

# Treatment options, clinical outcome (quality of life) and cost benefit (quality-adjusted life year) in varicose vein treatment

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## Abstract

Varicose veins are an extremely common condition causing morbidity; however, with current financial pressures, treatment of such benign diseases is controversial. Many procedures allow the treatment of varicose veins with minimal cost and extensive literature supporting differing approaches. Here we explore the underlying evidence base for treatment options, the effect on clinical outcome and the cost-benefit economics associated with varicose vein treatment. The method of defining clinical outcome with quality-of-life assessment tools is also investigated to explain concepts of treatment success beyond abolition of reflux.

**Keywords:** QALY; varicose veins; cost-effectiveness

## Background

With the onset of the global economic crisis and the threat of world recession, health economics has become increasingly important in health-care decision-making. Discussions on the health economic benefits or burdens of new endovascular techniques are common.

Health-care costs are spiralling; in the UK they have doubled over the last decade to £126 billion annually,<sup>1</sup> and a similar picture is seen in the USA with spending now at \$1.2 trillion/year,<sup>2</sup> equivalent to over 8% GDP, a value seen throughout Europe as well.<sup>3</sup> In the National Health Service (NHS), austerity measures require a saving of £20 billion on this budget of £126 billion (16%), whilst caring for an ever more elderly and frail population.<sup>4</sup>

Although costs and value for money have always had a role in the decision-making processes, these

increasing financial pressures at the hospital, regional and national level have caused hospital managers to look at ways to cut costs at all levels. Varicose veins have been labelled as a 'Procedure of Low Clinical Value' due to the low mortality rates associated with this benign disease, leading to a reduced rate of referral for treatment.<sup>5,6</sup>

With the majority of patients with varicose veins being young and otherwise systemically well and with varicose veins rarely having a significant effect on mortality, they are afforded low priority. Therefore, by reporting crude outcomes through serious morbidity (or complications) and mortality, the object of treatment is missed and it allows questions to be raised over the necessity for intervention. In benign diseases quality-of-life (QOL) assessments are invaluable in revealing the true clinical benefit of intervention.<sup>7,8</sup>

Varicose veins are extremely common (approx. 25% of the population),<sup>9</sup> and so even moderate improvements in patient outcome generate large overall population improvements.<sup>10</sup>

## QOL assessment

QOL instruments include both generic and disease-specific surveys. Generic surveys assess global

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states of wellbeing and provide a subjective measure of treatment efficacy, while disease-specific surveys focus on elements associated with particular disease processes and treatment effects.<sup>11–14</sup>

In the UK, the National Institute for Health and Clinical Excellence (NICE) was founded in 1999. NICE is an independent government-funded organization that advises the National Health Service and has become a role model for the development of clinical guidelines and attempts to evaluate the cost and cost-effectiveness of potential new treatments and technologies within the NHS. It has set a cost-effectiveness threshold of £20–£30,000 per QALY (quality-adjusted life year) gain for appraisal of surgical procedures.

Vascular surgery is a specialty where there has been an ever-expanding introduction of new and often expensive technologies, some of which have not been fully evaluated.

## Varicose veins

Varicose veins affect approximately 25–50% of the adult population,<sup>15</sup> and complications arising from them are a significant cause of patient morbidity and health service expense.<sup>16</sup>

Symptoms are often vague and non-specific but include aching, discomfort, pruritus and muscle cramps; however, there are more obvious and objective symptoms which include varicose eczema, pigmentation, bleeding and ulceration.<sup>17</sup> Extensive previous work has shown that venous disease significantly impairs QOL.<sup>18–20</sup>

There are widespread misconceptions held by both the general public and primary care physicians with regard to varicose veins. The public fear that there is an increased likelihood of deep vein thrombosis (DVT) and that chronic venous changes are a common cause of limb amputation. However, primary care physicians are often mistaken in believing varicose veins are merely a cosmetic concern and even the skin changes of chronic venous insufficiency (a precursor to ulceration) are inconsequential. Extensive evidence exists to show the outcome of treatment of venous disease, but this requires the use of QOL measures. All forms of venous treatment have been shown to improve QOL.<sup>10,21–26</sup>

## Varicose vein assessment

### CEAP classification

Varicose veins have often been inadequately defined and have variously been described as

being visible subcutaneous veins, to dilated palpable subcutaneous veins generally larger than 3 mm in the upright position. Due to this lack of consensus in the reporting and classification in the published literature, the CEAP (Clinical severity, AEtiology, Anatomy, Pathophysiology) classification for chronic venous disorders was developed in 1994 by an international *ad hoc* committee of the American Venous Forum, endorsed by the Society for Vascular Surgery, and this classification became incorporated into 'Reporting Standards in Venous Disease' in 1995, with further refinements made to it in 2004.<sup>27</sup> This classification has been ubiquitously adopted and so allows more a direct comparison between studied modalities.

This is a clinician-implemented categorization tool. The clinical component indicates disease severity, ranging from zero points, for completely asymptomatic patients, up to six points for active ulcers. The aetiological component denotes the venous disease as congenital, primary or secondary in nature. The anatomic classification pinpoints the veins involved as superficial, deep or perforating. The pathophysiological classification identifies the presence of reflux in the superficial, communicating, or deep systems, as well as the existence of outflow obstruction. The CEAP classification is doctor driven, and highlights the cause of the underlying venous abnormality; however, it is not sensitive enough to track progressive changes.

### Venous clinical severity score

The venous clinical severity score (VCSS) is a clinician-completed tool, which includes nine hallmarks of venous disease, each scored on a severity scale from 0 to 3. In order to generate a dynamic score, VCSS categories are scored individually. These include skin changes and pigmentation, inflammation and induration, and ulcers (including number, size and duration). In 2007, an international *ad hoc* working group was created to revise the VCSS to update the terminology, simplify the application and clarify ambiguities, which was completed in 2010.<sup>28</sup>

The value of the VCSS is its ease of use along with an emphasis on the most severe manifestations of venous disease which are likely to show the greatest response to therapy allowing tracking and quantification of improvement (or deterioration).

### Aberdeen varicose vein questionnaire

The Aberdeen varicose vein questionnaire is a 13-question patient-completed survey addressing multiple elements of varicose vein disease, first

developed in 1993.<sup>29</sup> It has subsequently been translated into many languages.

Physical symptoms along with social issues, including pain, ankle oedema, ulcers, compression therapy use and limitations on daily activities are examined, as well as the cosmetic effect of varicose veins. The questionnaire is scored from 0 (no effect) to 100 (severe effect).

#### **Short form health survey (SF-36, SF-12, SF-8)**

A widely used and well-validated generic health QOL assessment tool is the short form health survey (QualityMetric, Lincoln, RI, USA), developed over time with questions in physical and mental health. These two categories have been broken down into eight domains that include physical and social functioning, role limitations due to physical or emotional problems, mental health, pain, vitality and health perception. The survey generates a score ranging from 0 to 100, with higher scores indicating better general health perception.

#### **EuroQOL 5 domain**

The EuroQOL 5 domain survey (Euroqol, Rotterdam, The Netherlands) is an alternative validated patient completed generic health QOL questionnaire that measures mobility, self-care, usual activities, pain and anxiety domains. The domains generate a unique QOL outcome between  $-0.594$  and 1 with 1 being perfect health.

It also provides a separate visual analogue scale rendering of global health status, from 0 to 100, with higher scores indicating better health.

### **Treatment of varicose veins**

The treatment of patients with superficial venous reflux has changed in recent years following the widespread acceptance of minimally invasive, endovenous modalities including ultrasound-guided foam sclerotherapy (UGFS), radiofrequency ablation (RFA) and endovenous laser ablation (EVLA).<sup>30,31</sup> All interventions are aimed at principally abolishing truncal reflux and then removing or occluding any incompetent varicosities.

Postal surveys carried out in 2008 and 2009 revealed that most surgeons who performed varicose vein surgery still regularly performed traditional open surgery, but over one-third also offered minimal access techniques either instead of open surgery, or as an adjunct procedure.<sup>32,33</sup> In the UK, an average of 40,000 NHS-funded interventional procedures are completed each year.<sup>34</sup>

### **Compression**

Compression stockings may be employed as a primary treatment for patients with symptomatic varicose veins. They act by providing graduated radial pressure between ankle and knee/thigh, and this along with the calf muscle pump returns venous blood cranially. Stockings are extremely attractive for the cost-conscious initially; however, the need for replacements (4 times per year) and poor compliance greatly reduce their effectiveness.<sup>35</sup> Additionally some patients (37%) still complain of persistent venous symptoms despite stockings.<sup>36</sup>

### **Conventional surgery**

Standard surgery for varicose veins was first described over 100 years ago, and is still considered the gold standard against which other treatment modalities are tested. The results of surgery are good and patients are generally satisfied. Surgery is associated with an improvement in QOL in most patients. However, there is a significant rate of minor complications.<sup>37</sup> Rates of morbidity vary from series to series.<sup>21,22,38</sup>

New techniques that have arisen interrupt the reflux haemodynamics while preserving the long saphenous vein and include the ASVAL and CHIVA techniques.<sup>39,40</sup> These provide minimally invasive treatments performed under tumescent local anaesthesia, and have produced good results. One single-centre series has shown that while CHIVA offers improved recurrence rates compared with open stripping in experienced hands, it has a steep learning curve and can lead to worse outcomes.<sup>41</sup>

### **Endovenous ablation**

In the last decade the introduction of minimally invasive endovenous ablation therapy has revolutionized the treatment of varicose veins.<sup>30</sup>

Three endovenous modalities offer thermal ablation – RFA, EVLA and steam (SVS). RFA and EVLA have 10 years of evidential data, though with rapid advances in technology many series have now been superseded.

Current RFA technology includes the VNUS ClosureFAST catheter and the Olympus CELON RFITT catheter. These offer effective reproducible treatments under local anaesthetic in the outpatient setting.<sup>30,42</sup> Direct comparisons with laser ablation have shown an equivalent efficacy with a reduced side-effect profile.<sup>22,24,43</sup>

Laser treatment has expanded from the original 810 nm wavelength laser to a wealth of different wavelengths, with different treatment profiles.<sup>30,31</sup> These different wavelengths offer a flexibility of treatment not found in other endovenous modalities.<sup>44,45</sup>

Steam is a new technology of thermal ablation, with only limited evidence of proof of concept at present.<sup>46</sup> Puffs of steam provide the energy for thermal denaturing of the long saphenous vein.

New developments include Clarivein mechanochemical ablation and Saphoon cyanoacrylate glue closure. Clarivein has shown encouraging early results of 96.7% closure at six months.<sup>47</sup> This technique of mechanical scarifying of the vein and instillation of liquid sclerotherapy needs no tumescent and so offers a less invasive alternative to thermal ablation. A further option is the Saphoon Venaseal Closure System, which utilizes proprietary glue to seal the vein; however, this has only been described at conference presentations so far.

### Ultrasound-guided foam sclerotherapy

UGFS is an effective and cheap method of chemically ablating incompetent varicosities. It is truly minimally invasive, requiring only a single needle puncture and no catheterization<sup>48</sup> and has been shown to be more effective than conservative therapy with compression.<sup>49</sup> The literature on foam sclerotherapy is extensive and it can provide similar closure rates and significant improvements in QOL outcomes at one year.<sup>22,50</sup> It appears to be more user-dependent than other modalities, though in experienced hands can provide excellent treatment at an unbeatable price.<sup>51</sup> Recurrence, however, can be a problem in some series.<sup>52</sup>

### Cost-effectiveness

Despite being one of the most commonly performed surgical procedures, very few cost-effectiveness evaluations have been calculated. Ratcliffe *et al.*<sup>53</sup> conducted a randomized trial comparing open surgery with conservative management.

The surgical group was a heterogeneous collection of unilateral and bilateral procedures performed under general anaesthesia as a day case, and the conservative group was treated with compression hosiery or bandaging. Not only did they demonstrate that open surgery was cost-effective using £20,000 QALY level, but a third of patients allocated to the conservative group dropped out to undergo surgery before the trial had finished.

The main aim of the REACTIV (Randomized and Economic Assessment of Conservative and Therapeutic Interventions for Varicose Veins) study was to investigate the clinical and cost-effectiveness of varicose vein treatments.<sup>54</sup> Patients were split into three groups:

*Group 1* – minor below knee varicose veins without truncal reflux, randomized to conservative or sclerotherapy treatment,  $n = 34$ ;

*Group 2* – moderate below knee varicose veins with truncal reflux, randomized to standard surgery or sclerotherapy treatment,  $n = 77$ ;

*Group 3* – significant varicose veins above and below the knee with truncal reflux, randomized to conservative treatment or standard surgery,  $n = 246$ .

Once again, a significant number of patients allocated to a conservative management path became dissatisfied and dropped out of the study so that they could undergo surgery. Although numbers were small in some groups, this study demonstrated the economic value in treating patients with symptomatic varicose veins.

Subramonia and Lees performed a study comparing surgery and RFA<sup>55</sup> which incorporated cost analysis into the design.<sup>56</sup> This study randomized 88 patients into RFA (VNUS ClosurePlus™) and conventional surgery (RFA 47, surgery 41) under general anaesthetic. RFA was found to be significantly more expensive (£1276 versus £559); however, the RFA group returned to work an average of one week earlier (10 days versus 18.5 days), at a cost of £6.14 per additional working hour gained. However, this study utilized the VNUS ClosurePlus™ catheter, which is six times slower than the current VNUS ClosureFAST™ catheter (0.05 cm/second versus 0.33 cm/second). The cost difference was due to increased theatre time (83.6 minutes versus 55.7 minutes, additional cost £171.01) and catheter cost (£550).

Gohel *et al.*<sup>57</sup> produced a Markov model to evaluate the cost-effectiveness of traditional and endovenous treatments for patients with primary great saphenous varicose veins. Day-case surgery or endovenous ablation using EVLA or RFA performed as an outpatient were shown to be the most likely cost-effective treatment strategies for patients with primary unilateral great saphenous vein reflux requiring treatment. However day-case traditional surgery was also shown to be below the conventional threshold of the cost-per-QALY in the UK and therefore cost-effective.

Recent work by Rasmussen *et al.*<sup>22</sup> showed equivalence between all available modalities, in a direct comparison trial of 580 legs. All procedures were under local anaesthetic and treatment time was 19–32 minutes. RFA was shown to be associated with less postoperative pain leading to a faster return to work and therefore a better cost-effectiveness analysis compared with open surgery or laser ablation. Catheter costs were EVLA £307 and RFA £371. Foam sclerotherapy remained the cheapest option, but was associated with a significantly higher recurrence rate at one year (16% versus 5–6%).<sup>22</sup>

With a wide range of available treatments and few comparative studies, treatment choices are currently made on the basis of local availability and clinician preference, rather than clinical evidence. All procedures have been shown to be effective at both abolishing reflux and improving QOL.<sup>22,24,52,55,58,59</sup> Additionally, day-case surgery, RFA, EVLA and UGFS have been demonstrated to be cost-effective at the limit of £20,000 per QALY.<sup>57</sup>

## Patient preference

With the evolution of a patient-centred model of health care, the preferences of the patient must be one of the major contributors to the treatment plan. Varicose veins have many options and these should all be offered to patients with appropriate guidance before a definitive plan is agreed. Recent studies show that while patients felt unable to access modalities formally, they had significant preferences for local anaesthetic and one sitting treatment,<sup>60</sup> though expectations need to be managed prospectively to avoid patient disappointment.<sup>61</sup>

## Conclusion

Varicose veins have a multitude of treatment options, all of which provide excellent improvements in QOL at a cost-effective level. Overall costs have fallen dramatically despite material requirements, and no patient should be without a treatment option. The treatment of varicose veins is one of the few treatments that offer low morbidity for large improvements in QOL. Importantly, despite the higher incidence of varicose veins in older patients, a high percentage of patients are of working age when health improvements are most cost-effective.

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## References

- 1 HM Treasury. *HM Treasury Budget 2011*. HM Treasury, The Stationery Office Publications, London, 2011
- 2 US Government Spending [Internet]. See <http://www.usgovernmentspending.com/> (last checked 14 December 2011)
- 3 Przywara B. Projecting future health-care expenditure at European level: drivers, methodology and main results. *Eur Commission Econ Papers* 2010;**417**:1–85
- 4 Oksanen H. Saving in an ageing society with public pensions: implications from lifecycle analysis. *Eur Commission Econ Papers* 2009;**370**:1–31
- 5 Kanwar A, Hansrani M, Lees T, Stansby G. Trends in varicose vein therapy in England: radical changes in the last decade. *Ann R Coll Surg Engl* 2010;**92**:341–6
- 6 Audit Commission. *Reducing Spending on Low Clinical Value Treatments* [Internet]. London: Audit Commission, 2011. See <http://www.audit-commission.gov.uk/sitecollectiondocuments/downloads/20110414reducingexpenditure.pdf> (last checked 1 December 2011)
- 7 Beattie DK, Golledge J, Greenhalgh RM, Davies AH. Quality of life assessment in vascular disease: towards a consensus. *Eur J Vasc Endovasc Surg* 1997;**13**:9–13
- 8 Ratcliffe J, Brazier J, Palfreyman S, Michaels J. A comparison of patient and population values for health states in varicose veins patients. *Health Econ* 2007;**16**:395–405
- 9 Callam MJ. Epidemiology of varicose veins. *BJS* 1994;**81**:167–73
- 10 Carradice D, Mazari FAK, Samuel N, Allgar V, Hatfield J, Chetter IC. Modelling the effect of venous disease on quality of life. *BJS* 2011;**98**:1089–98
- 11 Brazier J, Walters S, Nicholl J. Using the SF-36 and Euroqol on an elderly population. *Qual Life Res* 1996;**5**:195–204
- 12 Romney DM, Evans DR. Toward a general model of health-related quality of life. *Qual Life Res* 1996;**5**:235–41
- 13 Gudex C, Dolan P, Kind P, Williams A. Health state valuations from the general public using the visual analogue scale. *Qual Life Res* 1996;**5**:521–31
- 14 Dolan P, Gudex C, Kind P, Williams A. Valuing health states: a comparison of methods. *J Health Econ* 1996;**15**:209–31
- 15 Maurins U, Hoffmann BH, Löscher C, Jöckel K-H, Rabe E, Pannier F. Distribution and prevalence of reflux in the superficial and deep venous system in the general population – results from the Bonn Vein Study, Germany. *J Vasc Surg* 2008;**48**:680–7
- 16 Rabe E, Pannier F. Societal costs of chronic venous disease in CEAP C4, C5, C6 disease. *Phlebology* 2010;**25**(Suppl 1):64–7
- 17 Raju S, Neglén P. Clinical practice. Chronic venous insufficiency and varicose veins. *N Engl J Med* 2009;**360**:2319–27
- 18 Smith JJ, Garratt AM, Guest M, Greenhalgh RM, Davies AH. Evaluating and improving health-related quality of life in patients with varicose veins. *J Vasc Surg* 1999;**30**:710–9
- 19 Franks PJ, Wright DD, Fletcher AE, *et al.* A questionnaire to assess risk factors, quality of life, and use of health resources in patients with venous disease. *Eur J Surg* 1992;**158**:149–55
- 20 Smith JJ, Guest MG, Greenhalgh RM, Davies AH. Measuring the quality of life in patients with venous ulcers. *J Vasc Surg* 2000;**31**:642–9

- 21 Carradice D, Mekako AI, Mazari FAK, Samuel N, Hatfield J, Chetter IC. Clinical and technical outcomes from a randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. *BJS* 2011;**98**:1117–23
- 22 Rasmussen LH, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklöf B. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. *BJS* 2011;**98**:1079–87
- 23 Shepherd AC, Gohel MS, Lim CS, Davies AH. A study to compare disease-specific quality of life with clinical anatomical and hemodynamic assessments in patients with varicose veins. *J Vasc Surg* 2011;**53**:374–82
- 24 Shepherd AC, Gohel MS, Brown LC, Metcalfe MJ, Hamish M, Davies AH. Randomized clinical trial of VNUS ClosureFAST radiofrequency ablation versus laser for varicose veins. *BJS* 2010;**97**:810–8
- 25 Vasquez MA, Munschauer CE. Venous Clinical Severity Score and quality-of-life assessment tools: application to vein practice. *Phlebology* 2008;**23**:259–75
- 26 Darvall KAL, Sam RC, Bate GR, Silverman SH, Adam DJ, Bradbury AW. Changes in health-related quality of life after ultrasound-guided foam sclerotherapy for great and small saphenous varicose veins. *J Vasc Surg* 2010;**51**:913–20
- 27 Eklof B, Rutherford RB, Bergan JJ, *et al.* Revision of the CEAP classification for chronic venous disorders: consensus statement. *J Vasc Surg* 2004;**40**:1248–52
- 28 Vasquez MA, Rabe E, McLafferty RB, *et al.* Revision of the venous clinical severity score: venous outcomes consensus statement: special communication of the American Venous Forum Ad Hoc Outcomes Working Group. *J Vasc Surg* 2010;**52**:1387–96
- 29 Garratt AM, Macdonald LM, Ruta DA, Russell IT, Buckingham JK, Krukowski ZH. Towards measurement of outcome for patients with varicose veins. *Qual Health Care* 1993;**2**:5–10
- 30 Lane TRA, Pandey VA, Davies AH. Superficial venous disease treatment – is there still a role for open surgery in 2011? *Acta Chir Belg* 2011;**111**:125–9
- 31 Boezem PBVD, Klem TMAL, d’Armandville ELC, Wittens CHA. The management of superficial venous incompetence. *BMJ* 2011;**343**:d4489
- 32 Winterborn RJ, Corbett CRR. Treatment of varicose veins: the present and the future – a questionnaire survey. *Ann R Coll Surg Engl* 2008;**90**:561–4
- 33 Edwards AG, Baynham S, Lees T, Mitchell DC. Management of varicose veins: a survey of current practice by members of the Vascular Society of Great Britain and Ireland. *Ann R Coll Surg Engl* 2009;**91**:77–80
- 34 Lim CS, Gohel MS, Shepherd AC, Davies AH. Secondary care treatment of patients with varicose veins in National Health Service England: at least how it appeared on a National Health Service website. *Phlebology* 2010;**25**:184–9
- 35 Ziaja D, Kocelak P, Chudek J, Ziaja K. Compliance with compression stockings in patients with chronic venous disorders. *Phlebology* 2011;**26**:353–60
- 36 Palfreyman SJ, Michaels JA. A systematic review of compression hosiery for uncomplicated varicose veins. *Phlebology* 2009;**24**(Suppl 1):13–33
- 37 Subramonia S, Lees T. Sensory abnormalities and bruising after long saphenous vein stripping: impact on short-term quality of life. *J Vasc Surg* 2005;**42**:510–4
- 38 Nesbitt C, Eiffel RK, Coyne P, Badri H, Bhattacharya V, Stansby G. Endovenous ablation (radiofrequency and laser) and foam sclerotherapy versus conventional surgery for great saphenous vein varices. *Cochrane Database Syst Rev* 2011;**(10)**:CD005624
- 39 Pittaluga P, Chastanet S, Rea B, Barbe R. Midterm results of the surgical treatment of varices by phlebectomy with conservation of a refluxing saphenous vein. *J Vasc Surg* 2009;**50**:107–18
- 40 Parés JO, Juan J, Tellez R, *et al.* Varicose vein surgery: stripping versus the CHIVA method: a randomized controlled trial. *Ann Surg* 2010;**251**:624–31
- 41 Milone M, Salvatore G, Maietta P, Sosa Fernandez LM, Milone F. Recurrent varicose veins of the lower limbs after surgery. role of surgical technique (stripping vs. CHIVA) and surgeon’s experience. *G Chir* 2011;**32**:460–3
- 42 Boon R, Akkersdijk GJM, Nio D. Percutaneous treatment of varicose veins with bipolar radiofrequency ablation. *Eur J Radiol* 2010;**75**:43–7
- 43 Almeida JI, Kaufman J, Göckeritz O, *et al.* Radiofrequency endovenous ClosureFAST versus laser ablation for the treatment of great saphenous reflux: a multicenter, single-blinded, randomized study (RECOVERY study). *JVIR* 2009;**20**:752–9
- 44 Proebstle TM, Moehler T, Gül D, Herdemann S. Endovenous treatment of the great saphenous vein using a 1,320 nm Nd:YAG laser causes fewer side effects than using a 940 nm diode laser. *Dermatol Surg* 2005;**31**:1678–83; discussion 1683–4
- 45 Doganci S, Demirkilic U. Comparison of 980 nm laser and bare-tip fibre with 1470 nm laser and radial fibre in the treatment of great saphenous vein varicosities: a prospective randomized clinical trial. *Eur J Vasc Endovasc Surg* 2010;**40**:254–9
- 46 Van Den Bos RR, Milleret R, Neumann M, Nijsten T. Proof-of-principle study of steam ablation as novel thermal therapy for saphenous varicose veins. *J Vasc Surg* 2011;**53**:181–6
- 47 Elias S, Raines JK. Mechanochemical tumescentless endovenous ablation: final results of the initial clinical trial. *Phlebology* 2011 in press [Epub ahead of print 29/07/2011]
- 48 Bergan J. Sclerotherapy: a truly minimally invasive technique. *Perspect Vasc Surg Endovasc Ther* 2008;**20**:70–2
- 49 Schul MW, Eaton T, Erdman B. Compression versus sclerotherapy for patients with isolated refluxing reticular veins and telangiectasia: a randomized trial comparing quality-of-life outcomes. *Phlebology* 2011;**26**:148–56
- 50 Darvall KAL, Bate GR, Adam DJ, Silverman SH, Bradbury AW. Duplex ultrasound outcomes following ultrasound-guided foam sclerotherapy of symptomatic primary great saphenous varicose veins. *Eur J Vasc Endovasc Surg* 2010;**40**:534–9
- 51 Darvall KAL, Bate GR, Adam DJ, Silverman SH, Bradbury AW. Duplex ultrasound outcomes following ultrasound-guided foam sclerotherapy of symptomatic recurrent great saphenous varicose veins. *Eur J Vasc Endovasc Surg* 2011;**42**:107–14
- 52 van den Bos R, Arends L, Kockaert M, Neumann M, Nijsten T. Endovenous therapies of lower extremity varicosities: a meta-analysis. *J Vasc Surg* 2009;**49**:230–9
- 53 Ratcliffe J, Brazier JE, Campbell WB, Palfreyman S, MacIntyre JB, Michaels JA. Cost-effectiveness analysis of surgery versus conservative treatment for uncomplicated varicose veins in a randomized clinical trial. *BJS* 2006;**93**:182–6

- 54 Michaels JA, Campbell WB, Brazier JE, *et al.* Randomized clinical trial, observational study and assessment of cost-effectiveness of the treatment of varicose veins (REACTIV trial). *Health Technol Assess* 2006;**10**:1–196, iii–iv
- 55 Subramonia S, Lees T. Randomized clinical trial of radiofrequency ablation or conventional high ligation and stripping for great saphenous varicose veins. *BJS* 2010;**97**:328–36
- 56 Subramonia S, Lees T. Radiofrequency ablation vs. conventional surgery for varicose veins – a comparison of treatment costs in a randomized trial. *Eur J Vasc Endovasc Surg* 2010;**39**:104–11
- 57 Gohel MS, Epstein DM, Davies AH. Cost-effectiveness of traditional and endovenous treatments for varicose veins. *BJS* 2010;**97**:1815–23; discussion 1823–4
- 58 Nesbitt C, Wilson WRW, Lees TA, Stansby G. Interpretation of patient-reported outcome measures for varicose vein surgery. *Phlebology* 2011 in press [Epub ahead of print 21/09/2011]
- 59 Carradice D, Mekako AI, Mazari FAK, Samuel N, Hatfield J, Chetter IC. Randomized clinical trial of endovenous laser ablation compared with conventional surgery for great saphenous varicose veins. *BJS* 2011;**98**:501–10
- 60 Shepherd AC, Gohel MS, Lim CS, Hamish M, Davies AH. The treatment of varicose veins: an investigation of patient preferences and expectations. *Phlebology* 2010;**25**:54–65
- 61 Darvall KAL, Bate GR, Sam RC, Adam DJ, Silverman SH, Bradbury AW. Patients' expectations before and satisfaction after ultrasound-guided foam sclerotherapy for varicose veins. *Eur J Vasc Endovasc Surg* 2009;**38**:642–7