

**CHRONIC VENOUS  
DISEASES OF THE LEG**

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## Introduction

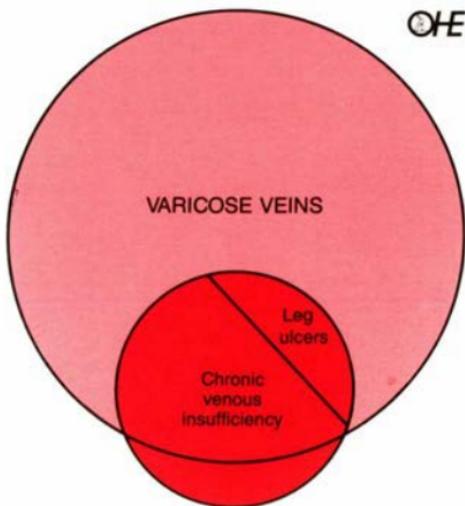
This report is about varicose veins and the range of venous diseases of the legs, including chronic venous insufficiency (CVI) and venous ulcers, that people with varicose veins are prone to develop. It collates information on the prevalence of these conditions, focusing on European populations, and presents estimates of their economic cost in five European countries, Britain, France, Germany, Italy and Spain. It reviews the benefits and risks of alternative treatments and highlights the potential for innovations in organising health services for people with venous diseases.

Venous diseases of the legs can be grouped into three broad entities which are, in ascending order of severity, varicose veins, CVI and venous ulcers of the leg. Figure 1 shows how they relate to each other.

### Varicose veins

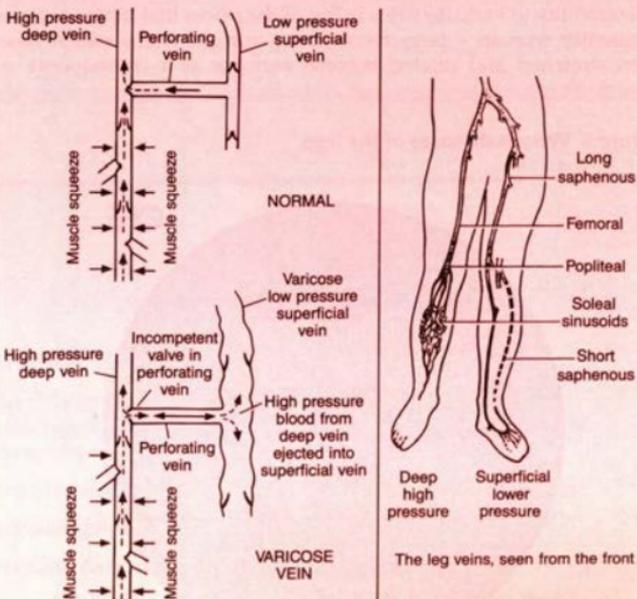
Vulnerability to varicose veins is one of the prices that man – or more frequently woman – pays for walking upright. Veins which have been stretched and dilated become varicose as a consequence of

Figure 1 Venous diseases of the legs



**BOX 1**

Man, as an upright biped, is a late evolutionary development. The force generated by man's heart cannot, unassisted, overcome the forces of gravity and drive the blood from the toes to the brain. A supplementary mechanism has evolved in which the muscles of the legs, when they contract, squeeze the deep veins and propel blood upwards. Downward flow is prevented by the presence of valves in the deep veins. In addition to the deep veins of the legs, which are surrounded by muscle and operate at high pressure in the muscles' contracting phase, there are also superficial veins of the legs which are embedded in the fatty tissue which surrounds the muscles. These are not squeezed and hence operate under lower pressure. The superficial and deep veins are connected at a number of points by perforating veins, which carry blood from the superficial to the deep compartment. Where they meet the deep veins, reverse flow is prevented by one way valves. Should these perforating vein valves fail, blood from the deep vein system is ejected at high pressure into superficial veins. This causes superficial veins to become congested and dilate, leading to the appearance of varicose veins close to the surface of the skin.



*Note:* The drawing of the deep and superficial leg veins is taken from 'The Oxford Companion to Medicine' edited by John Walton, Paul Beeson and Ronald Bodley Scott for the Oxford University Press, 1986.

incompetence or, rarely, the absence of valves of the vein, see Box 1. There are three sites where veins in man have a particular tendency to become varicose. These are at the lower end of the bowel, causing haemorrhoids, at the testicle, causing varicocele, and at the great saphenous vein and its branches on the inner side of the leg, knee and thigh. Animals which do not walk upright have no such predisposition to varicose veins. Foote (1960) made exhaustive enquiries but was unable to trace evidence of varicose veins in any quadruped.

Varicose veins are a very common condition, affecting about 50 per cent of the population in developed countries to some degree. In about two thirds of cases the condition is medically insignificant; that is, it may be diagnosed on clinical examination, but those affected do not consider it sufficiently important to mention it spontaneously in health questionnaires.

For the remaining third (approximately), varicose veins *do* present a significant medical problem – giving rise, in addition to their unsightliness, to physical symptoms of heaviness and aching in the limbs, sometimes accompanied by cramps. The effect on individuals' wellbeing tends to be underestimated. There have been few good studies of subjective perceptions of health, but one such British study which dealt specifically with peripheral vascular disease concluded that quality of life is much impaired (Hunt et al, 1982).

Moreover, varicose veins can be a progressive condition. Once a vein has started to dilate its walls become weak and its valves incompetent. The weight of blood pressing down tends to dilate the vein further and thus render other valves incompetent.

A minority of people with varicose veins develop chronic venous insufficiency, which can in turn lead to inflammation and eczema and ultimately – for a small but costly (in medical resources) part of the population – to venous ulcers of the leg.

### **Chronic venous insufficiency**

Chronic venous insufficiency (CVI) arises from a variety of causes, including deep vein thrombosis resulting in the post-thrombotic condition. Most frequently, however, CVI originates from the same underlying cause as varicose veins, that is incompetence of the valves in the perforator veins (or from their congenital absence).

These conditions allow the passage of high pressure blood during the contracting phase of the muscle pump from the deep compartment to the superficial compartment, causing an impulse which the superficial veins cannot withstand. This venous hypertension creates a disequilibrium at the level of the microvascular bed, thereby inducing capillary stretching with an increase in microvascular permeability and reduction in fluid resorption at the venular side of the microvascular bed. Accumulation of fluid in the pericapillary tissues leads to oedema

and symptoms which may include tired and heavy legs, swelling sensations, night cramps, restless legs, and paraesthesia.

Leakage of proteins into the extravascular tissue also induces an inflammatory process, reflected clinically as eczema, dermatitis, lipodermatosclerosis and a reduction of oxygen diffusion to the pericapillary tissues, while the passage of red blood cells outside the capillaries induces pigmentation.

### **Venous ulcers of the leg**

The end result of these processes, for a small but significant proportion of the population, is venous ulceration of the legs. Venous ulcers often develop as a result of scratching of the skin of a leg which has been rendered eczematous by CVI. They are frequently resistant to healing – though high healing rates have been demonstrated for newer methods of compression bandaging described below. They have a tendency to develop into callous ulcers where the edge is thick and hard, the colour pale and the discharge thin and light, though often offensive in smell.

## Prevalence of varicose veins, CVI and venous ulcers

Results of nineteen studies of the prevalence of venous diseases of the legs in Europe, the USA and New Zealand have been collated and analysed by Golden (1988). The best known is the large scale, in depth survey of cardiovascular disease among employees of the Basle chemical companies reported by Widmer and others (Widmer et al, 1977 and 1981; Widmer, 1978; Widmer and Biland, 1984). Because of its rigorous attention to detail (including a specific phlebologic examination with questionnaire, clinical examination and colour photographs of the legs) the diagnostic framework adopted by the Basle survey offers a suitable reference to which other studies of the prevalence of venous diseases of the legs can be compared, Table 1.

Table 1 Prevalence of venous diseases of the legs among male employees of Basle chemical companies, 1971-73

	<i>% of male subjects in Basle study</i>
'varicose disorders': ie reticular varicose veins or hyphen webs only or mild trunk varicose veins	44%
'varicose disease' or 'significant varicosity': pronounced trunk varicose veins or a combination of pronounced reticular varicose veins plus hyphen webs – but with little or no sign of CVI.	9%
'pathological' varicose veins with pronounced CVI	3%
Total (with some degree of varicosis)	56%

Source: Widmer et al, 1977 and 1981; Widmer, 1978; Widmer and Biland, 1984.

### Disorder or disease?

To what extent do varicose veins and other venous conditions of the legs represent a medical problem? Fifty-six per cent of male employees examined in the Basle study were found to have some degree of varicosity, but in the great majority of cases (44 percentage points) the condition was not considered by the investigators to be of sufficient clinical significance to merit medical intervention. A substantial minority, however, (the remaining 12 per cent) were classified as having 'severe' varicose veins of clinical importance, that is sufficiently severe to justify medical treatment. Severe varicose veins were further subdivided into 'relevant' varicose veins (with little sign of CVI – 9 per cent) and 'pathological' varicose veins (with pronounced CVI – 3 per cent).

Most other studies of employees give a somewhat lower prevalence than the Basle study, averaging approximately 45 per cent for all types of varicose veins and about 10 per cent for 'severe' varicose veins (Lake et al, 1942; Mekky et al, 1969; Guberan et al, 1973; Cassio et al, 1977; Giebler, 1986). However, because venous disease is more frequent among older age groups, and because it can prevent people from working, neither the Basle study nor other studies of working populations only provide a good measure of the prevalence of venous diseases among the population as a whole.

### **Prevalence in the general population**

Table 2 presents results from those studies in Anglo-Saxon and European countries which have been based on samples of the general population. At first sight, there appear to be wide variations in prevalence rates obtained. But these variations can be explained by differences in the age and sex of the populations studied and the survey techniques used. In particular, a distinction needs to be drawn between three early studies (Arnoldi, 1958; Bobek, 1966; Cepelak, 1970), based on patient responses to a questionnaire, and later, more complete studies including a clinical examination. Most subjects spontaneously report varicose veins only if they are relatively severe and this explains why prevalence as measured by questionnaire averages only 21 per cent – which is close to the average figure of 19 per cent for 'severe' varicose veins found by clinical examination of samples of the general population. Other reasons for variation in prevalence levels include the age and sex composition of the sample (venous disorders are increasingly prevalent with age and more common among women than men) and whether or not individuals in institutional care are included (they are typically old and frail with high frequencies of severe and disabling diseases of all types).

Finally, studies based on patient samples (hospital or GP) in France and Germany yield figures comparable to the general population. Ocelli and Langle (1970) and Eberth-Willerhausen (1984) found prevalence of 47 per cent for all varicose veins and approximately 20 per cent for severe varicose veins. Similarly, a study of patients attending a university health centre in Brazil found varicose veins of any grade in 48 per cent of cases and moderate to severe varicose veins among 21 per cent (Maffei et al, 1986).

### **Chronic venous insufficiency**

The seven general population studies which reported on CVI found prevalences varying from 3 per cent to 13 per cent, with an average around 6 per cent. The wide variation can be explained by differing criteria, often inadequately explained by the authors. At the time that

**Table 2 Prevalence of venous diseases of the legs of different degrees of severity among general population samples in industrialised countries**

<i>Study</i>	<i>Country</i>	<i>All degrees of varicose veins</i>	<i>Minor varicose veins</i>	<i>Severe varicose veins (clinically relevant)</i>	<i>CVI (skin changes)</i>	<i>Ulcers</i>
		%	%	%	%	%
Arnoldi	Denmark	29				3.9 ulcer history
Bobek	Czechoslovakia	11			3	1 ulcer history
Weddell	UK	46	35	11	3	1 active ulcers
Cepelak	Czechoslovakia	23 <sup>a</sup> 73 <sup>b</sup>	39	34		
Hackel	E Germany			18	2	
Coon	USA	20	8	12	3	0.2 ulcer history
Beaglehole	New Zealand	38	18	20		
Winkler	E Germany	58	35	23	10	4.5 ulcer history
Fischer	W Germany	86	58	28	13	2.7 ulcer history
Callam	UK	-	-	-	-	0.44 active ulcers
Cornwall	UK	-	-	-	-	0.15 active ulcers
Nelzen	Sweden	-	-	-	-	0.18 active ulcers
Henry	Eire	-	-	-	-	0.3 active ulcers (inc. non-venous)
						1.5 self diagnosis household survey

<sup>a</sup>questionnaire <sup>b</sup>clinical examination

Sources: Arnoldi (1958); Bobek et al (1966), Weddell (1966), Cepelak et al (1970), Hackel et al (1974), Coon et al (1973), Beaglehole et al (1976), Winkler et al (1980), Fischer (1989), Callam (1985), Cornwall (1986), Nelzén et al (1990), Henry (1986).

most of the studies were conducted, skin changes were used as a marker for CVI, in the absence of any objective test of venous function such as now exists with Doppler ultrasound. Subjective, visual tests are likely to underestimate the prevalence of CVI because many patients without skin changes, or even visible varicose veins, suffer from a degree of venous incompetence (Franks et al, 1989).

The end result of CVI may be venous ulcers of the leg, which represent the most serious and costly complication of venous disease. Data from the final phase of the Basle survey (Basle III) show that 21 per cent of people with pronounced CVI have leg ulcers (compared with 1 per cent of those with 'severe' varicose disease but little sign of CVI).

### **Venous ulcers of the leg**

Not all leg ulcers are venous. Some are of arterial origin – requiring entirely different treatment – and some are associated with diabetes. The great majority, however, are of venous origin.

Callam et al (1985) has suggested that about 20-25 per cent of venous ulcers are active (*ie* open) at any one time. Thus figures for 'active' ulcers should be raised by a factor of four or five to give an estimate of patients with a history of ulcers. Taking this into account, the general population studies listed in Table 2 indicate that about half a per cent of people have active ulcers at any one time and about 2 per cent have a history of venous ulceration.

Callam et al (1987) have described the natural history of venous ulcers using data from a longitudinal survey of 600 patients with leg ulcers (81 per cent of venous origin) in Scotland.

They show that ulcers can recur over long periods of time. Thus 45 per cent of patients surveyed had a history of venous ulceration stretching back more than 10 years. Two thirds of patients had at least one recurrence and one third had more than 3 recurrences.

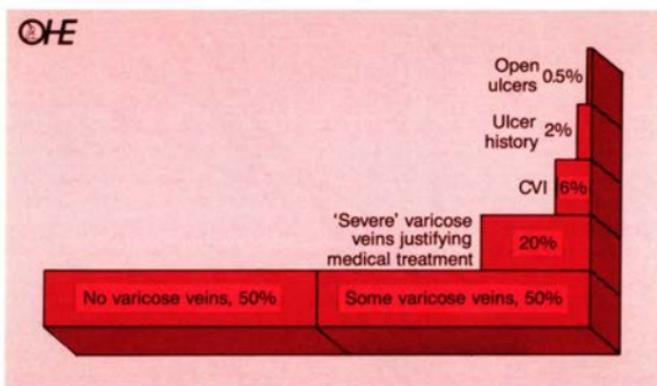
Venous ulcers are often resistant to healing. The mean duration of a single ulcer episode in Callam's sample was 9 months and 20 per cent of episodes lasted for more than 2 years without healing.

Venous ulcers are more common among elderly people but they are by no means confined to the elderly population. In the majority (66 per cent) of cases surveyed by Callam, the age of onset was below 65 years.

### **Summary of prevalence in developed western countries**

The prevalence data set out above is summarised in Figure 2. About half of the population of developed countries have some degree of varicosis, usually medically insignificant. About 20 per cent have varicose veins which justify medical intervention, about 6 per cent have CVI and, at the most severe and costly end of the spectrum, about 0.5 per cent have active venous ulcers.

Figure 2 Prevalence of varicose veins, chronic venous insufficiency and venous ulcers of the legs in developed western countries



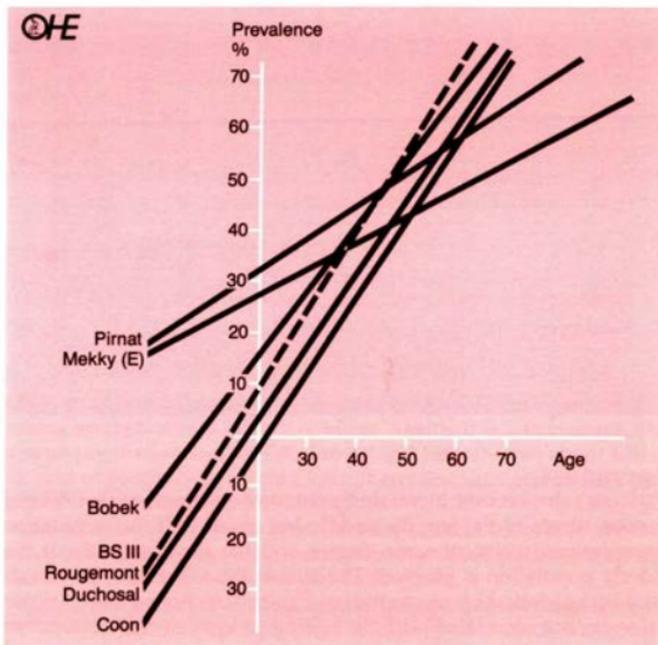
### Age and sex

Varicose veins become increasingly common with age, as do CVI and venous ulcers of the leg. By middle age about half the population have varicose veins of some degree and the great majority of the elderly population is affected. The almost linear increase in prevalence by age found by most studies, Figure 3, indicates that varicose veins are not associated with the ageing process as such, but rather with the cumulative effects over time of stresses to which the veins of the legs are subjected.

At the most severe end of the spectrum of venous diseases, the Skaraborg county leg and foot ulcer survey carried out in Sweden in 1988 ((Nelzén et al, 1990) found a point prevalence of 0.3 per cent for active varicose ulcers for the population as a whole, with a peak of 3 per cent for 80-89 year olds and 4 per cent for people over 90. This particular study included residents of long stay institutions where prevalence of leg ulcers is probably at its highest.

The female/male differential in frequency of varicose veins is less than is commonly supposed. The final phase of the Basle study (Basle III) found a prevalence of 61 per cent in females and 56 per cent in males, with an age range of 30-70 years. Other studies, on average, indicate a female/male prevalence ratio of about 1.5:1 for varicose veins. More severe venous disease is more common among women, for example varicose veins associated with pregnancy. But at least part of the perception of markedly higher rates in women is

Figure 3 Correlation of varicose veins prevalence with age in females



Among women, the correlation of varicose veins of all types and degrees with age is almost linear. A high regression coefficient of approximately 0.5 was observed by Bobek et al (1966), Coon et al (1973), Duchosal et al (1968), Widmer et al (1981) and a lower one by Pirnat (1970) and Mekky et al (1969).

Source: Reproduced from Madar, G et al (1986) *Varicose veins and chronic venous insufficiency: disorder or disease?* VASA 15 (2), 126-134.

due to the very high prevalence in old age and the preponderance of women in the elderly population.

Similarly, the impression of a markedly higher frequency of venous ulcers among women is not wholly borne out by prevalence studies. The Skaraborg county leg and foot ulcer study found an age adjusted female/male sex ratio of 1.4:1.

### International variations in prevalence of venous diseases of the legs

The range of prevalences found in different parts of the developed and developing world, according to Beaglehole (1986), is set out in Table 3.

In contrast to the high prevalence found among populations of industrialised countries, varicose veins appear relatively rare in Africa, Asia and most of the remainder of the developing world, even when the condition is specifically sought in patient or population studies (Burkitt, 1976).

Mekky et al (1969) reported a prevalence of 32 per cent among European cotton workers in contrast with 6 per cent among Egyptians in the same occupation. Banjo (1987) has reported a very low prevalence, just 0.12 per cent of a sample of 2340 Nigerian patients, and cites a maximum of 1-2 per cent in other studies of central Africans. Banjo attributes low prevalence in central Africa to a combination of factors including the higher number of valves found (on dissection) in African veins. He also cites the absence of a constipating diet (which in the developed world leads to straining and abnormal pressure on the valves of veins) and the absence of chronic bronchitic coughs, which also transmit abnormal pressure to valves in many industrialised populations.

In the Indian sub continent, Malhotra (1972) has reported prevalence of varicose veins among male railroad workers at 25 per cent in the south of India and 7 per cent in the north of India.

Table 3 Variations in the prevalence of varicose veins in adults

	Men %	Women %
New Zealand Maori	33	44
New Zealand Non-Maori	20	38
Cook Island Rarotonga	16	15
Cook Island Pukapuka	2	4
Tokelau Island	3	1
Israel	10	30
England	-	32
Egypt	-	6
Wales	37	53
United States	19	36
New Guinea	5	0.1
India - south	25	-
India - north	7	-

Sources: Beaglehole (1975), Abramson et al (1981), Mekky et al (1969), Weddell (1966), Coon et al (1973), Stanhope (1975), Malhotra (1972).

In Japan, the prevalence of varicose veins in women appears to be intermediate between Europe and developing countries. Hirai et al's (1990) study of 541 Japanese women used criteria similar to the Basle II study in Switzerland, counting all dilated, tortuous and elongated veins, however minor, and found a prevalence of 45 per cent. Age specific data showed a prevalence of 14 per cent among Japanese women aged 20-29 years compared with 25 per cent for the same age group in Switzerland. For the 60-69 age group, the prevalence was 69 per cent and 80 per cent respectively in Japan and Switzerland.

## **Causes of venous diseases of the legs**

At one level, the cause of varicose veins is well known to be the incompetence or absence of valves in the veins of the legs. But this begs the question, which is still not answered, of why this should happen in some individuals and populations and not in others. A recent paper by Franks et al (1989) has reviewed the evidence for various factors believed to be aetiologically important.

### **Heredity**

It has been shown by Matousek and Prerovski (1974) and Hauge and Gundersen (1969) that the predisposition to varicose veins is inherited. The Tubingen study in Germany (Fischer, 1981) found the risk of venous disease was doubled for people with a relative with the condition. A specific, though rare example of inheritance is congenital varicosity, caused by the congenital absence of venous valves (Sabiston, 1972). More generally, the thickness of vein walls and the number and position of vein valves varies greatly among individuals and the tendency for varicose veins to run in families may be due to inherited weakness of vein walls and low number of venous valves. Different racial groups also appear to vary in their vulnerability to varicose veins (see below). One recent hypothesis (Haardt, 1987) is that varicose veins may result mainly from genetically inherited enzyme defects responsible for collagen disruption and smooth muscle weakness in the vein wall.

### **Weight and height**

Franks et al (1989) cite a number of reports showing a positive relationship between body weight and varicose veins. In the Tubingen study, Fischer (1981) found a 20 per cent excess of varicose veins among patients classified as obese. The Framingham study also found that obesity was a positive risk factor in women, though not in

men (Brand et al, 1988). Height has been investigated in two studies and both found a positive relationship with varicose veins (Abramson et al, 1981; Beaglehole et al, 1976).

### **Pregnancy**

Pregnancy has long been recognised as a risk factor for varicose veins. The Tubingen study (Fischer, 1981), for example, found a doubling of risk in women with two or more pregnancies. However, varicose veins associated with pregnancy may be transient.

### **Occupation**

Textbook treatments of varicose veins stress the importance of occupational factors, with increased prevalence among people who stand for long periods of time without muscular exertion, for example barbers, barmaids, shop assistants and waitresses. The posited explanation is that the standing position not only places increased pressure on the walls and valves of veins in the leg, but without significant muscular contraction there is little of the ancillary pumping action normally provided by the legs themselves to empty the veins of blood.

### **Restrictive clothing**

Another element of the received wisdom about varicose veins is that restrictive clothing such as garters can be causative. But Geelhoed and Burkitt (1991) maintain that this has been disproved in both developing and developed countries.

### **Environment or race?**

The crucial fact that has to be explained by any theory of causation is why varicose veins are common in the west and rare in most developing countries. To what extent are the differences racial in origin, and to what extent are they environmental? Support for a racial component comes from Banjo's (1986) finding that Africans have more vein valves than Caucasians. Also, Abramson et al (1981) found that North Africans living in Jerusalem had a significantly lower prevalence of varicose veins than other racial groups in Jerusalem. But there is powerful evidence that environmental rather than racial factors predominate. Thus Mekky et al (1969) concluded that in the United States varicose veins are equally common in Negroes and Caucasians. Moreover, equivalence seems to be reached in the space of one or two generations. Another strong piece of evidence comes from work by Beaglehole (1975) who found that prevalence among Polynesians ranged from 3 per cent of men and 1 per cent of women living on Tokelau Island and up to 33 per cent of men and 44 per cent of women Maoris living on the New Zealand mainland.

Geelhoed and Burkitt (1991) suggest that western lifestyle, including components of exercise and diet, is the key to causation. They cite the hypothesis that straining at stool as a consequence of a fibre depleted diet can create abnormally high abdominal pressures, leading to failure of superficial vein valves progressively from above. While not necessarily invoking this abdominal pressure hypothesis, the authors maintain that prevention of varicose veins may be best achieved by the same changes in diet, and lifestyle generally, which are advocated to reduce atherosclerotic cardiovascular disease. What the abdominal pressure hypothesis itself fails to explain, however, is why studies which have investigated the relationship between constipation and varicose vein prevalence have not obtained conclusive results (Franks et al, 1989).

## **Treatment of venous diseases of the legs**

There are four broad groups of therapies for venous diseases of the legs: surgery, compression sclerotherapy, medicines and compression bandages/stockings.

Each has its advantages and disadvantages for particular groups of patients. Table 4 sets out the relative frequency of use of the various therapeutic alternatives among individuals surveyed in the Basle study in the 1960s and 1970s.

Sclerotherapy was the alternative that had most frequently been experienced by individuals in the Basle study – though that was in a period before it had been demonstrated by Chant (1972) and Hobbs (1974) that the excellent early results from sclerotherapy tend not to be sustained in the long term when compared with surgery for the main groups of patients. It is unlikely that a study carried out today would show the same predominance of sclerotherapy. Nevertheless, the Table does give an indication of the relative importance of different treatments in one European country.

Close examination of such evidence as there is on effectiveness and cost effectiveness of alternative therapies reveals more questions than answers. Clinical practices and fashions vary widely from one country to another within Europe and elsewhere and there is seldom incontrovertible evidence that one approach or combination of approaches is better than another. ‘Veno-active’ medicines, for example, are much more frequently used for CVI in France, Germany, Italy and Spain than in Britain and Scandinavian countries, where the alternative of elasticated hosiery is favoured. Because there are often several alternative courses of action, treatment of vari-

**Table 4 Experience of alternative therapies among employees of the Basle chemical industry**

	<i>Patients with 'severe' varicose veins (12% of study population)</i>					
	<i>Patients with all types of varicose veins (56% of study pop.)</i>		<i>'Relevant' varicose veins little sign of CVI (9% of study pop.)</i>		<i>'Pathological' pronounced CVI (3% of study pop.)</i>	
	M %	F %	M %	F %	M %	F %
Diuretics	5	6	na	na	na	na
Veno- active medicines	5	15	8	10	7	20
Bandages/ stockings	4	9	5	11	24	7
Sclero- therapy	7	26	11	22	31	70
Surgery	3	4	4	7	11	11
Combi- nation of above	6	15	3	10	18	29

Source: Widmer, L K (Ed.) (1978) *Peripheral Venous Disorders. Basle Study III*. Hans Huber (Berne, Stuttgart, Vienna).

cose veins is one of the areas of medical practice where doctors' and patients' own preferences for mode of treatment can be particularly important.

### **Surgery – stripping and ligation**

Stripping and ligation of varicose veins is one of the commonest elective operations. It can be conducted as day surgery but requires a general anaesthetic and still typically involves a two or three day stay as a hospital in-patient. The aim of surgery can be twofold, to cure symptoms (aching, heaviness and cramps) and/or to remove unsightly veins for cosmetic purposes. It has not yet been proved that surgery prevents the later development of leg ulcers.

Most cases of varicose veins are relatively minor and surgery may not be justified for either symptomatic or cosmetic reasons. In some countries, in particular those with budget capped healthcare systems like Britain, surgery for varicose veins may be considered a low priority use of scarce resources. Varicose veins is one of the commonest conditions on National Health Service waiting lists and

patients typically find themselves in the 'slow stream' and may wait for several months or, exceptionally, years for treatment – unless they are willing and able to pay privately. A survey conducted by the University of Sheffield Medical School (Nichol et al, 1989) estimated that a total of 52,800 procedures for stripping and ligation of varicose veins were carried out in England and Wales in 1986, representing a frequency of 1.1 procedures per 1000 population per year. 11,900 of the operations (23 per cent) were paid for privately and the remainder were carried out under the NHS. With the increase in private medical insurance since the time of the survey, and the increase in insurance claims rates, it is likely that about one third of stripping and ligation is privately paid in Britain in 1992.

### Vein valve transplantation

In more severe cases of CVI which have progressed to intractable venous ulcer - where stripping and ligation, sclerotherapy and other treatments may already have been tried - valvuloplasty or vein valve transplantation can be effective by repairing the underlying cause of the disease. Rai and Lerner (1991) have recently described a promising variation on vein valve transplantation in which vein valve segments, harvested from the patient himself/herself, are transplanted as close as possible to the symptomatic site. Among a series of 25 patients with severe CVI and ulcers, 15 were found to have valvular incompetence. Of the twelve who underwent valve transplantation, all obtained complete relief of pain, their ulcers healed and they were able to walk once again. Currently, however, this remains a research procedure.

### Compressive sclerotherapy

Compressive sclerotherapy is an alternative to stripping and ligation of varicose veins. A sclerosing substance is injected into the region of the incompetent perforator veins followed by compressive bandaging of the leg, resulting in obliteration of the affected perforator

**Table 5 Comparative results of sclerotherapy and stripping and ligation – Hobbs**

	<i>Compressive sclerotherapy</i>			<i>Surgery</i>		
	<i>1 year</i>	<i>3 years</i>	<i>6 years</i>	<i>1 year</i>	<i>3 years</i>	<i>6 years</i>
Cure*	82	31	7	62	40	22
Improved	17	44	27	33	51	56
Failed	1	25	66	5	9	22

Source: Hobbs (1974).

\*Cure: no recurrence of varicose veins; no symptoms or signs.

veins. This technique is practically painless and does not require anaesthetic but does need several out patient sessions (Chant, 1972). However, though short term results are excellent, there is a higher recurrence rate than with good surgery.

The two classical randomized controlled trials comparing stripping and ligation with sclerotherapy were undertaken in the UK in the late 1960s.

Hobbs (1974) rated 99 per cent of patients given sclerotherapy as 'cured' or 'improved' at one year. After 6 years follow up, however, the sclerotherapy success rate had fallen to 34 per cent compared with 78 per cent for stripping and ligation, Table 5, despite repeat courses of sclerotherapy during the follow up period.

Closer analysis of Hobbs's results, however, reveals two sub groups of patient. For those with long varicose veins or short saphenous varicose veins (61 per cent of the patients in the trial) surgery gave better results, though about 35 per cent required additional minor sclerotherapy. For those with trivial cosmetic veins, dilated superficial veins, lower leg perforators and those with post-thrombotic syndrome (the remaining 39 per cent of patients) compressive sclerotherapy gave better results.

The trial reported by Chant (1972) gave similar long term results (Table 6). At the end of 5 years follow up the results of surgery were clearly superior to sclerotherapy, for the patient sample as a whole, though patient preference at the outset was for sclerotherapy because of its perceived convenience. In the light of these results, stripping and ligation is usually the preferred surgical procedure, where indicated, though scleropathy is frequently used as a 'tidying up' adjunct.

**Table 6 Comparative results of sclerotherapy and stripping and ligation – Chant**

	<i>Compressive sclerotherapy</i>		<i>Surgery</i>	
	<i>3 years %</i>	<i>5 years %</i>	<i>3 years %</i>	<i>5 years %</i>
No further treatment required	78	51	86	70
Required support stockings	9	18	11	12
Required further treatment	13	22	3	12
Lost to follow up	–	–	9	6

Source: Chant (1972).

More recent surgical innovations have aimed at developing effective procedures which can be carried out on an out-patient basis. Belcaro et al (1991) have reported results of a randomized trial comparing compression sclerotherapy, the 'dentist's technique' (involving section under local anaesthesia of incompetent veins) and the SAVAS technique (Section en Ambulatoire des Varices avec Sclérothérapie) – being a combination of 'dentist's technique' and compression sclerotherapy. After 4 years of follow up, the SAVAS treatment was found to be the most effective, its haemodynamic value superior to sclerotherapy alone. SAVAS was also found to be less costly.

### **Elasticated stockings and compression bandages**

The first efforts to provide extrinsic calf compression were made in the seventeenth century with rigid lace up stockings applied over the lower calf in an attempt to heal ulceration (Burnand and Layer, 1986; Wiseman, 1676). The principle of compression is now used across the range of venous diseases of the legs. Compression works by decreasing superficial venous pressure, reducing the leakage of solutes and fluid from the affected microvasculature. It also assists the muscle pump in the lower limbs, thus improving venous return.

For varicose veins and CVI, elasticated stockings (compression hosiery) are the mainstay of conservative management in the UK and Scandinavian countries, though less so in other west European countries where pharmacotherapeutic alternatives are more widely used. Their efficacy in increasing the velocity of femoral vein flow (Lawrence and Kakkar, 1980), reducing ambulatory venous pressure (Jones et al, 1980; Horner et al, 1980) and relieving symptoms (Somerville et al, 1974) is well established. It is also believed that compression hosiery helps to prevent the recurrence of venous ulcers of the leg, after healing, though no definitive paper has yet been published quantifying its effectiveness in preventing ulcer recurrence. One of the aims of the continuing Lothian and Forth Valley leg ulcer study in Scotland is to provide more information on this, though this will only be obtained with difficulty, a randomised controlled trial of compression therapy versus no treatment being ethically unacceptable in Britain.

For maximum efficacy, it is believed that hosiery needs to be individually fitted and renewed at regular intervals to sustain graduated pressures in different parts of the leg, approaching a maximum of 60 mm Hg (Callam et al, 1987a). However, at optimal stocking pressures there is a non-negligible danger of provoking ischaemia in legs with occult arterial disease, leading to skin necrosis and possibly amputation.

Where active venous ulcers have formed, sustained compression using four layer bandages has been found to give better results (74

per cent healing at 12 weeks according to Blair et al, 1988) than use of ordinary elasticated bandages. When healed, the patient may revert to compression hosiery to prevent ulcer recurrence.

### **Unanswered questions on compression therapy**

Despite good evidence that compression therapy can be highly effective, many unanswered questions remain. The degree of compression required for optimal results is unknown and it is probable that it varies among patients by height, weight and severity of CVI. Nor is it clear to what extent the benefits of compression therapy and various forms of pharmacotherapy (the principal alternative therapeutic approach for CVI) are additive. As with other chronic conditions, controlled trials of treatment for venous diseases need many years of follow up, and information has been slow to emerge on the relative effectiveness of different therapeutic options as applied under carefully monitored conditions in centres of excellence.

The issue which is probably of more immediate importance, however, is the effectiveness *in use* of compression therapy, which may fall well short of the theoretical optimum because of poor patient compliance and inadequate dissemination of appropriate expertise.

Patient compliance is problematic with elasticated stockings because they are unsightly and can be uncomfortable to wear. Recent results from the Lothian and Forth Valley leg ulcer study (Gibson et al) show that non-compliance can be contained at a fairly low level with constant monitoring and persuasion by an expert team. But it is unlikely that similar levels are achieved outside a small number of centres of excellence. In the Lothian and Forth Valley study, two hundred and twenty patients with recently healed ulcers were considered for a trial to compare the effectiveness of low pressure (20 mm. Hg.) and medium pressure (30 mm. Hg) hosiery in controlling CVI and preventing ulcer recurrence. Forty-two of these patients (19 per cent) were deemed unsuitable on medical grounds (*eg* positive rheumatoid serology) and a further 18 patients (8 per cent) proved unable to wear even the lighter grade of stocking - despite strenuous efforts being made to assist patient compliance. The authors concluded that the higher the compression required for optimal effectiveness the more patients are likely to be excluded on safety grounds or to exclude themselves through failure to comply.

Dissemination of the appropriate expertise is also a major problem because compression hosiery and bandages are typically applied in community settings by healthcare professionals (usually nurses) who rarely have direct access to information and advice from centres of excellence. Most published studies on treatment of CVI and leg ulcers have been carried out in out-patient departments or clinics

under controlled conditions by medical and nursing staff with special experience in this area. But nearly two thirds of ulcer patients in Britain may never attend a hospital (Cornwall and Lewis, 1983). It is probable that the quality of stocking and bandage fitting and supervision is very variable, though no statistical data appear to have been published on this. At the most basic level, compression hosiery loses its elasticity over time and without careful monitoring, many patients may in fact be wearing stockings which have no therapeutic value.

Venous disease, like diabetes, illustrates the challenge of delivering expert medical management skills, traditionally found in hospitals, to community settings. In the case of diabetes, there is an extensive literature on different ways of organising care (OHE, 1989) including community diabetes centres and general practitioner mini-clinics. Little has been written specifically on venous diseases, but the issues are similar for this and other chronic diseases.

### **Pharmacotherapy**

According to a review by Cheatle et al (1991), a better understanding of the pathological mechanisms underlying skin damage in venous disease has allowed more rational pharmacotherapeutic approaches to be made in recent years.

Among the earlier experiments in drug treatment for venous ulcers, zinc supplements were found to be of value in treating leg ulcer patients with low serum zinc, but the conclusion drawn from a number of controlled trials has been that dietary zinc supplementation is unlikely to be of much benefit to the great majority of patients who do not have severe nutritional problems. Antibiotics are, of course, useful in treating infected ulcers by topical application, but despite extensive investigation of the possible effect of antibiotics in promoting ulcer healing, there is little evidence that systemic antibiotics have a role in the management of uncomplicated venous ulcers.

The two main classes of drugs currently used in the treatment of CVI are the hydroxyethylrutosides and fibrinolytic therapy. Hydroxyethylrutosides, which are the most frequently prescribed, were introduced in the 1970s and clinical trials published in the early 1980s showed them to be effective in alleviating symptoms of aching, tiredness, restless legs, pins and needles and muscle cramps, as well as in reducing oedema associated with CVI (Balmer and Limoni, 1980; Pulvertaft, 1983). Other reports have demonstrated that they reduce the capillary filtration rate in patients with CVI (Roztocil et al, 1977; Cesarone et al, 1992) and have confirmed their effectiveness in alleviating symptoms (de Jongste et al, 1989; Nocker et al, 1990). However, there is no convincing evidence of any beneficial effect of

hydroxyethylrutosides in promoting the healing of venous ulcers and only weak evidence that they may prevent their recurrence. The one published double-blind, placebo-controlled, multi-centre trial on ulcer recurrence (Ruckley et al, 1987) was inconclusive. It found that patients with recently healed ulcers put on hydroxyethylrutosides plus elastic stockings had an initially *higher* rate of recurrence than those on placebo plus elastic stockings, though by the end of 20 months the positions had reversed and the group on hydroxyrutosides did show a significantly lower cumulative rate of ulcer recurrence. Recent studies showing that hydroxyethylrutosides raise skin oxygen levels (TCPO<sub>2</sub>) indicate that further work in the field of venous ulcers appears justified (Burnand et al, 1989; Belcaro et al, 1989; Neumann and van den Broek, 1990).

The theoretical basis for fibrinolytic therapy was suggested by Browse and Burnand (1982). They proposed that venous hypertension in CVI causes fibrinogen leakage; the fibrinogen then polymerises into an insoluble pericapillary fibrin cuff which prevents the diffusion of oxygen and other nutrients from the blood vessel to the skin, leading to skin changes associated with CVI. Initial attempts to reverse skin damage by enhancing fibrinolysis using stanozolol, an anabolic steroid with profibrinolytic properties, were encouraging. But subsequent controlled trials (Burnand et al, 1980; Cheatle et al, 1991) found that fibrinolytic therapy offers only minor benefits in the symptomatic treatment of lipodermatosclerosis associated with CVI. Fibrinolytic therapy, such as stanozolol, appears to have no effect on ulcer healing, according to the one trial that has been reported (Layer et al, 1986).

With the disappointing results from fibrinolytic therapy, pharmacotherapeutic agents based on alternative theories of the underlying cause of skin damage have been tested. One recently proposed hypothesis (Coleridge Smith et al, 1988) is that raised venous pressure may lead to adherence of white cells to the capillary endothelium, releasing proteolytic enzymes and toxic free radicals. In line with this theory, the effect of prostaglandin E<sub>1</sub> has been studied and Rudofsky (1989) has reported a controlled trial in which venous ulcer patients on PGE<sub>1</sub> and compression therapy recorded a significantly better ulcer healing rate than patients on compression plus placebo. The disadvantage of PGE<sub>1</sub> is its expense and the inconvenience of administration by infusion. Pentoxifylline is a less expensive and orally administered agent which has also been shown to reduce white cell adhesion to endothelium. A number of trials have shown that pentoxifylline also has a significant effect on ulcer healing (eg Colgan et al, 1990).

## Cost of venous diseases of the legs

### Direct costs of healthcare provision

One of the principal objectives of this report is to estimate the cost of venous diseases and investigate how it varies from one European country to another. There is little published work on this particular group of conditions. Only one study (Dinkel, 1985) appears to have been published which makes estimates of the full range of costs - in this case in West Germany using 1981 data. Broadly, the results are comparable with those set out in Table 7, below, relating to the late 1980s. In Britain, the cost of venous ulcers alone has been variously estimated at £150m to £650m per annum. (Wilson, 1989). The lower end of this range is consistent with the figures in Table 7, below, but the upper range estimate of £650m is certainly too high.

To fill the gap in pan European information on the costs of venous diseases, health economists from France, W Germany, Italy and Spain were commissioned to provide data on healthcare costs within their own countries. In addition, the international market research group, Intercontinental Medical Statistics (IMS), made available information on the number of general practitioner consultations and prescriptions written for venous diseases - derived from information provided by a sample of primary care physicians in each country. IMS also provided information on expenditure on compression hosiery in the UK, derived from wholesalers' returns.

Table 7 summarises the overall results. Venous diseases of the legs are defined according to the International Classification of Diseases (ICD) to include ICD number 454 (Varicose veins of the lower extremities), ICD 459 (Other disorders of the circulatory system, including venous insufficiency and post phlebotic syndrome and one half of ICD 451 (Phlebitis and thrombophlebitis).

Using the available statistics on utilisation by ICD number, these conditions are estimated to absorb between 1.5 per cent and 2.0 per cent of total healthcare spending in the three European countries, UK, France and West Germany, where in-patient data are available for all three relevant ICD numbers. For the other two countries, Italy and Spain, where in-patient utilisation statistics were available only for ICD 454, the figure is 1.0 per cent.

Among the five countries, the UK spends the largest proportion - 2 per cent - of national healthcare resources on venous diseases, marginally more than France at 1.9 per cent. In cash terms, however, the UK's estimated £294 million in 1989 is substantially less than France's estimated FF 7834 m, because France spends substantially more on healthcare overall. The striking variations between French and UK general practitioner and prescribing costs are explained below.

**Table 7 Costs of venous diseases of the legs\* in the UK, France, W Germany, Italy and Spain**

**A) Cash**

	<i>UK £m<sup>1989</sup></i>	<i>France FF m<sup>1989</sup></i>	<i>W Germany DM m</i>	<i>Italy Ll bn<sup>1989</sup></i>	<i>Spain Ptas m</i>
Hospital in patient	89 <sup>1</sup>	1944	595 <sup>1987</sup>	333 <sup>2</sup>	4726 <sup>1987</sup>
Hospital out patient	na	609	na	na	na
District nursing service	180	–	–	–	–
General practitioners	8	1336	177 <sup>1986</sup>	58	5680 <sup>3</sup>
Prescription medicines	7	3945	575 <sup>1989</sup>	247	6841 <sup>1989</sup>
Compression hosiery <sup>10</sup>	1990/91	na	na	na	na
Total for sectors where data are available (local currency)	£294m	FF7834m	DM1426m	£1638bn	Ptas17247m
Total ECUs m (1992 exchange)	418	1135	696	412	134

**B) As a percentage of costs for all conditions**

	<i>UK %</i>	<i>France %</i>	<i>W Germany %</i>	<i>Italy %</i>	<i>Spain %</i>
Hospital in patient <sup>4</sup>	.96	.96	.97	.77 <sup>2</sup>	.52 <sup>2</sup>
Hospital out patient	na	1.6	na	na	na
District nursing service	30.0 (est.)	–	–	–	–
General practitioners	.42	4.90	2.47	1.40	1.35
Prescription medicines	.26	5.38	2.37	1.68	1.67
Compression hosiery <sup>10</sup>	100	na	na	na	na
Total for sectors where data are available	2.0	1.9	1.5	1.0	1.0

<sup>1</sup> \*Venous diseases of the legs are defined as ICD 454 (Varicose veins of the lower extremities), ICD 459 (Other disorders of the circulatory system, including venous insufficiency and post phlebotic syndrome and one half of ICD 451 (Phlebitis and thrombophlebitis).

Notes: 1 £55m. in the NHS and £34m privately paid. 2 ICD 454 only.

3 1985 figure for GPs and out patient clinics combined. 4 non psychiatric.

Sources: **UK:** OHE estimates. **West Germany:** estimates by Professor Dr J-Matthias von der Schulenburg of Department of Labour Economics, University of Hanover. **France:** estimates by Agnes Leclercq of CRESGE (Centre de Recherches Economiques Sociologiques et de Gestion). **Italy:** estimates by Professor Carlo Lucioni. **Spain:** estimates by Dr Joan Roviro of SOKOS at the Institute of Health Economics (Instituto di Economia Sanitaria), Barcelona.

There are gaps in the data, particularly in the area of hospital out-patient care, and comparisons by sub-sector are vitiated by national variations in healthcare organisation and reporting systems. It is believed, however, that Table 7 gives a fair reflection of how the magnitude of venous disease costs varies among major European countries.

### Hospital in-patient treatment

Venous diseases absorb a remarkably consistent 1 per cent of non-psychiatric hospital in-patient costs in the major EEC countries. Italy and Spain are lower at 0.8 per cent and 0.5 per cent respectively, but this is largely or wholly because their estimates cover ICD 454 only. The uniformity of in-patient costs contrasts strikingly with the massive inter-country variation in GP and prescribing costs. The method used to estimate in-patient costs is the same in each country; that is, the numbers of in-patient days recorded against each relevant ICD code are multiplied by revenue cost per in-patient day to arrive at an overall cost.

In those three countries where figures are available separately for

Table 8 Hospital in-patient costs absorbed by venous diseases of the legs

#### A) Cash

	UK £m <sup>1989</sup>	France FF m <sup>1989</sup>	W Germany DM m	Italy £l bn	Spain Ptas m
ICD 454	70 <sup>1</sup>	1519	313 <sup>1987</sup>	333	4726 <sup>1987</sup>
ICD 459	9	81	202 <sup>1987</sup>	na	na
one half ICD 451	9	344	80 <sup>1987</sup>	na	na
All in-patient costs for venous diseases	89	1944	595 <sup>1987</sup>	na	na

#### B) As a percentage of costs for all conditions

	UK %	France %	W Germany %	Italy %	Spain %
ICD 454	.76	.75	.51	.77	.48
ICD 459	.10	.04	.33	na	na
one half ICD 451	.10	.17	.13	na	na
All in-patient costs for venous diseases	.96	.96	.97	na	na

1 Consisting of NHS £36 million and private treatment £34 million.

Source: As Table 7.

each of the ICD numbers which make up venous diseases of the leg, ICD 454 (varicose veins) absorbs the largest share of resources (Table 8). Nearly all is spent on one procedure, stripping and ligation of varicose veins. The cost of in-patient treatment of venous ulcers, which is usually coded as ICD 459, is small in Britain and France, though it is substantial in West Germany. This difference may also reflect the more widespread use of the term 'venous insufficiency' in West Germany, in contrast to 'varicose veins' in Britain and France.

### **Hospital out-patient treatment**

Very few statistics are available on out-patient costs of treating venous diseases. This is a major gap in information because a great deal of treatment of CVI and varicose veins takes place on an out-patient basis, in particular sclerotherapy. Sclerotherapy is not now performed as often as it was in the late 1960s, when it was by far the most frequent intervention undergone by the sample of chemical industry employees surveyed by the Basle study. However, it still absorbs a large, but unknown, amount of resources. France is the only country where usable statistical information proved to be available, with an estimated expenditure of FF 609 million, being about one third of the estimated expenditure on hospital in-patient services for venous diseases. It is possible to estimate UK out-patient costs for venous diseases approximately, using out-patient referral rates from the National Morbidity Surveys organised by the Royal College of General Practitioners in association with the Office of Population, Censuses and Surveys. This method leads to a result similar to that found in France, *ie* that out-patient costs for venous diseases (for public and private sectors combined), at about £30 million in 1989, are about one third of in-patient costs. However, this method of estimation for Britain is regarded as too tenuous for inclusion in Table 7.

### **District nursing service**

One of the main differences between the UK and other European countries is the existence of 'Community Health Services' in the UK, funded and organised by district health authorities and NHS Trusts separately from the family doctor service and hospital out-patients. In the case of venous diseases, the key member of the community health services team is the district nurse. She usually advises on compression hosiery and bandages chronic leg ulcers in patients' own homes and this accounts for a major part of the overall cost of treating venous diseases to the British NHS.

Treating venous disease is one of the most time consuming of district nurses' activities. Bosanquet (1992a) reports that surveys in Walsall and Rochester have estimated that district nurses spend 30-50

per cent of their time dealing with patients with leg ulcers. In Norwich, an estimate of 10-20 per cent has been made and in the Riverside district of London a survey of district nurses found that 75 per cent of them were spending at least one quarter of their professional time treating leg ulcers. Taking a figure of 30 per cent as representative of the country as a whole, this percentage can be applied to the total £498.2 m. spent on district nursing in England 1988/9 according to Department of Health programme budget (HMSO, 1990). After adjustment to a UK basis, this implies that £180 million was spent on district nurse care of venous ulcers in 1989. The figure is for staff only and excludes the cost of materials such as compression bandages unavailable on the FP10 prescription form and consequently purchased out of the community health service budget.

This makes the district nursing service by far the largest component of the total cost of treating venous diseases in Britain. The figure of £180 million is, of course, subject to the same degree of error as the (approximate) estimate of 30 per cent for the proportion of time spent by district nurses on managing leg ulcers.

**Table 9 General practitioner costs absorbed by venous diseases of the legs**

**A) Cash**

	<i>UK £m<sup>1989</sup></i>	<i>France FF m<sup>1989</sup></i>	<i>W Germany DM m</i>	<i>Italy £l bn</i>	<i>Spain Ptas m</i>
ICD 454	7	341	120 <sup>1986</sup>	33	2956 <sup>1</sup>
ICD 459	1	959	49 <sup>1986</sup>	17	2533 <sup>1</sup>
one half ICD 451	1	35	9 <sup>1986</sup>	8	211 <sup>1</sup>
Total general practitioners	8	1336	177 <sup>1986</sup>	58	5680 <sup>1</sup>

**B) As a percentage of costs for all conditions, 1991**

	<i>UK %</i>	<i>France %</i>	<i>W Germany %</i>	<i>Italy %</i>	<i>Spain %</i>
ICD 454	.34	1.25	1.67	.80	.70
ICD 459	.05	3.52	.68	.40	.60
one half ICD 451	.03	.13	.12	.20	.05
Total general practitioners	.42	4.90	2.47	1.40	1.35

<sup>1</sup> 1985 figure for GPs and out patient clinics combined.

Source: As Table 7.

**Table 10 Prescription medicines costs absorbed by venous diseases of the legs**

**A) Cash**

	UK <i>£m</i> <sup>1989</sup>	France <i>FF m</i> <sup>1989</sup>	W Germany <i>DM m</i>	Italy <i>£ bn</i>	Spain <i>Plas m</i>
ICD 454	4	675	386 <sup>1989</sup>	119	3154 <sup>1989</sup>
ICD 459	2	3036	158 <sup>1989</sup>	85	3318 <sup>1989</sup>
one half ICD 451	1	235	32 <sup>1989</sup>	43	369 <sup>1989</sup>
Total prescription medicines	7	3945	575 <sup>1989</sup>	247	6841 <sup>1989</sup>

**B) As a percentage of costs for all conditions, 1991**

	UK %	France %	W Germany %	Italy %	Spain %
ICD 454	.15	.92	1.59	.81	.77
ICD 459	.07	4.14	.65	.58	.81
one half ICD 451	.04	.32	.13	.29	.09
Total prescription medicines	.26	5.38	2.37	1.68	1.67

1 1985 figure for GPs and out-patient clinics combined.

Source: As Table 7.

On the continent of Europe, there is no real equivalent to the district nurse. Patients with chronic venous ulcers have them bandaged in general practitioners' surgeries or sometimes at out-patient clinics and this is reflected in higher spending under those cost heads.

### General practitioners and prescription medicines

The existence of a district nursing service in the UK is presumably the reason why, according to audits carried out by Intercontinental Medical Statistics, consultations specifically for ICD 459 ('other disorders of the circulatory system') account for only 0.05 per cent of GPs' time in Britain compared with 0.4 per cent in Italy, 0.6 per cent in Spain and 0.68 per cent in West Germany. In France the proportion is *seventy* times higher than in Britain at 3.52 per cent, though this also reflects a very wide interpretation of ICD 459 in France (Table 9).

The management of leg ulcers and CVI by district nurses also helps to explain why Britain spends much less on prescription medicines for venous diseases than the other major EEC countries (Table 10). However, any 'savings' in GP time and medicines in Britain are probably less than the additional cost incurred by

Britain's district nursing service. After combining all cost heads, according to the calculations in Table 7, the 2.0 per cent of healthcare resources overall that Britain spends on venous diseases is a higher proportion than that spent in France, Germany, Italy or Spain. In the absence of any comparative data on outcome, however, no conclusions whatsoever can be drawn on the relative cost effectiveness of the different national models for managing venous disease and its complications.

The method for calculating General Practitioner and prescription medicine costs, using data from IMS, is identical for all five countries.

General practitioner costs are assumed to be proportional to the number of diagnoses recorded against each relevant ICD code and are calculated in Table 7 by applying each diagnosis percentage to total national expenditures on general practitioners.

The cost of prescription medicines is calculated by a similar method, after weighting prescription volumes by a relative price factor for venous products.

Non-prescribed medicines are excluded from the costs throughout.

### **Elastic hosiery**

Information on expenditure on compression hosiery is available only in Britain among the five European countries investigated. Data are available from two sources, the Prescription Pricing Authority and Intercontinental Medical Statistics' Patient Personal Care report. There is little difference between the two and the figure from IMS is given in Table 7 after an adjustment to include pharmacists' margins. This sum of £10 million in the year ending June 1991 does not include compression bandages for treatment of venous ulcers, which are rarely available on prescription. Compression bandages are usually purchased under district health authorities' out-patient or community health service budget heads.

### **Indirect cost of lost working time**

The 'cost of illness' framework proposed by Rice (1966) incorporates the costs of productive capacity lost as a consequence of illness. These are usually described as 'indirect' costs, in contradistinction to the 'direct' costs of healthcare services. Indirect costs are usually estimated by multiplying the number of days of invalidity attributed to the particular condition by average gross income per day from employment. There are two serious conceptual objections to this methodology. First, Rice proposed it at a time when full employment was seen as a credible object of government policy. But in the 1990s, when a substantial pool of unemployed people is widely regarded as

a permanent feature of the economy, it may be valid to regard the opportunity cost of long term non-participation in the workforce as zero. This is a general issue in economics, wherever resources lie idle, not one that is specific to health economics. The second conceptual problem is that sickness absence from work is not primarily a medical phenomenon. A multiplicity of non medical factors cause people to go off sick temporarily or leave the workforce permanently (OHE, 1981). The particular medical cause to which sickness absence is attributed may be no more than a convenient label. Low levels of sickness absence are more likely to be related to job satisfaction than to low levels of clinically defined morbidity. It is likely to be misleading, therefore, to base calculations of cost (or the potential benefit from effective prevention or cure) on the assumption that the eradication of a particular medical condition really would lead to a corresponding reduction in absence from work.

With these reservations, Table 11 provides an estimate of the indirect costs of venous diseases in those two countries, Britain and West Germany, where data are available. In each case, the source data are medical certificates of invalidity processed by the social security system. There are shortfalls in these data in Britain, but broadly the shortfalls are counterbalanced by other factors which tend to overstate days of absence experienced (OHE, 1981).

**Table 11 Indirect costs of invalidity attributed to venous diseases**

	<i>West Germany<sup>1987</sup></i>			<i>Great Britain<sup>1989</sup></i>		
	<i>Days of invalidity</i>	<i>As percent of invalidity</i>	<i>Cost</i>	<i>Days of invalidity</i>	<i>As percent of invalidity</i>	<i>Cost</i>
	<i>All causes</i>			<i>All causes</i>		
	days	%	DM m	days	%	£ m
ICD 454	1,580,000	.4	313	818,000	.2	33
ICD 459	2,437,000	.6	483	903,000	.2	36
one half ICD 451	790,000	.2	157	115,000	.02	5
All venous diseases	4,807,000	1.2	953	1,836,000	.4	73

*Sources:*

West Germany: – estimates by Professor Dr J-Matthias von der Schulenburg based on Der Bundesminister für Arbeit und Sozialordnung, Arbeitsunfähigkeit und Krankenhausbehandlung nach Krankheitsarten 1987, Bonn 1990 and Institut der Deutschen Wirtschaft, Zahlen zur wirtschaftlichen Entwicklung der Bundesrepublik Deutschland 1990, Köln 1990. Great Britain: OHE estimates based on DSS sickness and invalidity statistics and Department of Employment data on average gross income.

In West Germany, 1.2 per cent of all days of certified invalidity are attributed to venous diseases, representing a theoretical loss of productive capacity of 953 million DM in 1987. The figure is comparable with results obtained by Dinkel (1985) for West Germany in 1981. In Britain, the lower figure of 0.4 per cent (implying a loss of productive capacity of £73 million in 1989) is probably related to the existence of the district nursing service which draws patient traffic away from general practitioners' surgeries and leads to fewer requests for sick notes attributable to episodes of venous disease.

### **Cost of reduced quality of life**

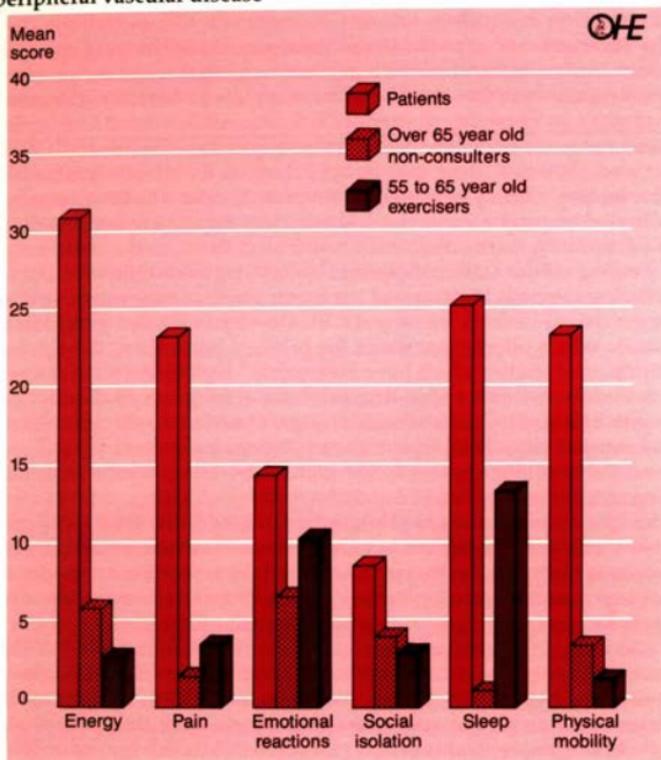
There are many papers on the frequency of symptoms associated with venous disease, but few which give any indication of the degree to which individuals are disabled as a consequence of the condition or the extent to which their quality of life suffers. Only one well constructed study could be found which measures subjective perceptions of the health impact of venous diseases (Hunt et al, 1982). The authors applied the Nottingham Health Profile to 93 patients attending an outpatient clinic. These were patients, therefore, who had undergone surgery for vascular disease, and were attending for review, or who had been referred for possible surgery. Figure 4 shows how their health profile scores compared with healthy individuals in similar age groups. The results, according to the authors show that:

'patients with peripheral vascular disease have many problems with functioning – low levels of energy, pain, sleep disturbance and limitations on physical mobility being the most serious. Feelings of social isolation are less marked and emotional problems are fewer than might be expected.'

Quality of life, therefore, appears to be significantly impaired for individuals with vascular disease, but what is lacking is data on how much surgery, sclerotherapy or pharmacotherapy improves it. Nearly all controlled trials to date have used clinical end points. These do, of course, indicate whether intervention is effective, and if cost data are included they may show which one of alternative treatments for the same condition is the most cost effective. But typically they yield no information on patients' subjective perceptions of the benefits of treatment, of the sort that could assist in determining whether treatments for venous disease represent a good use of scarce healthcare resources compared with treatments for other diseases.

An exception is the Riverside study, conducted in inner London, which breaks new ground by incorporating 'quality of life' measures of the outcome of treatment for venous ulcers (see below).

Figure 4 Nottingham Health Profile scores for patients with peripheral vascular disease



Source: Reproduced from Hunt, S et al (1982) *Subjective health of patients with peripheral vascular disease*. *The Practitioner* 226, 133-136.

## The future

### Prevention or cure?

In the absence of any established theory on the underlying cause of most venous diseases of the legs, there is limited scope for primary prevention strategies. Little can be done about heredity. Pregnant women's vulnerability to varicose veins cannot be altered in the present state of knowledge. With greater emphasis on health and safety at work, however, there may be opportunities for initiatives aimed at preventing employment related venous disease. Health education directed at people in service industry jobs which involve standing (hairdressing, bartending, etc.) could alert them to the dangers of standing *still* for extended periods. By moving from time to time and causing the muscle pumps of the leg to contract they might reduce their risk of varicose veins and CVI. Obesity is another aetiological factor which offers some scope for primary prevention, though the findings of studies which have investigated the link between obesity and varicose veins imply that even the eradication of obesity (an optimistic goal) would not make major inroads into the prevalence of varicose veins in Europe. If the hypothesis proposed by Geelhoed and Burkitt (1991) proves to be valid (that western lifestyle, including components of exercise and diet, is the underlying cause of venous disease) then current changes towards healthier behaviour patterns may yield a pay off in venous as well as cardiovascular diseases more generally. As yet, however, there is insufficient evidence of any causal connection between lifestyle factors and venous disease for any specific preventive measures to be promoted.

Secondary prevention holds more promise than primary prevention. It is possible, though understandably no clinical trial has ever tested the hypothesis, that varicose veins and CVI in western countries could be all but eradicated if everyone wore the appropriate grade of compression hosiery from early childhood; but, of course, indiscriminate intervention on this scale is not a practical option. More realistically, there may be potentially significant returns from proactive care management programmes developed with the specific objective of preventing progression to severe CVI and venous ulceration among individuals at risk, applying the entire range of therapies – surgery, medicines and compression.

### Innovation and clinical research

Though most of the therapies available for venous diseases are long established, recent years have seen a quickening of the pace of innovation. Surgical procedures for varicose veins and even severe CVI have been refined and extended, for example with vein valve transplantation, while greatly improved results in the treatment of venous

ulcers have been achieved by modifications in compression bandages. In each case the new therapies can be best described as small step innovation. In the area of pharmacotherapy, the last two decades have witnessed no major innovations in the treatment of venous diseases, but early results from trials of prostaglandin E<sub>1</sub> and pentoxifylline, both of which are believed to work by reducing white cell adhesion to endothelium, have raised the prospect of a fundamental advance in medical treatment for severe CVI and venous ulceration.

There remain many unanswered questions on the impact of treatment for venous diseases and there is a need for further, well constructed, randomised controlled trials to establish the effectiveness – under controlled conditions and with optimum patient compliance – of various alternative therapies, both individually and in combination.

### Organisational change

A second challenge, which is only beginning to be addressed, is how to maximise the cost effectiveness *in use* of such treatments as there are. The massive variations between European healthcare systems, in how much they spend on treating venous diseases in non-institutional settings, is indicative of extensive differences in clinical practice. Identifying best practice may involve evaluation of a range of different organisational models, not so much for varicose veins – which seems to fit naturally into existing systems of acute in-patient and out-patient treatment – but for individuals with chronic, severe CVI and a history of leg ulceration.

- **Out patient clinics**, as used by academic centres with a particular interest in venous diseases. The difficulty lies in replicating the high quality of service undoubtedly provided in academic centres of excellence in ordinary out-patient clinics.
- **GP clinics**, which are unusual in Britain where management of severe CVI and leg ulcers has traditionally been undertaken by district nurses.
- **District nursing service**, where the challenge is to ensure that nurses have the full range of skills to deal with routine cases and appropriately to refer cases which are outside their competence. It is likely, though there are no supporting data, that the effectiveness of district nursing services varies widely in different parts of Britain.
- **Special community clinics**, combining medical and nursing skills to offer a local, proactive, non hospital based service.

Management of venous diseases exemplifies one of the principal challenges faced by health services in Europe as they approach the end of the twentieth century; that is, how best to organise continuing

services for people at risk of serious but not immediately life threatening conditions in middle and old age. The classical paradigm here is provided by diabetes. Venous disease presents a challenge which is similar in many ways to diabetes, but there are important points of difference. Venous disease is – in principle at least – a simpler condition, in the sense that the complications are all concentrated in the leg, whereas the complications of diabetes affect the kidneys, the cardiovascular system, the peripheral nervous system and the eyes. Another point of difference is that the population at risk of leg ulcers does not represent a target group with such a clear potential for benefit from long term management. It would not make economic sense to target the 50 per cent of the population with venous diseases of some degree, since just 1-2 per cent of national healthcare resources are consumed in their treatment. The marginal cost burden that venous disease represents is fairly small and the potential benefits from even a large proportionate reduction in those costs are correspondingly small as well. In contrast, the 1 per cent of the population with diabetes (in Britain) consume 4 per cent of all healthcare resources (OHE, 1989). A more manageable target group would be individuals with CVI, but with 6 per cent of the population affected, and no clear way of identifying those most at risk of progressing to severe symptoms and leg ulcers, any programme more formalised than opportunistic assessment in primary care of patients at risk would be expensive.

The question that needs to be posed is at exactly what point in the spectrum of venous disease does it become valid to move from a demand led 'repair' model of healthcare, which is quite appropriate for varicose veins, to one where proactive management and continuing monitoring are appropriate, as in severe CVI and leg ulcers?

The answer to this question requires a great deal more information than is presently available on the costs and benefits of alternative therapies for venous diseases and on how costs and benefits vary according to the mode of healthcare delivery adopted. The limited amount of work that has been done has inevitably focused on patients with a history of leg ulceration, at the most severe and costly end of the spectrum of venous disease.

The most promising evaluative exercise to date, in Britain, is the King's Fund sponsored study of six community venous ulcer clinics in the Riverside Health Authority in inner London, linked to the vascular surgery service at Charing Cross Hospital and offering – in addition to treatment – a focus for community training in ulcer management. The study incorporated a controlled trial of the four layer bandaging system, which had already achieved venous ulcer healing rates at 12 weeks of 74 per cent, according to results reported by Blair et al (1988). More broadly, the study sought to evaluate the

concept of specialist community venous ulcer clinics in terms of costs and effectiveness, the latter being measured in both healing rates and changes in the quality of life.

Among patients referred in the first three months, the 12 week leg ulcer healing rate was 55 per cent. This was below average for the four layer bandaging method, reflecting the relatively intractable core of chronic patients referred at the outset, but still substantially higher than the 22 per cent 12 week healing rate found by the control audit carried out prior to the commencement of the Riverside clinics. Healing rates improved for subsequent referrals, to 78 per cent for those referred between 6 and 9 months after the start of the programme and 86 per cent for those referred 15-18 months after the start.

The Riverside initiative has also provided strong evidence that healing of venous ulcers leads to an improvement in the quality of life. A symptom rating test carried out among patients prior to and after treatment found that 12 weeks of treatment in a specialist leg ulcer clinic (using the four layer bandage method) improved quality of life by significantly reducing depression, anxiety and hostility whilst improving cognitive function, Franks et al (1992). The reductions in depression and hostility were related to the complete healing of the ulcer. Much of this change, according to the authors, may be due to significant reductions in pain following treatment, improvements in performing everyday tasks and reduced interference in social activities.

According to Moffatt et al (1992) the results from the first 18 operational months of the Riverside initiative demonstrate that leg ulcer care can be delivered with greatly enhanced effectiveness by dedicated community leg ulcer clinics using existing staff – provided adequate training, equipment and effective elastic bandages are available.

Moreover, Bosanquet (1992b) points out that the cost of the special leg ulcer clinics could be significantly less than the cost of the old (ineffective) service in the long term. The Riverside leg ulcer clinic programme involves an investment of £170,000 a year over 3 years for a population of 287,000. After that a continuing programme will be required to treat new patients and to prevent relapse, but this continuing programme could cost less than the present £416,000 per annum expenditure for the old type of service.

The health service reforms in Britain have encouraged experimentation in new styles of healthcare delivery and the announcement in February 1992 that GP fundholders will be given a budget to purchase district nursing services from NHS community units, from April 1993, holds intriguing possibilities for management of venous diseases. It is estimated, Table 7, that about 30 per cent of district nurse

time is spent on care of people with leg ulcers. The government's proposal will, therefore, affect primary care management of venous diseases more than any other medical condition. When implemented, it will mean that GP fundholders will have discretionary budgets covering virtually the entire range of services for people with venous diseases – elective surgery, out-patient treatment, medicines, compression hosiery and district nursing services, the latter including (presumably) compression bandages which general practitioners have hitherto been excluded from prescribing under publicly funded pharmaceutical services. The only element of healthcare not covered by GP fundholder budgets will be the relatively small amount of spending on 'core' (*ie* non elective) in-patient treatment. Traditionally, and because of the separate organisation of district nursing, British general practitioners have played a relatively minor role in management of chronic venous disease. It will be of interest to see whether GP fundholders take advantage of their increased financial powers to extend their role and develop new models of integrated care. NHS Trusts, a number of which specialise in community services, may also make use of their greater flexibility to lead the development of new services for people with chronic conditions such as venous disease. As Bosanquet (1992b) points out, there is an attractive role for Trusts – as well as for GP fundholders – to transform what are now disconnected 'maintenance' activities carried out by various arms of the health service into a coherent programme of investment in benefits for patients, based on achieving clearly defined service goals at a given cost. The British health care reforms certainly present an opportunity for experiments in innovation. And, though the administrative context differs, the issue of how to promote innovation in the management of chronic illness is equally relevant in other countries of Europe.

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