▪ 3 vascular surgeons ▪ local tumescent anesthesia	▪ 980nm ▪ 10-14W power on continuous mode with pull back rate 3-5 mm/sec	▪ 187 p (88% F) mean age 53 yrs (range: 14-89) ▪ 210 Legs ▪ 210 SSV	At least 1 concomitant procedure performed in 94% of patients – GSV ELT in 156, sclerotherapy in 120, perforator ligation in 136, microphlebectomy in 35	Evaluate safety and effectiveness	3 month Mean 4 months (range: 2 – 11)
Huisman 2009 (77) Netherlands	▪ 1 outpatient vein clinic ▪ 3 vascular surgeons ▪ local tumescent anesthesia	▪ 810nm ▪ 14 W power on continuous mode ▪ 70 J/cm	▪ 150 p (82% F) ▪ Mean age 57 yrs (range: 23-87) ▪ 169 Legs	Staged sclerotherapy or phlebectomy if required at 6 weeks	Determine if ELT in SSV can achieve the same results as in the GSV	3 month
Kontothanassis 2009 (78) Italy	▪ 5 centers (4 Italy, 1 France) ▪ Surgeons ▪ local tumescent anesthesia	▪ 980nm ▪ Mode NR ▪ mean energy density ▪ 49.2 J/cm	▪ 204 p (77%) mean age 57 yrs (range: 23-87) ▪ 229 Legs	Concurrent phlebectomy (n=177), vein ligation, foam sclerotherapy to treat incompetent tributaries and perforate veins [40 limbs had ELT ablation only. GSV reflux treated prior to SSV].	Safety and efficacy	3 year Mean 16 months (range: 2 – 390)
Nwaejike 2009 (82) United Kingdom	▪ 1 outpatient site ▪ 2 surgeons ▪ local tumescent anesthesia (for 40%),	▪ 810nm ▪ 10 W power ▪ mean energy density 53 J/cm	▪ 61 p (59% F) mean age 47 yrs (range: 23-80) ▪ 66 SSV ▪ 5 underwent bilateral ELT SSV	Concomitant phlebectomies (n=52), foam sclerotherapy (n=1)	Safety and efficacy	2 year Median 14 months
Park S.J. 2008 (83) Korea	▪ 1 outpatient site ▪ Phlebologist ▪ local tumescent anesthesia	▪ 980nm ▪ 12-15 W power pulse mode, laser withdrawal at 2 mm/sec ▪ median energy density 62.1J/cm (12W), 77.5 J/cm (15W)	▪ 344 p (65%) mean age 47 yrs (range: 19-69) ▪ 390 Legs ▪ 45 underwent bilateral and 113 also ELT GSV reflux	Concomitant phlebectomy (n=72) only for severe varicosities. After 2-3 months sclerotherapy for distal varicose tributaries	Safety and effectiveness of the 980 diode laser for refluxes of incompetent SSV	1, 2 years Mean 9 months (SD 7 months)

Author, Year, Country	Sites Operators Anesthesia	Laser Wavelength (λ), Mode, Energy (J/cm)	Sample (% Female)	Concomitant or Staged Procedures	Objective	Follow-Up
Park S.W. 2008 (80) Korea	▪ 1 site (angiography suite) ▪ Interventional radiologists ▪ local tumescent anesthesia	▪ 980nm ▪ 10-12 W power continuous mode with pullback rate 5 mm / second with fluoroscopy and ultrasound guidance	▪ 84 p (55% F) mean age 50.1 yrs (range: 22-67) ▪ 96 Legs	Staged sclerotherapy performed for remaining varicose tributaries by vascular at 1 month follow-up	Long term safety and effectiveness with 980nm diode laser for	3 year
Theivacumar 2007 (81) United Kingdom	▪ 2 sites (venous outpatient clinics) ▪ Surgeon ▪ local tumescent anesthesia	▪ 810nm ▪ 12 W power pulse mode ▪ energy density 60-72 J/cm	▪ 65 p (66%F) ▪ median age 48 yrs (range: 28-82) ▪ 68 Legs	Staged foam sclerotherapy for residual varices at 6 weeks on patient request	Safety and effectiveness	6 months

Table A4: Complications and Adverse Events following Ablation of the Great Saphenous Vein

Author, Year, Country	Patients (p) Legs (L) Veins (V)	Follow-Up	Laser λ	DVT	PE	Phlebitis	Hematoma	Skin Burns or Necrosis	Parasthesia Dysesthesia	Nerve Damage	Infection
Barucchello 2009 Italy	473 p 535 Legs 301 GSV	3 years	808nm	0	0	44/535 L (8.2%)	0	0	?	0	0
Desmyttere 2007 France	500 p 511 L 500 GSV	4 years	980nm	0					7% L (temporary, medium duration of 2 wks		
D'Othee 2008 US	112 p 122 L		980nm	NR	NR	NR	NR	NR	NR	NR	NR
Elmore 2008 US	516 p 685 L 475 GSV, 325 SSV, 9 other V		810nm	0	0			2 (0.4%)	11 (2.1%) 8 GSV, 3 SSV		0
Fernandez* 2008 Venezuela	1559 p 1985 L 1652 GSV, 285 SSV, 40 ALT, 8 PMT	30 months	810nm	2 (in GSV)		58 p (2.9%)			38 (2.4%) Transient resolved after 2 wks		
Hamel-Desmos 2008 France Switzerland	1422 p 1703 V 1394 GSV, 309 SSV	6 months	980nm	5 (4 GSV, 1 SSV)	1 (GSV)	4 SVT	5: 4 GSV, 1 SSV	0	12 dysesthesia (9 GSV, 3 SSV); all resolved within 3 months)	0	2
Jung 2008 Korea	148 p 169 L 176 V (135 GSV, 41 SSV)		810nm	0	0	5 (All GSV)		0	12 (7 GSV, 5 SSV)	1 foot drop (SSV), recovered in 2 weeks	
Knipp 2008 US	364 p 460 L	1 year	810nm	3 l (0.7%)	1 (0.2%)	32 (7.2%) SF thrombus extension 11 (2.5%) superficial thrombus			2 (0.5%)		
Lu 2008 China	1060 p 1186 L	Mean 27 months± 11	810nm	0	0	Superficial phlebitis 5%	0	Spot skin burns 12 L (1.01%)	Parasthesia in gaiter area 65 L (5.48%)		7 L (0.59%)
Mackenzie 2008 UK	640 p 713 V (579 GSV, 119 SSV, 6 AA-GSV)	3 months	810nm	0	1		0	0		0	0

Author, Year, Country	Patients (p) Legs (L) Veins (V)	Follow-Up	Laser λ	DVT	PE	Phlebitis	Hematoma	Skin Burns or Necrosis	Parasthesia Dysesthesia	Nerve Damage	Infection
Marston 2008 US	70 p 75 L	6 months	810nm	NR	NR	NR	NR	NR	NR	NR	NR
Myers† 2009 Australia	361 p 494 L 509 V	NR	NR	0	1	11 (3.0%) thromboembolic events (thrombus extensions)		0		1 partial sural nerve palsy at 18 months post SSV ELT	
Pannier 2009 Latvia	100 p 117 L 134 v (108 GSV, 26 SSV)	6 months Mean 184 days (± 27)	1470nm	0	0	3 (2.2%)		0	9.5% L parasthesia at 6 months, 7.6% at 1 year	0	
Park, SW 2009 Korea	312 p 411 L 437 V (331 GSV, 106 SSV)	6 months	980nm	0	0	3 L (0.8%) at 1 month delayed superficial thrombophlebitis		0	Parasthesia /tingling 6/373L (1.6%) at 1 month, resolved by 3 months)		
Prince 2008 US	474 p 471 V (365 GSV, 49 SSV, 60 other V)	Average of 5 months (range: 0.5 - 26.3)	980nm	0	0			0	Parasthesia in 16 (3.3%) but none at lower energy dose < 60 j/cm)	0	0
Sadik 2007 US	90 p 94 L 94 GSV	Minimum of 1 year	810nm					0	4 (4.3%)		
Tan 2009 Singapore	169 p 270 GSV	Median: 6 months	940nm	0	0			0	Hypoesthesia (numbness) in 18 (10.7%)	0	
Theivacumar 2008 UK	582 p 644 L	Minimum of 3 months	810nm	1	0	phlebitis 66 (10.2%)		0	Transient numbness 7 (1.1%)	0	0
van den Bremer 2009 Netherlands	323 p 403 L	6 weeks	980nm	0	0			0		0	0
Vuylsteke 2008 Belgium	97 p 129 GSV	6 months	980nm	0	0	Periphlebitis 12 (all resolving with NSAIDs)	Small hematomas 8 (associated with phlebectomy and punctured successfully)	0	Temporary parasthesia or hypoesthesia 6; all resolved in 6 months	0	1

* One patient (0.06%) in Fernandez et al. 2009 also died from lidocaine toxicity

† One patient (0.28%) in Myers et al. 2009 also died from cardiac disease unrelated to ELT at 18 months post op

Table A5: Complications and Adverse Events Following Ablation of the Small Saphenous Vein

Author, Year, Country	Patients (p) Legs (L) Veins (V)	Follow-Up	Laser λ	DVT	PE	Phlebitis	Parasthesia Dysesthesia	Nerve Damage
Gibson 2007 United States	187 p 210 L 366 V (54 SSV only, 156 GSV and 156 SSV)	Mean 4.0 months	980nm	12 l (5.7%) at 2-4 days none were occlusive, (none at 2-11 months)	0		Numbness lateral malleolus of distal posterior calf at 2 and 6 weeks in 3 L (1.6%) – had also miniphlebectomy of vein branches near lateral malleolus	0
Huisman 2009 Netherlands	150 p 169 L 248 V (98 GSV and 98 SSV and 52 SSV)	3 months At 2 months 150 L of 169	810nm	0	0	6 superficial thromboplebitis (resolved spontaneously)	Numbness lateral lower leg and foot (sural nerve) 2 (1.3%); resolved after 2 months	
Kontothanas 2009 Italy	204 p 229 L	Mean 16 months (range: 2-39)	980nm	3 at 7 days none after 2 months	0	Superficial vein thrombosis 3 (1.3%)	Parasthesia from sural nerve injury 5 L (2.2%) at post op persisting in follow-up.. parasthesia was not noted in later series with increased amount tumescent saline	1 sural nerve injury with permanent numbness at bilateral malleolus (sustained after redo laser)
Nwaejike* 2009 United Kingdom	66 p 66 SSV	6 weeks	810nm	0	0	2 superficial thrombophlebitis (resolved within 3 months)	0	0
Park, SW 2008 Korea	84 p 96 L	3 year	980nm	0	0	0	4 (4%) parasthesia mid and distal aspect posterior calf at 1 week post-op (resolved by 1 year without treatment)	
Park, SJ 2008 Korea	344 p 390 SSV	12 months	980nm	0	0	8 (2.3%) palpable induration along vein overt phlebitic reaction treated by NSAIDs and compression	7 (2%) localized skin parasthesia in lateral malleabar region (2p), lateral dorsum foot (4p) and lateral calf region (1 p); disappeared after 3 months in 6 p).	In 1 of the 7 with parasthesia SSV ran further laterally than usual in one assumed lateral cutaneous nerve injury cause parasthesia
Theivacumar 2007 United Kingdom	65 p 68 L	6 months	810nm	0	0	3 (4.4%) superficial phlebitis (treated with diclofenac sodium 50 mg)		

Note: No instances of skins burns, skin necrosis, or infections were reported in any of the included studies.

* Two patients in Nwaejike et al. 2009 also suffered hematomas at the phlebectomy sites.

Table A6: Study Quality of Controlled Clinical Trials

Author, Year	Study Design	Randomize	Allocation Concealment Blinding	Inclusion Exclusion Criteria Stated	Intention to Treat Analysis	Power Calculation	Baseline Characteristics	Attrition Reported Loss to Follow-Up		Overall Study Quality
								Laser	Surgery	
Endovascular Laser Ablation vs. Surgery										
Darwood et al, 2006 (89)	3-arm RCT	Sealed envelopes	No/not clear	Yes	Yes	Yes	Similar	9/80*	2/34	high
DeMedeiros et al, 2005 (90)	2-arm within-person RCT	Drew lots	No/not clear	Yes	Yes	No	Similar	0/20	0/20	moderate
Disselhoff et al, 2008 (90;92;96)	2-arm RCT	Sealed envelopes	No/not clear	Yes	Yes	Yes	Similar	4/60*	5/60	high
Kalteis et al, 2008 (93)	2-arm RCT	Randomization method not stated	Patient informed of assignment after treatment	Yes	Yes	Yes	Similar	3/50	2/50	moderate
Rasmusson et al, 2007 (94)	2-arm RCT	Sealed envelopes	Data collection and analysis by research team	Yes	Yes	Yes	Similar	15/62	18/59	high
Theivacumar et al, 2009 (95)	2-arm Mixed RCT	68 randomized and 59 treated as preference	No/not clear	Yes	Yes	No	Similar	5/49	4/46	low
Endovascular Laser Ablation vs. Radiofrequency Ablation or Sclerotherapy										
Almeida et al, 2009 (98)	2-arm multi-center RCT	Web based random assignment	Patients unaware of assignment	Yes	Yes	Yes	Similar	0/34 (laser)	0/35 (radiofreq.)	high
Morrison et al, 2005 (100)	2-arm within-person RCT	Randomization method not stated	No/not clear	Yes	Yes	No	Not Reported	0/50 (laser)	0/50 (radiofreq.)	moderate
Almeida et al, 2006 (97)	CCT	Contemporary comparison group	No/not clear	No	No	No	Similar	Not reported	Not reported	low
Gonzales et al, 2008 (99)	CCT	Assignment by patient choice	Recruiting and follow-up investigators by physicians blind to initial treatment	Yes	Yes	Yes	Similar	0/45 (laser)	0/53 (sclerotherapy)	low

Author, Year	Study Design	Randomize	Allocation Concealment Blinding	Inclusion Exclusion Criteria Stated	Intention to Treat Analysis	Power Calculation	Baseline Characteristics	Attrition Reported Loss to Follow-Up		Overall Study Quality
								Laser	Surgery	
Endovascular Laser Ablation With and Without Concomitant Phlebectomy										
Carradice et al, 2009 (101;123)	2-arm RCT	Sealed envelopes	No/not clear	Yes	Yes	Yes	Similar	5/25* (laser and phlebectomy)	4/25 (laser only)	high
Kim et al, 2009 (103)	CCT	Cross over by time period	No/not clear	Yes	Yes	No	Similar	Not reported	Not reported	low
Endovascular Laser Ablation With and Without Surgical Ligation										
Disselhoff et al, 2008 (112)	2-arm within-person RCT	Numbered sealed envelopes	No/not clear	Yes	Yes	Yes	Similar	4/43*	4/43	high
Endovascular Laser Ablation with Different Above and Below the Knee Treatment										
Theivacumar et al, 2008 (113)	3-arm RCT	Randomization method not stated	No/not clear	Yes	Yes	No	Similar	0//43 (ELT only)	0/22 (ELT and sclerotherap.y)	moderate
Endovascular Laser Ablation With and Without Eccentric Leg Compression										
Lugli et al, 2009 (104)	2-arm RCT	Telephone randomization service	Surgeon blind to post surgery assignment	Yes	Yes	No	Similar	0/94 (ELT only)	0/92 (ELT with compression)	high

Table A7: Study Outcomes and Endpoints Reported in Clinical Trials Involving Endovascular Laser Treatment of VV

Author, Intervention Arms	Primary Outcome	Secondary Outcomes	Other Outcomes
ELT vs. Surgery			
Darwood et al. 2008 ELT vs. high ligation GSV and inversion stripping	▪ Reflux in treated vein segment at 3 months ▪ Vein disease specific QOL (AVVSS) at 3 months, 1 year	▪ Postoperative complications and pain ▪ Time to return to work/usual activities ▪ Cosmesis at 3 months ▪ Patient satisfaction at 3 months	▪ ND
DeMedeiros et al. 2005 ELT + surgical ligation GSV vs. surgical ligation GSV and stripping	▪ ND	▪ ND	▪ Post operative pain- 30 days ▪ Bruising – 30 days ▪ Cosmesis – 30 days ▪ Satisfaction – 60 days ▪ GSV recanalization
Disselhoff et al. 2008 ELT vs. surgical ligation GSV and cryostripping	▪ Recurrent vein incompetence on duplex imaging at 6,12,24 months ▪ Venous clinical severity score (VCSS) at 6,12 and 24 months ▪ Venous disease specific QOL (AVVSS) at 6, 12 and 24 months	▪ ND	▪ Procedure duration ▪ Post procedural complications ▪ Time to return to usual activities ▪ Postoperative pain and in duration
Disselhoff et al. 2009 ELT vs. surgical ligation GSV and cryostripping	▪ Clinical effectiveness [QALY (SF – 6D)] at 2 years ▪ Direct and indirect costs ▪ ICER	▪ ND	▪ ND
Kalteis et al. 2008 ELT and surgical ligation GSV vs. surgical ligation GSV and stripping	▪ Haematoma at 1 week ▪ Venous disease specific QOL (CIVIQ) at 4 weeks	▪ Post operative pain and analgesic use ▪ Time to work recovery ▪ Cosmetic result 4 months ▪ Patient satisfaction at 4 months ▪ Complications (parasthesia)	▪ ND
Rasmussen et al. 2007 ELT vs. surgical ligation GSV and perforate invagination stripping	▪ Closed or absent GSV at 6 months	▪ Technical results and post procedural complications ▪ Post operative pain ▪ Return to work/normal activities ▪ Venous clinical severity score (VVSS) ▪ Venous specific QOL (AVVSS) ▪ Generic QOL (SF-36) ▪ Direct and indirect costs	▪ Adverse events

Author, Intervention Arms	Primary Outcome	Secondary Outcomes	Other Outcomes
Rasmussen et al. 2009 ELT vs. surgical ligation GSV and perforate invagination stripping	▪ Closed or absent GSV at 2 years	▪ Venous clinical severity (VCSS) ▪ Venous specific QOL (AVVSS) ▪ Generic QOL (SF-36) ▪ Complication rates	▪ ND
Theivacumar et al. 2009 ELT vs. surgical ligation GSV and stripping	▪ Recurrence and neovascularization at 2 years	▪ Patient satisfaction at 2 years	▪ ND
Endovascular Laser Treatment vs. Radiofrequency or Sclerotherapy			
Almeida et al. 2009 ELT vs. RF	▪ Post operative pain ▪ Ecchymosis ▪ Adverse procedural sequelae (deep vein thrombosis, parasthesia, phlebitis, hyperpigmentation and infection)	▪ Vein occlusion and elimination truncal reflux at 48 hours, 1 month ▪ Venous disease severity (VCSS)at 48 hrs, 1 week, 2 weeks, 1 month ▪ Limb tenderness at 48 hrs, 1 week, 2 weeks, 1 month ▪ Postoperative pain and analgesic use ▪ Vein disease specific QOL (CIVIQ)	▪ ND
Morrison et al. 2005 ELT vs. RF	▪ Vessel ablation with no flow on color doppler in any portion of the treated vessel at 1 year ▪ Recurrent patency in any portion at 1 year	▪ ND	▪ ND
Almeida et al. 2006 ELT vs. RF	▪ Vein closure rate in follow-up to 500 days ▪ Recanalization rate in follow-up to 500 days	▪ ND	▪ Adverse events
Gonzales et al. 2008 ELT vs. foam sclerotherapy	▪ Presence reflux on duplex imaging at 1 year ▪ Success as vein occlusion	▪ Post procedural pain (diary) ▪ Venous clinical severity score (VCSS) ▪ Post procedural complications (deep vein thrombosis, phlebitis, ecchymosis and paresthesia)	▪ ND
Disselhoff et al. 2008 ELT GSV with and without surgical ligation GSV	▪ Recurrent VV in the groin at 2 years	▪ Ablation reflux in GSV ▪ Venous clinical severity score (VCSS) ▪ Recurrent VV Procedural complications	▪ ND

Author, Intervention Arms	Primary Outcome	Secondary Outcomes	Other Outcomes
ELT Technical Issues			
Carradice et al. 2009 ELT GSV and concomitant or with sequential phlebectomy	▪ Disease specific QOL (AVVQ) at 3 months	▪ Technical success (completion of procedure, ablation of flow in GSK at 1 week and freedom from recurrent reflux on duplex ultrasound) ▪ Procedural duration, complications and post-procedural pain ▪ Time to return to work/usual activity ▪ Patient satisfaction ▪ Venous disease severity (VCSS) ▪ Generic QOL (SF36 / EQ50) ▪ Need for secondary procedures at 6 weeks	▪ ND
Kim et al. 2009 ELT GSV and ELT or phlebectomy of varicose tributaries	▪ ND	▪ ND	▪ Postoperative complications ▪ Recanalization ▪ Recurrent varicosities
Lugli et al. 2009 ELT GSV with and without eccentric vein compression	▪ Post-operative pain	▪ ND	▪ Postoperative complications
Theivacumar et al. 2008 ELT and varying below the knee vein GSV ablations	▪ Residual varicosities requiring sclerotherapy ▪ Vein symptom severity score (AVVSS)	▪ Post-operative pain ▪ Patient satisfaction ▪ Complication rates	▪ ND

ND; not done

Table A8: Clinical Trials Involving Endovascular Laser Ablation vs. Surgical Treatment for VV

Author, Year, Country	Trial Design, Sample	Setting, Operator, Anesthesia	Endovascular Laser		Surgical Arm		Follow-Up
			Laser λ, Power Mode, Energy (J/cm)	Concurrent or Staged Procedures	Surgical Technique	Concurrent or Staged Procedures	
Darwood 2006 UK	3-arm RCT 118 p (57%F)	▪ Outpatient clinic ▪ Vascular surgeons ▪ Local tumescent anesthesia (ELT) vs. day case general anesthetic (surgery)	810nm Arm 1: 12W power on pulse mode with pullback rate 2-3 mm/sec with 60.9 J/cm (49.2-68.8) Arm 2: 14 W continuous mode withdraw rate 2-3 mm/sec with 71.1 J/cm (64.7-80.6)	Staged sclerotherapy at 6 wks for residual varices if requested by patient	Arm 3. High ligation SFJ and inversion stripping GSV to the knee	Concurrent multiple phlebectomies	12 month
DeMedeiros 2005 Brazil	2-arm within person RCT, 20 p (95% F)	▪ Vascular surgery clinic ▪ Vascular surgeons ▪ Epidural block (ELT) and subarachnoid (60%)/ epidural block (surgery)	810nm 12-14 W on pulsed mode	Concurrent high ligation GSV and all tributaries, mini phlebectomies and ligation insufficient perforator veins	High ligation GSV and forward total stripping GSV to the ankle	Concurrent mini phlebectomies and ligation all GSV tributaries and insufficient perforator varices	9 month (range: 2-18)
Disselhoff 2008, 2009 Netherlands	2-arm RCT + CE study 120 p (69% F)	▪ Outpatient (ELT), day case (surgery) ▪ Surgeon doing surgery and ELT ▪ Patient choice anesthesia – tumescent anesthetic	810nm 14 W continuous pulse mode 57 (41-86) J/cm	Staged 6-wk post-op sclerotherapy or phlebectomy for persistent varices	Ligation and liquid cryosurgery stripping and avulsion of tributaries	Staged at 6-wk post-op sclerotherapy or phlebectomy for persistent varices	2 year
Kalteis 2008 Austria	2-arm RCT 100 p (75% F)	▪ Outpatient clinic ▪ >1 surgeon (>50 vein surgeries / yr) ▪ No tumescent anesthesia	810nm Variable watts declining down leg (10-12W, 6 W, 4-6W) Targeted energy level 20-30 J/cm	Concurrent high ligation of GSV and ligation of all side tributaries followed by ELT. and stab avulsions of all side tributaries	Dissection SFJ junction, high ligation of GSV, ligation of all side tributaries followed by GSV stripping	Concurrent stab avulsions of all marked tributaries	4 week

Author, Year, Country	Trial Design, Sample	Setting, Operator, Anesthesia	Endovascular Laser		Surgical Arm		Follow-Up
			Laser λ, Power Mode, Energy (J/cm)	Concurrent or Staged Procedures	Surgical Technique	Concurrent or Staged Procedures	
Rasmusson 2007, 2009 Denmark	2-arm RCT + costing study 121 p (69% F)	▪ Outpatient setting for ELT and surgery ▪ 2 experienced surgeons (>100 ELT) ▪ Tumescent anesthesia	980nm 12 W pulse mode mean delivered energy 73.5 J/cm (range 57 – 95.4)	Concurrent all varices removed by miniphlebectomies	High ligation and perforate invagination stripping of GSV	Concurrent all varices removed by miniphlebectomies	6 month 2 year
Theivacumar 2009 UK	2-arm mixed RCT 127 p (68 randomized) (61% F)	▪ Outpatient clinic ▪ Vascular surgeon ▪ All treatments general anesthesia	810nm 12 W pulse mode	Staged within 12 wks foam sclerotherapy of residual varicoses	SFJ ligation and division of all tributaries with GSV stripping to the knee	Concurrent multiple stab avulsions of varices	2 year

* RCT refers to randomized controlled trial; GSV, great saphenous vein; SFJ, saphenofemoral junction

Table A9: Clinical Trials Comparing Endovascular Treatment Approaches

Author, Year, Country	Trial Design, Sample	Setting, Operator, Anesthesia	Laser λ, Power Mode, Energy (J/cm)	Concurrent or Staged Procedures	Surgical Technique	Concurrent or Staged Procedures	Follow-Up
ELT vs. Radiofrequency			**ELT Arm**		**Radiofrequency Ablation Arm**		
Almeida, 2009 US	2-arm RCT 69 p (87 Legs)	▪ Multicenter: 6 outpatient clinics (5 US and 1 European) ▪ Interventional radiologists ▪ Local tumescent anesthesia	980-nm 12 W power continuous mode 80 J /cm	Ablation GSV and staged phlebectomies permitted after 30 days post op	Closure-FAST® device, 7-cm heating element, 1200C in 20 sec cycles, 2 cycles proximal	phlebectomies permitted after 30 days post op	1 month
Morrison 2005 US	2-arm within-person RCT 50 p (50 Legs)	▪ 1outpatient clinic ▪ Surgeon ▪ Anesthesia NR	810-nm pulse mode (early cases) and continuous mode (later cases)	Ablation GSV	Closure® device	NR	1 year
Almeida 2006 US	CCT (Early ELT cases were compared with recent RF cases) ELT 819 V (483 GSV) RF 128 V (95 GSV)	▪ Outpatient vein clinics for both procedures ▪ Vascular surgeon ▪ Local tumescent anesthesia	810-nm (17p) 940-nm (4p) 980-nm (460p) 1320 (2p) 50-90 J/cm (based on vein diameter)	Concurrent phlebectomies or sclerotherapy	Closure® device RF temp 850 C for early cases and 95 0 C for later cases	Concurrent phlebectomies or sclerotherapy	500 days
ELT vs. Foam Sclerotherapy			**ELT Arm**		**Foam Sclerotherapy Arm**		
Gonzales 2008 Chile	CCT (assignment to ELT or RF by patient choice) 98 p (45 ELT, 53 UFS)	▪ Outpatient clinic ▪ Surgeon (>800 ELT, >2000 UFS) for both procedures ▪ Local tumescent anesthesia	980-nm 15 W power continuous mode with withdraw rate 1-2 mm/sec target delivering energy 70-90 J/cm	NR	3% sclerosing foam (Polidocanol), foam to air ratio of 1:4	NR	I year

Table A10: Clinical Trials of Alternate Technical Approaches to Endovascular Laser Ablation

Author, Year, Country	Trial Design, Sample	Setting, Operator, Anesthesia	Standard Arm	Comparator Arm	Follow-Up
Laser Ablation With and Without Concomitant Phlebectomy					
Carradice 2009 UK	2-arm RCT 50 p	▪ Outpatient clinic ▪ Vascular surgeon ▪ Local tumescent anesthesia	ELT only - 810nm laser 14 W continuous pulse mode, targeted energy density 80-100 J/cm Secondary procedures offered if necessary 6 weeks post op	Combination Group – 810nm laser 14 W continuous pulse mode, targeted energy density 80-100 /cm and concomitant ambulatory phlebectomy of marked varices Secondary procedures offered if necessary 6 weeks post op varicoses.	1 year
Kim 2009 South Korea	CCT – cross over trial 132 p with ELT and phlebectomy (Aug.2003 - Feb.2005) 133 p with ELT only (Mar.2005 - July 2006)	▪ Hospital clinic ▪ Surgeons ▪ Patient choice: general, spinal or local anesthesia + local tumescent anesthesia for all treatments	Combination group - 980nm laser continuous mode 10 W or 8 W followed by concomitant Muller ambulatory phlebectomy of remaining associated tributaries	ELT only - 980nm laser continuous mode 10 W or 8 W followed by tributaries also treated by laser	ELT: 11.8 ± 8.2 months range: 1.3 - 18.5 Combination group: 25.6 ± 12.8 months range: 15 - 37
Laser Ablation with and without Surgical Ligation and Stripping					
Disselhoff 2008 Netherlands	2-arm within person RCT 43 p	▪ Day procedure ▪ 1 surgeon for all procedures ▪ Spinal or general anesthesia with local tumescent anesthesia	ELT without SFJ ligation Early cases (first 20 patients)- 810nm laser with 12W power intermittent mode to later cases (next 23 patients) 14W power with continuous mode with pullback rate 0.2 cm/sec.	ELT with SFJ ligation performed through groin incision with flush division of tributaries beyond the second level of division	2-year
Laser Ablation With and Without Eccentric Compression					
Lugli, 2009 Italy	2-arm RCT 186 p	▪ Outpatient setting ▪ Phlebologist ▪ Local tumescent anesthesia	ELT without post procedural eccentric bandage compression of the treated leg	ELT with post procedural eccentric bandage compression of the treated leg	1 week
Laser Ablation GSV with Varying Below the Knee GSV Treatment					
Theivacumar 2008 UK	3-arm RCT 65 p	▪ 1 site ▪ Surgeons ▪ Local tumescent anesthesia	<u>Group A</u> ▪ Standard ELT above the knee ▪ 810nm laser 12W pulsed mode, energy density 60-70 J/cm ▪ At 6 weeks foam sclerotherapy for residual VV	<u>Group B</u> ▪ Standard ELT above and below the knee ▪ 810nm laser 12W pulsed mode, energy density 60-70 J/cm ▪ At 6 weeks foam sclerotherapy for residual VV	<u>Group C: Comparator Arm</u> ▪ Standard ELT above the knee and 1% foam sclerotherapy below the knee ▪ 810-nm laser 12W pulsed mode, energy density 60-70 J/cm ▪ At 6 weeks foam sclerotherapy for residual VV	3 months

Table A11: Endovascular laser treatment resources – estimates from a vascular surgeon in Toronto

Resources	Unit	Unit Cost	Utilization 1	Cost 1	Assumptions	References
Equipment						
Acquisition cost	per case		1	$285.71	$100,000/machine; Duplex machine plus laser generation unit; lifetime of machine = 5-7 years; practice conducting 60-80 procedures per year and could easily double/triple	Vascular surgeon in Toronto
Maintenance cost	per case		1	$10.00	$1,000/yearly maintenance	Vascular surgeon in Toronto
Laser fibres (EVLT kit)	per case		1	$200.00	$200/case	Vascular surgeon in Toronto
Disposables	per case		1			
Tumescent delivery system	per case					
Core Pak	per case					
EVLT						
EVLT procedure	per leg		1	$3,500.00		vascular surgeon in Toronto
Medical Visits						
Vascular surgeon	per consult	$32.50	1	$132.50	Assumed that procedural visits are billed to the province separately and not absorbed within the hospital/clinic procedural cost; assumed 1 consult and visit pre, 4 visits post	vascular surgeon in Toronto; OSB A935 www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html; Last updated September 2009; Accessed November 2009
	per visit	$29.20	5	$146.00		OSB C092
Interventional radiologist	per consult	$132.50		-		
	per visit	$29.20		-		
GP	per consult	$56.10		-		Vascular surgeon in Toronto; OSB C005
	per visit	$29.20		-		OSB C002
Nurse	per visit	$32.73	2	$65.46	Assumed that procedural visits are billed to the province separately and not absorbed within the hospital/clinic procedural cost; assumed 2 visits post	Vascular surgeon in Toronto; http://www.health.gov.on.ca/transformation/fht/guides/fht_inter_provider.pdf, Last updated May 2009; Accessed November 2009

Laboratory Tests						
none				-		
Medical Procedures						
Duplex venous imaging	per technical test	$34.35	3	$103.05	Assumed 3 procedures; 1 pre, 1 during and 1 post	Vascular surgeon in Toronto; OSB J202
	per professional test	$21.40	3	$64.20		
Bilateral	per technical test	$7.60	1	-		Vascular surgeon in Toronto; OSB J198
	per professional test	$12.70	1	-		
Vascular ultrasounds	per technical test	$22.60		-		
	per professional test	$18.60		-		
Bilateral	per technical test	$7.60		-		
	per professional test	$12.70		-		
Drugs						
Ibuprofen (200 mg)	per tablet	$0.02	70	$1.70	Assumed 6-8 tables a day for 10 days	Vascular surgeon in Toronto

Table A12: Endovascular laser treatment resources – estimates from an interventional radiologist in Toronto

Resources	Unit	Unit Cost	Utilization 2	Cost 2	Assumptions	References
Equipment						
Acquisition cost	per case		1	$145.24	$61,000/machine; Assumed lifetime = 4-5 years, conducting 84 procedures per year	Interventional radiologist in Toronto
Maintenance cost	per case		1	$41.67	$3,500/yearly maintenance	Interventional radiologist in Toronto
Laser fibres (EVLT kit)	per case		1	$662.00	$662/case	Interventional radiologist in Toronto
Disposables	per case		1	$85.00	$85/disposables	Interventional radiologist in Toronto
Tumescent delivery system	per case					
Core Pak	per case					
EVLT						
EVLT procedure	per leg		1	$2,950.00		Interventional radiologist in Toronto
Medical Visits						
Vascular surgeon	per consult	$132.50				Interventional radiologist in Toronto; OSB A935; www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html Last updated September 2009, Accessed November 2009
	per visit	$29.20				OSB C092
Interventional radiologist	per consult	$132.50	1	$132.50	Assumed that procedural visits are billed to the province separately and not absorbed within the hospital/clinic procedural cost; assumed 1 consult and visit pre, 4 visits post	interventional radiologist in Toronto; OSB A365
	per visit	$29.20	5	$146.00		OSB C002
GP	per consult	$56.10	1	$56.10	Assumed that procedural visits are billed to the province separately and not absorbed within the hospital/clinic procedural cost; assumed 1 consult pre	Interventional radiologist in Toronto; OSB C005
	per visit	$29.20		-		OSB C002
Nurse	per visit	$32.73		-		

Laboratory Tests						
None				-		
Medical Procedures						
Duplex venous imaging	per technical test	$34.35		-		
	per professional test	$21.40		-		
Bilateral	per technical test	$7.60				
	per professional test	$12.70				
Vascular ultrasounds	per technical test	$22.60	6	$135.60	Assumed 1 pre, 3 during, 2 post	Interventional radiologist in Toronto; OSB J193
	per professional test	$18.60	6	$111.60		
Bilateral	per technical test	$7.60	1	$7.60		Interventional radiologist in Toronto; OSB J198
	per professional test	$12.70	1	$12.70		
Drugs						
Ibuprofen (200 mg)	per tablet	$0.02	126	$3.06	Assumed 9 tablets a day for 14 days	Interventional radiologist in Toronto

Table A13: Vein stripping surgery resources – estimates from a vascular surgeon #1 in Toronto

Resources	Unit	Unit Cost	Utilization 1	Cost 1	Assumptions	References
Day Surgery						
Hospital	per case	$1,058.72	1	$1,058.72	Procedure: 1KR87LA,1KR87LAXXA,1KR87WK,1 KR87WKXXA,1KR87WM - see vein stripping spreadsheet for details on costing	Canadian Classification of Health Interventions - ICD-10-CA/CCI, Version 2006 License Agreement for CD; Accessed November 2009; The Ontario Case Costing Initiative - www.occp.com; accessed October/November 2009; Last updated September 2009.
Medical Visits						
Vascular surgeon	per consult	$132.50	1	$132.50	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 consult and visit pre, 1 labour, 1 visit post.	Vascular surgeon in Toronto; OSB A935 http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html, Last updated September 2009, Accessed November 2009
Long saphenous veins	per labour	$148.60	1	$148.60	100% of the time R868 plus R837; R869 would be a minority (~10 to 15% as an isolated procedure); Recurrent veins occur in anywhere from 20 to 50% of patient after vein stripping, some would say an even higher percentage.	Vascular surgeon in Toronto; OSB R868
Phlebectomy	per labour	$148.60	1	$148.60		OSB R837
Short saphenous veins	per labour	$107.50	1	$107.50		OSB R869
Recurrent veins	per labour	$353.80	1	$353.80		OSB R844
	per visit	$29.20	2	$58.40		OSB C092
Anesthetist	per consult	$103.85	1	$103.85	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 consult pre and 1 labour.	Vascular surgeon in Toronto; OSB A015
	per labour	$119.16	1	$119.16	Assumed 2 hour surgery, therefore base units plus 1 unit in the first hour and 2 units after the first hour up to and including the first 1.5 hours.	Vascular surgeon in Toronto; OSB R868
	per labour	$119.16	1	$119.16		Vascular surgeon in Toronto; OSB R837
	per labour	$119.16	1	$119.16		Vascular surgeon in Toronto; OSB R869
	per labour	$119.16	1	$119.16		Vascular surgeon in Toronto; OSB R844

Resources	Unit	Unit Cost	Utilization 1	Cost 1	Assumptions	References
Surgical assistant	per labour	$102.60	1	$102.60	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 labour; assumed 2 hour surgery therefore base units plus 1 unit in the first hour and 2 units after the first hour.	Vascular surgeon in Toronto; OSB R868
	per labour	$102.60	1	$102.60		Vascular surgeon in Toronto; OSB R837
	per labour	$102.60	1	$102.60		Vascular surgeon in Toronto; OSB R869
	per labour	$102.60	1	$102.60		Vascular surgeon in Toronto; OSB R844
GP	per consult	$56.10	1	$56.10	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 consult and 1 visit post.	Vascular surgeon in Toronto; OSB C005
	per visit	$29.20	1	$29.20		OSB C002
Nurse	per visit	$32.73	1	$32.73	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 post-op hour visit by a nurse.	Vascular surgeon in Toronto; http://www.health.gov.on.ca/transformation/fht/guides/fht_inter_provider.pdf, Last updated May 2009, Accessed November 2009
Laboratory Tests						
CBC	per test	$ 8.27	2	$ 16.54	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre and 1 post test.	Vascular surgeon in Toronto; OSLF L393 http://www.health.gov.on.ca/english/providers/program/ohip/sob/lab/lab_mn.html, Last updated June 2009, Accessed November 2009
Electrolytes (3 tests: Cl, K and Na)	per test	$ 7.76	1	$ 7.76	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test.	Vascular surgeon in Toronto; OSLF L053, L204, L226
BUN	per test	$ 2.59		$ -		
Creatinine	per test	$ 2.59		$ -		
Medical Procedures						
Duplex venous imaging	per technical test	$34.35	1	$34.35	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test.	Vascular surgeon in Toronto; OSB J202
	per professional test	$21.40	1	$21.40		
Bilateral	per technical test	$7.60	1	$7.60		Vascular surgeon in Toronto; OSB J198

Resources	Unit	Unit Cost	Utilization 1	Cost 1	Assumptions	References
	per professional test	$12.70	1	$12.70		
Chest x-ray (3 views or more)	per technical test	$28.85	1	$28.85	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test.	Vascular surgeon in Toronto OSB X092
	per professional test	$12.80	1	$12.80		
Electrocardiogram	per technical test	$6.75	1	$6.75	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test.	Vascular surgeon in Toronto; OSB G310
	per professional test	$9.75	1	$9.75		OSB G313
Ultrasound doppler	per technical test	$22.60		$ -		
	per professional test	$18.40		$ -		
Bilateral	per technical test	$7.60				
	per professional test	$12.70				
Drugs						
Tylenol 3 (30 mg)	per tablet	$0.05	168	$8.80	Assumed all drugs during visit are absorbed by hospital cost per case; assumed 240 mg codeine per day for 3 weeks post.	Vascular surgeon in Toronto; ODB formulary https://www.healthinfo.moh.gov.on.ca/formulary/SearchServlet, Last updated April 2009, Accessed November 2009
Keflex (500 mg)	per tablet	$0.47	21	$9.95	Assumed all drugs during visit are absorbed by hospital cost per case; assumed 1-2 gms PO per day for 7 days post.	Vascular surgeon in Toronto; ODB formulary https://www.healthinfo.moh.gov.on.ca/formulary/SearchServlet, Last updated April 2009, Accessed November 2009

Table A14: Vein stripping surgery resources – estimates from a Vascular surgeon #2 in Toronto

Resources	Unit	Cost/Unit	Utilization 2	Cost 2	Assumptions	References
Day Surgery						
Hospital	per case	$1,058.72	1	$1,058.72	Procedure: 1KR87LA,1KR87LAXXA,1KR87WK,1KR87WKXXA,1KR87WM - see vein stripping spreadsheet for details on costing	Canadian Classification of Health Interventions - ICD-10-CA/CCI, Version 2006 License Agreement for CD; Accessed November 2009; The Ontario Case Costing Initiative - www.occp.com; accessed October/November 2009; Last updated September 2009.
Medical Visits						
Vascular surgeon	per consult	$132.50	1	$132.50	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 consult pre, 1 labour, 2 visits post	Vascular surgeon in Toronto; OSB A935 http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html, Last updated September 2009, Accessed November 2009
long saphenous veins	per labour	$148.60	1	$148.60		Vascular surgeon in Toronto; OSB R868 + R837
Phlebectomy	per labour	$148.60	1	$148.60		Vascular surgeon in Toronto; OSB R868 + R837
Short saphenous veins	per labour	$107.50				OSB R869
Recurrent veins	per labour	$353.80				OSB R844
	per visit	$29.20	2	$58.40		OSB C092
Anesthetist	per consult	$103.85	1	$103.85		
	per labour	$119.16	1	$119.16	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 labour	Vascular surgeon in Toronto; OSB R868 + R837
	per labour	$119.16	1	$119.16		Vascular surgeon in Toronto; OSB R868 + R837
	per labour	$119.16				OSB R869
	per labour	$119.16				OSB R844

Resources	Unit	Cost/Unit	Utilization 2	Cost 2	Assumptions	References
Surgical assistant	per labour	$102.60	1	$102.60	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 labour	Vascular surgeon in Toronto; OSB R868 + R837
	per labour	$102.60	1	$102.60		Vascular surgeon in Toronto; OSB R868 + R837
	per labour	$102.60				OSB R869
	per labour	$102.60				OSB R844
GP	per consult	$56.10	1	$56.10	Assumed that procedural visits are billed to the province separately and not absorbed by the hospital/clinic procedural cost; assumed 1 consult pre	Vascular surgeon in Toronto; OSB C005
	per visit	$29.20		$ -		
Nurse	per visit	$32.73		$ -		
Laboratory Tests						
CBC	per test	$8.27	1	$8.27	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test	Vascular surgeon in Toronto; OSLF L393 http://www.health.gov.on.ca/english/providers/program/ohip/sob/lab/lab_mn.html, Last updated June 2009, Accessed November 2009
Electrolytes (3 different tests Cl, K and Na)	per test	$7.76	1	$7.76	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test	Vascular surgeon in Toronto; OSLF L053, L204, L226
BUN	per test	$2.59	1	$2.59	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test	Vascular surgeon in Toronto; OSLF L251
Creatinine	per test	$2.59	1	$2.59	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test	Vascular surgeon in Toronto; OSLF L067
Medical Procedures						
Duplex venous imaging	per technical test	$34.35		$ -		
	per professional test	$21.40		$ -		
Bilateral	per technical test	$7.60				
	per professional test	$12.70				
Chest x-ray (3 views or more)	per technical test	$28.85		$ -		
	per professional test	$12.80		$ -		
Electrocardiogram	per technical test	$6.75	1	$6.75	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test	Vascular surgeon in Toronto; OSB G310

Resources	Unit	Cost/Unit	Utilization 2	Cost 2	Assumptions	References
	per professional test	$9.75	1	$9.75		OSB G313
Ultrasound doppler	per technical test	$22.60	1	$22.60	Assumed all tests during visit are absorbed by hospital cost per case; assumed one pre test	Vascular surgeon in Toronto; OSB J193
	per professional test	$18.40	1	$18.40		
Bilateral	per technical test	$7.60	1	$7.60		Vascular surgeon in Toronto; OSB J198
	per professional test	$12.70	1	$12.70		
Drugs						
Tylenol 3 (30 mg)	per tablet	$0.05	110	$5.76	Assumed all drugs during visit are absorbed by hospital cost per case; assumed 10-12 tablets a day for 10 days post	Vascular surgeon in Toronto; ODB formulary https://www.healthinfo.moh.gov.on.ca/formulary/SearchServlet, Last updated April 2009, Accessed November 2009
Keflex (500 mg)	per tablet	$0.47		$ -		

Appendix 3: Resource utilization questionnaire – endovascular laser treatment (ELT)

EQUIPMENT

Based on your experience with treating patients eligible for EVLT what is the acquisition cost associated with the laser equipment? What is the lifetime of the laser? Are there maintenance fees with the equipment? How many EVLT procedures do you conduct a year on one laser machine? Are there any other costs related to equipment?

Equipment related costs	Cost
Acquisition cost	
Lifetime of equipment (years)	
Maintenance cost per year	
Procedures per year	
Other costs:	

MEDICAL VISITS

Based on your experience with treating patients eligible for EVLT please specify all types of specialists and/or healthcare staff (i.e. nurse, counsellor, dietician, etc.) involved in the pre and post-procedure consultations and visits AND during the procedure stay at the clinic/hospital (i.e. surgeon, anesthesiologist, etc.).

Visit	Number of visits pre-procedure	At clinic/hospital	Number of visits post-procedure
Specialist:_____			
Specialist:_____			
Specialist:_____			
Specialist:_____			
GP			
Healthcare staff:_____			
Healthcare staff:_____			
Healthcare staff:_____			
Healthcare staff:_____			

LABORATORY TESTS

Based on your experience with treating patients eligible for eligible for EVLT please specify the laboratory tests (i.e. CBC, electrolytes, etc.) required in the pre and post-procedure stages AND during the procedure stay at the clinic/hospital.

Laboratory Test	Number of tests pre-procedure	At clinic/ hospital	Number of tests post-procedure

MEDICAL PROCEDURES/DEVICES

Based on your experience with treating patients eligible for EVLT please specify the medical

procedures/devices (i.e. ultrasounds, x-rays, etc.) required in the pre and post-procedure stages AND during the procedure stay at the clinic/hospital.

Medical Procedure	Number of procedures pre-surgery	At clinic/hospital	Number of procedures post-surgery

MEDICATIONS

Based on your experience with managing patients undergoing EVLT please identify the standard therapy used in the pre and post-procedural stages AND during the stay at the clinic/hospital.

Drug	Typical Daily Dose (mg/day)	Number of tablets per day	Specify if PRE, POST or AT-HOSP

Appendix 4: Existing Guidelines

The Canadian Societies of Interventional Radiology and the Canadian Society of Vascular Surgery do not have official positions on endovascular laser treatment for venous reflux. (Personal Communication, clinical experts, November 2009) However, the American societies of the Society of Vascular Surgery, Society Interventional Radiology and American Society Phlebology all have official positions affirming ELT as a safe and effective treatment for venous reflux. The majority of major health insurers in the United States currently provide coverage for this therapy. In general, endovascular treatment is considered medically necessary and insured only for symptomatic VV and is not insured when provided solely for cosmetic purposes or to treat psychological symptomatology.

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