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DJ Torgerson on behalf of the VenUS Team

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Abstract

VenUS I: a randomised controlled trial of two types of bandage for treating venous leg ulcers

C Iglesias, EA Nelson, NA Cullum* and DJ Torgerson on behalf of the VenUS Team

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Objectives: To compare the clinical and cost-effectiveness of two different compression bandages for the healing of venous leg ulcers.
Design: A pragmatic, randomised controlled trial with an economic evaluation.
Setting: Community, district nurse-led services; community leg ulcer clinics; hospital leg ulcer clinics with community outreach. A range of urban and rural settings in England and Scotland.
Participants: Patients with a venous leg ulcer of at least 1-week's duration, at least 1 cm in length or width and an ankle:brachial pressure index of at least 0.8.
Interventions: The four-layer bandage (4LB) (which is multilayer elastic compression) compared with the short-stretch bandage (SSB) (multilayer, inelastic compression).
Main outcome measures: The primary end-point was complete healing of all the ulcers on the trial leg. Secondary outcomes were the proportion of patients healed at 12 and 24 weeks, rate of recurrence, costs of leg ulcer treatment and quality of life.
Results: Between April 1999 and December 2000 the trial recruited 387 people aged from 23 to 97 years at trial entry. The majority of patients in this trial (82%; 316/387) had a reference ulcer of area ≤ 10 cm^2. To test the difference over time of Kaplan–Meier curves for the two bandage groups, the distribution of the cumulative times to healing of individuals in the two trial groups was compared using the log-rank test. The difference in the distribution of cumulative healing times between the individuals in the two groups was not statistically significant at the 5% level. Adjusting for the effects of variables which may influence healing (centre, baseline ulcer area, duration, episodes, ankle mobility, weight) in a Cox proportional hazards model, a statistically significant treatment effect in favour of the 4LB was identified. At any point in time, the probability of healing for individuals in the SSB treatment arm is significantly lower than that for people treated with the 4LB. Our base case economic analysis showed that the 4LB is the dominant strategy, that is, it is associated with a greater health benefit and lower costs than the SSB, although the differences are not statistically significant. This result is explained largely by the greater number of community nurse visits required by participants in the short-stretch arm.
Conclusions: The 4LB, which is currently the UK standard compression bandage for people with venous leg ulcers, was more clinically and cost-effective than the SSB. The bandage costs were less important than the costs of treatment visits, and patients in SSBs required more treatment overall. Generally, this trial supports the use of the 4LB in preference to the SSB. Recommendations for future research include: exploration of the relationship between bandager skill, application technique and ulcer healing; the relative cost-effectiveness of community leg ulcer clinics; and the study of nurse decision-making in venous ulcer management.

Contents

List of abbreviations

ABPI	ankle:brachial pressure index
AE	adverse event
CI	confidence interval
CIVIQ	Chronic Venous Insufficiency Questionnaire
CONSORT	Consolidated Standards of Reporting Trials
DVT	deep vein thrombosis
FLQA	Freiburger Questionnaire of QoL in Venous Diseases
4LB	four-layer bandage
HLFVQ	Hyland Leg and Foot Ulcer Questionnaire
HR	hazard ratio
ITT	intention-to-treat
ICER	incremental cost-effectiveness ratio
HRQoL	health-related quality of life
LCMHT	Leeds Community and Mental Health Trust
LFV	Lothian and Forth Valley Leg Ulcer Study
LREC	Local Research Ethics Committee
MAI	Multilevel Assessment Instrument
MREC	Multicentre Research Ethics Committee
MSC	mental component of Short Form 12
NHP	Nottingham Health Profile
NHS	National Health Service
PGC	Philadelphia Geriatric Center
PSC	physical component of Short Form 12
QoL	quality of life
QALY	quality-adjusted life-year
RCT	randomised controlled trial
RPI	resting pressure index
SD	standard deviation
SF-12	Short Form 12
SF-36	Short Form 36
SSB	short-stretch bandage
VenUS	Venous Ulcer Study

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Objectives

To compare the clinical and cost-effectiveness of two different compression bandages for the healing of venous leg ulcers.

Methods

Design

A pragmatic, randomised controlled trial (RCT) with an economic evaluation.

Setting

Community, district nurse-led services; community leg ulcer clinics; hospital leg ulcer clinics with community outreach. A range of urban and rural settings in England and Scotland.

Subjects

Patients were eligible to participate in the trial if they presented with a venous leg ulcer of at least 1-week's duration, at least 1 cm in length or width and an ankle:brachial pressure index of at least 0.8.

Interventions

The four-layer bandage (4LB) (which is multilayer elastic compression) compared with the short-stretch bandage (SSB) (multilayer, inelastic compression).

Main outcome measures

The primary end-point was complete healing of all the ulcers on the trial leg. Secondary outcomes were the proportion of patients healed at 12 and 24 weeks, rate of recurrence, costs of leg ulcer treatment and quality of life.

Results

A total of 387 people were recruited to the trial between April 1999 and December 2000; this represents 39% (387/988) of those approached. Patients ranged in age from 23 to 97 years at trial entry, with a mean age of 71 years. Most frequent reasons for exclusion from the trial were patients not suitable for compression, ankle/brachial pressure index lower than 0.8, diabetes mellitus and maximum ulcer <1 cm. The majority of patients in this trial (82%; 316/387) had a reference ulcer of area ≤ 10 cm^2. To test the difference over time of Kaplan–Meier curves for the two bandage groups, the distribution of the cumulative times to healing of individuals in the two trial groups was compared using the log-rank test. The difference in the distribution of cumulative healing times between the individuals in the two groups was not statistically significant at the 5% level (log rank = 2.46, $p = 0.12$). Adjusting for the effects of variables which may influence healing (centre, baseline ulcer area, duration, episodes, ankle mobility, weight) in a Cox proportional hazards model, a statistically significant treatment effect in favour of the 4LB was identified. At any point in time, the probability of healing for individuals in the SSB treatment arm is significantly lower than that for people treated with the 4LB (hazard ratio 0.72, 95% confidence interval 0.58 to 0.91).

Our base case economic analysis showed that the 4LB is the dominant strategy, that is, it is associated with a greater health benefit and lower costs than the SSB, although the differences are not statistically significant. This result is explained largely by the greater number of community nurse visits required by participants in the short-stretch arm.

Conclusions

The 4LB, which is currently the UK standard compression bandage for people with venous leg ulcers, was more clinically and cost-effective than the SSB.

Implications for healthcare

This trial found a higher healing rate, a reduced median time to healing and lower costs associated with 4LB treatment compared with SSB. The bandage costs were less important than the costs of treatment visits, and patients in SSBs required more treatment overall. Generally, this trial supports the use of the 4LB in preference to the SSB. However, if healing rates are good, and patients and/or their carers are able to launder and re-apply the bandage, then the treatment is likely to become cost-effective.

The SSB would be a reasonable alternative for those patients who like it and will not tolerate the 4LB.

Recommendations for future research

- Exploration of the relationship between bandager skill, application technique and ulcer healing, including the potential for patients and/or their carers to apply bandages effectively.
- The relative cost-effectiveness of community leg ulcer clinics should be re-examined using modelling (the only RCT, incorporating an economic evaluation, comparing home visits with clinic treatment was confounded by major differences in bandage provision).
- Study of nurse decision-making in venous ulcer management to understand better the influences on treatment choice and the frequency of treatment visits (since the latter drives costs in the treatment of venous leg ulceration).

Chapter 1
Background

> "Even though my ulcer has healed, I am still troubled by some aspects of having a leg ulcer. I now have to wear compression stockings for the rest of my life. I feel very aware of them all the time and feel very self-conscious. ... I still avoid busy shops, crowded places and friends with dogs and cats. The ulcer may be healed but it still interferes with my day to day life."
>
> Patient 1361, VenUS

The epidemiology of venous leg ulceration

Leg ulceration remains a relatively common condition, particularly in the elderly, and as the quotation above shows, leg ulcers have far reaching consequences on quality of life even after healing.

There have been several epidemiological studies of leg ulceration within the UK and around the world, with variation in the definition of a leg ulcer used between studies. Some studies have included ulcers anywhere on the lower limb; others have excluded toe or forefoot lesions; some studies have incorporated an element of chronicity in the definition; and some have only included open, active ulcers. The largest epidemiological study of leg ulceration in the UK was undertaken in the Lothian and Forth Valley (LFV) in the early 1980s and defined a leg ulcer as[1]

> "… loss of skin below the knee on the leg or foot which takes more than 6 weeks to heal."

The LFV study aimed to identify all patients receiving treatment for leg ulceration from GPs, community nurses and in nursing homes. Healthcare professionals reported 1477 people with active leg ulcers from a total population of approximately 1 million (a point prevalence of people with active leg ulcers known to the health service of 1.48 per 1000). Six hundred of the patients received a clinical examination from a vascular surgeon.[2] This study yielded new data regarding the numbers, clinical histories and healthcare of people with chronic leg ulceration in the UK. Important findings were that 76% of the 600 people examined had venous disease, 22% arterial disease, 9% rheumatoid arthritis and 5% diabetes.[3] More than one of these factors was present in a proportion of patients with 'mixed aetiology' ulcers. This and subsequent similar studies in the UK and elsewhere have broadly agreed that the point prevalence of active leg ulceration is between 1 and 2 per 1000 and that at any one time only about 20% of people with this chronic condition have an open ulcer, hence the prevalence of people with open ulceration or a history of ulceration is approximately 1% of the total population. More women than men are affected, with nearly four times as many women than men affected in the 70+ years age group.[3]

Risk factors for leg ulceration

Most leg ulcers are found in association with venous disease, but there has been relatively little prospective epidemiological research to ascertain risk factors. A history of deep vein thrombosis (DVT) has long been thought significant and when Kahn and co-workers reviewed the literature on long-term outcomes post-DVT they concluded that postphlebitic syndrome is established by 1 year after DVT in 17% to 50% of patients.[4] Moher and co-workers ascertained the outcomes of a cohort of 1527 people who had DVT or pulmonary embolus and concluded that 245 (16%) went on to develop venous disease and 3.7% had developed leg ulcers after 20 years.[5]

DVT is thought to cause damage to the deep veins, leading to venous insufficiency and venous ulceration, but the cellular mechanisms involved in tissue breakdown are poorly understood.[6] Venous insufficiency has been shown to be associated with increased hydrostatic pressure in the veins of the leg,[7] and it is in an attempt to reverse this and aid venous return that external compression in various forms is applied as a therapy for venous leg ulcers.

Prognosis after ulceration

Short-term outcomes

Margolis and colleagues[8] in Pennsylvania have

undertaken the most sophisticated work to date exploring predictors of healing a venous leg ulcer. By following cohorts of patients with venous leg ulcers, treated with compression bandaging, they showed that:

- initial wound area
- wound duration at presentation
- history of venous ligation/venous stripping
- history of knee or hip replacement
- ankle:brachial pressure index (ABPI) of <0.8
- >50% of wound surface covered in fibrin at baseline

are all independently associated with failure of the ulcer to heal within 24 weeks.[8] They then proceeded to develop a prediction rule from a cohort of 260 patients treated with compression and validated it in an independent cohort of 219 patients. This simple rule (1 point if ulcer duration >6 months; 1 point if baseline area >5 cm^2; score of 0 predicted healing; score of 2 predicted failure to heal) discriminated between ulcers healed or not healed at 24 weeks in 87% of cases.[9] This group's most recent work showed that it is the percentage change in ulcer area during the first period of treatment that distinguishes between healers and non-healers at 24 weeks. A wound whose area increases by ≥ 3% over the first 4 weeks of treatment has a 68% probability of failing to heal by 24 weeks; conversely, an ulcer whose area increases by <3% in the first 4 weeks has a 75% chance of healing.[10]

Long-term outcomes

The LFV study showed that leg ulceration is typically a chronic condition with periods of ulceration followed by healing and then recurrence; 20% of ulcers in the LFV study had been open for more than 2 years and 66% of patients had experienced previous episodes of ulceration.[3] Nelzen and colleagues in Sweden followed 382 patients who had open leg and/or foot ulcers in 1988 (206 with predominantly venous aetiology) for 5 years to determine healing and recurrence outcomes.[11] At follow-up, 58% of all patients had healed ulcers, 38% had open ulcers and 4% had undergone amputation. Looking at patients with ulceration due to venous incompetence (n = 135 at 54 months), only 44% had healed their original ulcer without subsequent recurrence compared with 59% of patients with arterial ulcers and 59% of people with diabetes. Four patients with venous ulcers had undergone amputation.[11]

Impact of ulceration on quality of life

Studies of quality of life (QoL) in people with leg ulceration fall into four categories:

- qualitative, inductive in-depth studies of what life with a leg ulcer is like from a patient's perspective
- cross-sectional measurement using generic health-related quality of life (HRQoL) instruments, for example, Short Form with 36 Items (SF-36), Nottingham Health Profile (NHP) or leg ulcer specific measures, in people with leg ulcers
- cross-sectional measurement using generic and/or leg ulcer-specific HRQoL measures in people with leg ulcers and people of a similar age without leg ulcers
- prospective collection of data on HRQoL during intervention studies.

Qualitative studies

Several studies have used inductive approaches such as phenomenology to enquire about life with a leg ulcer from the patient's perspective.[12–14] Living with chronic pain is a theme that consistently emerges from these studies and yet venous leg ulcers were traditionally not regarded as painful.[12,14,15] Other themes which recur are the restrictions on social, leisure and work activities,[12–14] the hope and despair experienced throughout the long healing trajectory[13,14] and the restrictions that ulceration places on clothing and footwear that can be worn.[14,15]

HRQoL measurement

A number of studies have used established generic measures to capture HRQoL in people with venous leg ulceration. Flett and colleagues[16] compared HRQoL in 14 people with and 14 without leg ulcers using several scales:

- General Disability Spectrum
- the Medical Problems Scale
- an unnamed, nine-item scale for measuring psychosomatic symptoms
- three single-item measures taken from an early version of the SF-36
- the revised UCLA Loneliness Scale
- the Closeness of Relationships scale
- the Short Form of the Affectometer 2.

They found that leg ulceration was associated with significantly greater problems with activity and mobility, significantly more pain, lower levels of self-esteem and higher levels of negative affect.

Roe and colleagues[17] compared HRQoL in 88 people with leg ulceration and 70 people of a similar age without leg ulcers using the NHP, the Life Satisfaction Index, the Hospital Anxiety and Depression Scale, the Short Form McGill Pain Questionnaire and the Health Locus of Control. People with leg ulcers scored significantly worse for pain, energy, life satisfaction and depression.[17] Wissing and colleagues[18] used the Philadelphia Geriatric Center Multilevel Assessment Instrument (PGC MAI) to compare HRQoL in 144 people with and without leg ulcers and reported that people with leg ulcers had significantly lower mean values for physical health, activities of daily living, cognition, time use/social behaviour, personal adjustment and environmental quality. These studies indicate that leg ulcers have a far-reaching impact on various aspects of QoL.

Performance of different HRQoL measures in people with leg ulcers

Walters and colleagues[19] described the discriminative and evaluative properties of four instruments (SF-36; EuroQol; Short Form McGill Pain questionnaire; Frenchay Activities Index) prospectively during a randomised controlled trial (RCT) comparing community leg ulcer clinics with standard care in 233 patients. They concluded that the Short Form McGill Pain Questionnaire was the most responsive at 3 and 12 months, whilst the SF-36 and the EuroQol also detected changes in HRQoL at 12 months. Franks and Moffatt compared the NHP with the SF-36 before and after 12 weeks of high-compression bandaging in 383 patients.[20] Both the NHP and SF-36 had good internal consistency. Whereas the NHP determined that a large proportion of patients had scores of 'best possible health' on entry, it was more sensitive to changes in patients' health status, such as leg ulcer healing, than the SF-36.

Three disease-specific measures of QoL for venous ulcers have been published: the Hyland; the Chronic Venous Insufficiency Questionnaire (CIVIQ) and the Freiburger Questionnaire of QoL in Venous Diseases (FLQA). The oldest measure is the Hyland, which has the disadvantage that it only measures QoL of people with open ulceration.[21] The more recent CIVIQ is a health measure for venous insufficiency and so can be used during and after the healing of venous leg ulcers. CIVIQ measures four dimensions: psychological, physical and social functioning and pain.[22] It has been shown to have good reliability (Cronbach $\alpha > 0.8$ for three out of four dimensions) and reproducibility over time ($r = 0.94$). The FLQA has 83 items within 7 scales. It has been reported to have good validity and sensitivity to changes in health status; however, an English language translation has not been validated.[23]

Cost of venous leg ulceration

There have been few studies of the cost of managing venous leg ulcers in the UK. In 1989, Wilson estimated that the management of active leg ulcers cost the UK £294 million per year,[24] and Laing estimated that venous disease (which includes people without leg ulcers) costs £650 million per year.[25] The greatest element of cost is nursing time. In the UK, most people with leg ulcers are assessed and treated by community nurses either via domiciliary visits or in dedicated leg ulcer clinics and many patients require daily dressings and visits. In 1992, Bosanquet[26] reported that community nurses spent 30–50% of their time dressing leg ulcers. A survey of community nursing activity found that leg ulcer management was the most prevalent 'purpose of visit' with nursing costs alone having been estimated at £100–£180 million per year in the UK.[27]

Effective treatments

Treatment of an active leg ulcer involves management of the wound and compression therapy to reverse the high venous pressures caused by venous incompetence. Several systematic reviews[28–31] have failed to find a major benefit associated with any local treatment of venous leg ulcers, but have concluded that external graduated compression therapy is beneficial. External compression therapy has been used as a treatment for venous insufficiency and leg ulceration since at least the late 19th century. Compression is most commonly applied using bandages, although hosiery and pneumatic devices are also used. The magnitude of applied compression is usually graduated, decreasing from toe to knee. This graduated, external compression has been regarded as the most important element in the conservative treatment of venous leg ulcers for at least a decade.[32]

Compression bandages are made either of highly extensible, elastomeric fibres or of relatively inextensible, short-stretch materials such as cotton and wool. It is imperative that patients are fully assessed by an adequately trained health

professional before the application of compression, since although the majority (70–80%) of leg ulcers are associated with venous disease, at least 20% are associated with peripheral vascular disease (with the two often occurring together). Poorly perfused legs and feet are at high risk of ischaemia if compression bandages are applied and a survey undertaken in Scotland identified 147 reported cases of compression damage over a 5-year period, including seven cases requiring arterial reconstruction and 12 amputations.[33] The measurement of the ratio between arterial pressure at the ankle and arterial pressure at the brachial plexus is widely used as a basic measure of arterial competence – the ankle:brachial pressure (ABPI) or resting pressure index RPI. Generally, patients are regarded as being candidates for compression if their ABPI is ≥ 0.8.

Extending a bandage generates tension in its fibres; this produces a pressure on the limb to which the bandage is applied. Elastomeric bandages, the most widely used in the UK, contain rubber or Lycra and can sustain high pressures for about 1 week, as many patients only need their bandage replaced weekly. Since nursing costs comprise the largest element of the cost of managing venous leg ulcers, any therapy which reduces the necessity for regular nurse visits or clinic time reduces costs to the NHS and inconvenience to the patient. A number of elastomeric bandages are washable, allowing re-use of the bandages if the patient is able to wash them. The inclusion of Lycra or rubber in a bandage means that the washing instructions must be closely adhered to, otherwise the properties of the elastomeric fibres can be affected by heat and the resultant compression application may be altered.[34]

Extensible bandages are classified in the Drug Tariff based on their performance and function. Compression bandages are Type 3 extensible bandages, further subdivided according to their ability to deliver a predetermined level of pressure (see *Table 1*).

Inextensible bandages and supports have been used as a treatment for venous incompetence in mainland Europe, North America and Australasia for decades, but until recently were little used in the UK (although the old-fashioned paste bandages used here have similarities with these systems). In North America, the gold standard compression treatment has long been Unna's boot, a semi-rigid plaster-type dressing wrapped around the leg which hardens to provide compression and a wound dressing. In Europe and Australasia, the short-stretch bandage (SSB) is widely used. SSBs have a number of potential advantages. First, the bandages are made of 100% cotton and hence there is a low likelihood of contact sensitivity (common in patients with venous ulceration) and minimal damage on laundering. Second, the tension in the bandage falls when the patient is resting and therefore the bandage exerts high compression levels only when the patient is active (reported to result in a greater margin of safety as compression levels are lower at night and at rest than elastomeric bandages). SSBs are applied at full stretch, usually over a layer of cotton wadding which protects bony prominences from pressure damage. It has been suggested that SSBs might exert their effect by forming a semi-rigid sleeve against which the calf muscles pump during exercise, thus increasing the pressure within the veins and aiding venous return.

Clinical effectiveness of different bandage systems

A systematic review[35] (updated by Cullum and colleagues[31]) concluded that patients with venous leg ulcers who receive compression therapy are

TABLE 1 *Classification of type 3 (compression) bandages*

Type 3a: Light-compression bandages	Provide and maintain low compression up to 20 mmHg[a] on the average ankle Indications: early varices; varicosis during pregnancy
Type 3b: moderate-compression bandages	Compression up to 30 mmHg[a] on the average ankle. Indications: varicosis during pregnancy; prevention and treatment of ulcers; mild oedema
Type 3c: high-compression bandages	Compression up to 40 mmHg[a] on the average ankle. Indications: gross varices; post-thrombotic venous insufficiency; management of leg ulcers; gross oedema
Type 3d: extra-high-performance compression bandages	Compression in excess of 50 mmHg[a] at the ankle Indications: venous insufficiency; management of leg ulcers; oedema

[a] Pressures based on the assumption that the bandage has been applied as a spiral with 50% overlap at each turn.

more likely to heal than those who do not, and that multilayer high-compression systems are more effective than single layers of bandage or low-pressure alternatives. However, only nine RCTs have compared different high-compression systems (either multilayer or inelastic, high-compression types) and the review was unable to draw any conclusions about their relative merits. To date six trials have compared multilayer high-compression [e.g. four-layer bandages (4LBs)] with inelastic high-compression bandages (e.g. SSBs); however, these trials involved only 328 patients in total, and therefore even taken together they lacked power to detect clinically important differences in leg ulcer healing.

Trials comparing inelastic high compression with multilayer systems

Danielsen and colleagues, 1998[36,37]

This RCT in 43 patients was undertaken in Sweden and compared the SSB over gauze padding (SSB applied in a spiral with 50% overlap between turns; changed every 1 or 2 days) with a long-stretch elastomeric bandage over gauze padding (also applied in a spiral with 50% overlap; changed every 7 days). Outcomes were reported as proportion of initial ulcer area remaining at 1, 6 and 12 months and number of ulcer-free limbs at 1, 6 and 12 months. The latter outcome potentially underestimates the healing rates compared with other trials where incidence of healing is reported. The method of randomisation used for this trial (and hence extent of allocation concealment) was unclear and the outcome assessor is presumed to be aware of the treatment group. Groups were not comparable at baseline for ulcer area, with smaller ulcers in the SSB group. Furthermore, a research nurse applied the bandages in the long-stretch group and a range of community nurses bandaged patients receiving SSBs. There were 43% (9/21) ulcers healed at 6 months in the multilayer bandage group compared with 26% (5/19) ulcers healed in the SSB group.

Duby and colleagues, 1993[38–40]

In this UK-based trial, 63 people with 76 ulcerated legs were randomised between three treatment groups: SSB, 4LB and a paste-bandage three-layer system. All bandages were changed approximately twice per week. Outcomes were reported as ulcers completely healed at 12 weeks and percentage reduction in ulcer area at 12 weeks. The report of this study does not detail the patient inclusion and exclusion criteria, the method of randomisation, whether the outcome assessment was masked to treatment group or whether the analysis was by intention to treat. A total of 44% of patients in the 4LB group were described as healed at 12 weeks compared with 40% in the SSB group.

Knight and McCulloch, 1996[41]

In this USA-based RCT, only 10 patients were randomised (by an undescribed method) to either the 4LB or Unna's boot. No patient in either group healed within the follow-up period.

Moody, 1999[42]

Fifty-two patients were randomised between a long-stretch bandage or an SSB. All patients received orthopaedic wool padding under the bandage. Eight patients in each group of 26 (31%) were completely healed by 12 weeks. Intriguingly, by the end of the study approximately seven patients in each group were able and wiling to apply their own bandages.

Scriven and colleagues, 1998[43]

Fifty-three patients with 64 ulcerated limbs were randomised between the 4LB and the SSB. Patients in the SSB group in this trial also received a cohesive long-stretch bandage over the SSB with the aim of keeping the SSB in place for longer. It was reported that 34% of ulcerated limbs were healed with 4LB at 3 months compared with 41% with SSB (no statistically significant difference); these figures were 55 and 57%, respectively, at 1 year. Unfortunately, the ulcers of patients with multiple ulcers were randomised independently, thus potentially biasing the results. Outcome assessment was blind to treatment group.

Partsch and colleagues, 2001[44]

The largest comparison of 4LB and SSB was undertaken in Austria and The Netherlands and recruited 112 participants. All patients received knitted viscose dressings (the UK standard) underneath their bandages. This study had clear inclusion criteria (presence of venous reflux or history of DVT and stigmata of the post-thrombotic limb), and randomisation was stratified by important prognostic variables. However, the method of randomisation and extent of blinding at outcome assessment were not clear. The primary analysis used a Cox proportional hazards model and reported a higher healing rate under the SSB regime, i.e. 73% at 16 weeks compared with 62% in the 4LB group [hazard ratio (HR) 1.19, 95% confidence interval (CI) 0.73 to 1.91], but this difference was not statistically significant.

It is possible to pool the data from these six RCTs to derive an overall point estimate. However, most of these trials are of poor quality and only the

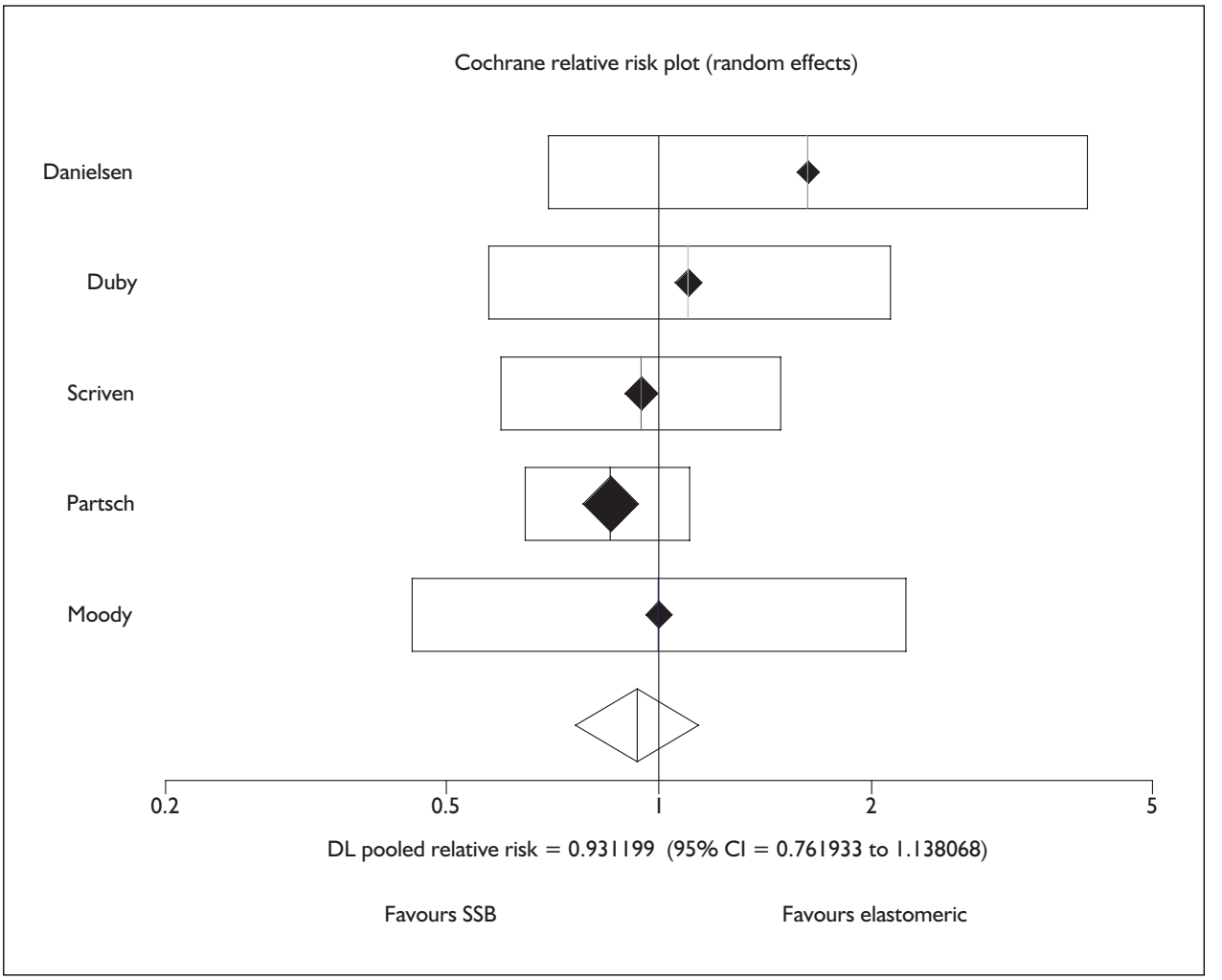

FIGURE 1 *Meta-analysis of RCTs comparing elastomeric high-compression bandages with inelastic high compression, for the outcome of complete ulcer healing during the trial (different durations of follow-up)*

recent trial by Partsch and colleagues used survival analysis and a hazards model to explore time to healing and determinants of healing fully. Apart from that of Partsch and colleagues, these trials reported crude, unadjusted healing data, after different periods of follow-up, and several analysed separate ulcers within an individual patient as independent. The variability in these studies, including variations in the forms of inelastic and multilayer elastic bandage systems used, led us to adopt a random effects model for this meta-analysis (see *Figure 1*). This analysis gives a pooled relative risk of healing for multilayer compared with inelastic compression of 0.93 (95% CI 0.76 to 1.14) (no statistically significant difference).

Background to Venous Ulcer Study (VenUS) trial

Because of the methodological weaknesses of studies identified in the review by Fletcher and colleagues[35] we felt that a study that examined the clinical and cost-effectiveness of different compression systems was justified.

Different bandage systems have different performance and economic characteristics, which make their comparison in a large RCT particularly worthwhile. The reusability and low cost price of the SSB (between £3.08 and £4.08 for a 10-cm wide bandage plus padding at 2001 prices), compared with a cost of approximately £8 for the disposable 4LB, makes a strong economic argument for a robust head-to-head comparison with economic evaluation. During the execution of our trial, the completion of new studies, particularly the trial of Partsch and colleagues did not alter our view that a large RCT of the SSB and 4LB was required. In 1996, the NHS HTA programme put out a call for a large RCT of different compression systems. In our application, we sought to test the hypothesis that the SSB would be more cost-effective than the 4LB.

Chapter 2
Methods

Design of trial

A pragmatic RCT to compare the clinical and cost-effectiveness of four layer and short-stretch compression bandages for healing venous leg ulcers.

The Northern and Yorkshire Multicentre Research Ethics Committee (MREC) approved the final protocol on 18 June 1998. The details of MREC and Local Research Ethics Committee (LREC) approval are provided in Appendix 1.

Sample size

The sample size calculation was based on the proportion of patients achieving complete ulcer healing at 12 weeks. Rates of healing under 4LB quoted in the literature range between 34 and 70% at 12 weeks.[31] Using a conservative estimate of 50% of ulcers healed at 12 weeks with 4LB, and assuming that an absolute increase in ulcers healed of 15% would be worthwhile, we calculated that 400 patients (200 in each arm) would give us 80% power to detect an increase in healing rates from 50 to 65% at 12 weeks (α = 5%) [see Consolidated Standards of Reporting Trials (CONSORT) Statement 7a].

Trial sites

The study was conducted in nine areas: four large sites (North Yorkshire; Leeds; West London; Cumbria) and five smaller sites (Calderdale, West Yorkshire; East London; Falkirk, Scotland; Newmarket, Cambridgeshire; Southport, Merseyside). The centres represented a range of urban and rural settings and also a number of different models of leg ulcer service (domiciliary visits; nurse-led community clinics; tertiary referral clinics, etc.) (CONSORT Statement 3b).

Clinical collaborators from four large clinical centres were involved in the development of the trial protocol and recruited patients from April 1999 to December 2000. Details of the study sites are provided in Appendix 2.

Patient entry to the trial

The precise route by which patients entered the trial depended on the participating centre. Community nurses or trial nurses recruited people to the trial during a routine scheduled consultation, either during a home visit or in a clinic. Any nurse responsible for the day to day care of a patient with a leg ulcer, or the local research nurse, could enrol a patient into the trial (CONSORT Statement 10b). All patients with new, existing or recurrent ulceration who fulfilled the criteria (below) were considered for entry into the trial.

Patients with existing ulceration were eligible for inclusion as it was assumed that they could still benefit from improved healing rates given the opportunity of entering the trial. As the treatments under evaluation do not have any systemic effect, a period of washout was considered unnecessary. Patients who had previously failed to improve while using one of the trial bandages were excluded as it was considered unethical to randomise them to a previously discarded treatment.

The nurse considering recruiting a patient to the trial made an informal assessment of the ability of the patient to consider the purpose and responsibilities of taking part in the trial. In the event that they were considered able to understand the objectives of the trial and their role, then the patient was provided with written and verbal information about the trial and invited to participate (see Appendix 3). The patient was given a minimum of 24 hours to consider the information and make a decision.

Eligibility criteria

All persons presenting to one of the trial centres, whether to the leg ulcer clinic or to the community nursing service, who had a venous leg ulcer of at least 1 week's duration, at least 1 cm in length or width, were candidates for inclusion in the study (CONSORT Statement 3a). The clinician made a diagnosis of venous ulceration by observing signs of venous disease (e.g. lipodermatosclerosis, varicose veins or a history of DVT) and excluding the presence of arterial

disease (i.e. ABPI of at least 0.8). People with diabetes were not eligible for inclusion since they are regarded as at higher risk of compression damage due to increased microvascular disease.

Where a patient presented with multiple ulcers (on either one leg or both), the largest ulcer was chosen as the 'reference' ulcer and follow-up was continued until all ulcers on the trial leg had healed. Although relatively few people have bilateral ulcers, it would be inappropriate to recruit both legs into the trial as they could not be regarded as independent for the purposes of statistical analysis. We therefore recruited the leg with the 'worst prognosis' based on the assumption that the second leg will have healed already at the primary end-point.

Patients previously enrolled into the study were not eligible for re-randomisation into the trial when an ulcer recurred or new ulcers developed.

Baseline assessment

Once the recruiting nurse had discussed the trial and had completed the consent form with the patient, she undertook the baseline assessment. The following data were collected.

Area of the reference ulcer

The ulcer outline was traced on to an acetate film grid, and the area was estimated by counting the number of whole and partial squares falling mainly within the ulcer outline. This method is accurate and reliable.[45] Ulcer area was required at randomisation for the purposes of stratification. After randomisation, the original ulcer tracing was forwarded to the Trial Coordinator and the ulcer area was accurately calculated by computerised planimetry.

Measurement of ankle brachial pressure index (ABPI)

The ABPI was measured using a mercury sphygmomanometer and a hand-held Doppler ultrasound probe using a standardised technique.[46] The patient lay supine for at least 10 minutes prior to measurement of the systolic pressure in the arm and at the ankle. A minimum of two systolic pressures were measured at the ankle, using the peroneal, posterior tibial and dorsalis pedis arteries. To calculate the ABPI, the highest ankle pressure was divided by the higher of the two arm systolic pressures. Values of <0.8 show that peak arterial blood pressure at the ankle is significantly less than that in the arm, indicating a degree of arterial insufficiency. National clinical practice guidelines state that compression bandages should only be used where there is adequate arterial supply, commonly defined as an ABPI of ≥ 0.8.

Ulcer duration

The duration of ulceration, in months, as reported by the patient, was recorded. This information was necessary for stratification of randomisation as longer duration is associated with longer time to healing.[9,47]

Ulcer episode

One previous study demonstrated that recurrent ulcers healed more slowly.[47] Randomisation was stratified by number of ulcer episodes as reported by the patient.

Sex

This was recorded in order to describe the population recruited and to allow comparison with the general population of people with venous ulcers, in which women outnumber men.[48]

Date of birth

Age at recruitment was derived from the patient's date of birth. Increased age was associated with slower healing rates in one study,[47] therefore age would be considered as a potential factor influencing healing. Only patients of 18 years and over were entered into the trial.

Ankle circumference

The circumference of the ankle at the start of the trial was measured at its narrowest point. This was necessary to assess whether having a large ankle circumference is associated with slower healing. Laplace's law as applied to compression bandaging states that for a higher circumference limb, a compression bandage needs to be applied at a higher tension in order to generate the same level of compression. This means that larger limbs/ankles may require stronger bandages to apply therapeutic levels of compression.

The precise choice of 4LB regimen depends on the ankle circumference (<18 cm, 18–25 cm or >25 cm) and ankle circumference is measured routinely in order to choose the appropriate formulation of 4LB.

Ulcer position

A record of the position of all ulcers on the trial leg including the reference ulcer was made.

Ankle mobility

The patient's ankle mobility was recorded as this may be a risk factor for healing.[49] Venous return is

assisted by flexion of the ankle and contraction of the calf muscle. This leads to high pressures in the tissues surrounding the veins of the leg, and the pressure changes in conjunction with one-way valves in the veins propel blood towards the heart. This mechanism is called the calf pump. The SSB system is thought to work by providing a firm outer bandage layer which does not yield when the calf muscle contracts. This means that the high pressure in the leg compresses the deep veins and propels blood up towards the heart, reducing oedema and venous hypertension. Hence these bandages are thought to depend, to some extent, on the patients' ability to flex their ankle. By contrast, the 4LB system is made up of elastic layers that apply constant high pressures and are reported to encourage venous return regardless of the calf muscle pump. These layers do yield when the ankle is flexed, and there are relatively small changes in sub-bandage pressure. There may be an interaction, therefore, between ankle mobility and bandage effectiveness.

Patient mobility

During walking, the foot is slightly flattened at each step, at the moment of contact with the floor. This causes the plexus of veins in the foot to empty, venous blood being forced up towards the calf veins (and the calf pump). This 'foot pump' may contribute to ulcer healing. Whether the patient is fully mobile without an aid, uses an aid and is mobile, or is chair- or bed-bound was recorded in order to allow us to explore whether there was any relationship between the effectiveness of the two compression systems and patients' mobility levels.

Polaroid photograph

A dated photograph of the reference ulcer with grid film was taken at baseline to provide a visual record of ulcer size and condition at enrolment. These data were recorded on the trial entry form (see Appendix 4).

Health-related quality of life

The patient was given a QoL questionnaire booklet to complete immediately after recruitment. This was designed to be filled in by the patient and returned to the Trial Coordination Office using a reply-paid envelope. The questionnaire comprised three tools; a generic HRQoL profile, a generic utility measure and an ulcer-specific HRQoL measure.

In order to ensure that any small changes in HRQoL specifically associated with leg ulceration were recorded, the Hyland Leg and Foot Ulcer Questionnaire (HLFUQ) (a leg ulcer-specific measure) was also used.[21] The HLFUQ is a 34-item instrument derived from conversations with patients and measures HRQoL across four categories: pain; restriction of activities; mood and feelings; and ulcer preoccupation and treatment.[21] To the best of our knowledge, this instrument has not been previously used as an outcome measure in an intervention study and we therefore decided to test its validity and reliability.

Allocation to treatment

After the baseline clinical assessment was completed, the nurse recruiting the patient telephoned the Randomisation Service at the Trial Support Unit, Department of Health Sciences, University of York (freephone number). This service was open from 8.30 to 17.30 Monday to Friday. The person staffing the randomisation service would ask the nurse for the patient's name, address and stratification variables (ulcer area, duration, episode and trial centre) prior to revealing the allocation and study number, hence allocation was concealed until randomisation (CONSORT Statement 10b).

The clinician was asked to provide the following information for randomisation:

- **Clinical Centre**: Cumbria, Leeds, West London, North Yorkshire or 'Other' site (covering the five smaller centres).
- **Area of ulcer**: two strata: >10 and ≤ 10 cm^2.
- **Ulcer episode**: two strata: first or recurrent ulcer.
- **Ulcer duration**: two strata: duration ≤ 6 or >6 months.

Patients had an equal probability of assignment to either treatment group. The randomisation code was developed using computer-generated permuted blocks, which were randomly of size four or six (CONSORT Statement 8a). The allocation sequence was generated by the trial statistician (AF) in the Trial Support Unit, Department of Health Sciences, University of York (CONSORT Statement 10a).

Initiation of allocated treatment, including blinding

At randomisation, the nurse applied the allocated bandage system (4LB or SSB as described in Appendix 5) at that visit. Community nurses and leg ulcer clinics were supplied with sufficient bandages to allow immediate supply of the allocated system. A letter was sent to the patient's GP informing them of the treatment allocation.

As the two bandage systems are different in appearance, it was not possible to blind the patient or nurse to the allocated treatment.

Interventions (CONSORT Statement 4)

Four-layer bandage

4LB systems are available in proprietary kit form (not prescribable on the NHS) and the individual components are available as separate items (these are prescribable). One of the kits (Profore®, Smith and Nephew) has been demonstrated to have similar effectiveness to the original system developed at Charing Cross Hospital.[50] Within the trial, any of the following were permitted for patients allocated to the 4LB arm:

- Profore (Smith and Nephew)
- System 4 (SSL)
- Original 4LB.[51]

For participants with an ankle circumference between 18 and 25 cm, the bandages used are listed in *Table 2*.

Two layers of the padding bandage were used for participants with an ankle circumference of <18 cm.

The third bandage layer was a class 3C high-compression bandage such as Tensopress [Tensopress® Class 3C elastomeric compression bandage (Smith and Nephew)] for participants with an ankle circumference >25 cm.

All the 4LB components were used once only and then discarded, according to the manufacturers' instructions. Bandages 10 cm wide were used throughout.

Both bandage systems were applied on the day of trial entry and were then replaced as dictated by clinical need, until complete ulcer healing on the trial leg.

Short-stretch bandage

A multilayer SSB system was used; the first layer was orthopaedic wool padding and the upper layers were cotton SSBs. Comprilan [Comprilan® 100% cotton bandage (Beiersdorf)] or Rosidal K [Rosidal K® 100% cotton bandage (Lohmann Rauscher)] was used throughout. Nurses were trained to apply the SSB using any one of three techniques:

1. Spiral technique: two bandages are applied at full extension in opposite directions up the leg (i.e. clockwise and counter-clockwise) with 50% overlap.
2. Figure-of-eight technique: two bandages are applied at full extension in a figure-of-eight formation, in opposite directions up the leg (i.e. clockwise and counter-clockwise) with 50% overlap.
3. Modified Putter technique: two bandages are applied at full extension, in opposite directions up the leg (i.e. clockwise and counter-clockwise). The position of the bandage is dictated by the curvature of the leg rather than following a conventional spiral of figure-of-eight. Overlap is variable.

TABLE 2 *Four-layer bandage systems and method of application (ankle circumference 18–25 cm)*

Profore[a]	System 4[b]	Original 4-layer
Soffban[c]: spiral	Softexe[d]: spiral	Velband[e]/Soffban[c]: spiral
Soffcrepe[f]: spiral	Setocrepe[g]: spiral	Crepe BP: spiral
Litepress[h]: figure-of-eight	Elset[i]: figure-of-eight	Elset[i]: figure-of-eight
Co-Plus[j]: spiral	Coban[k]: spiral	Coban[k]: spiral

[a] Profore®, Smith and Nephew.
[b] System 4®, SSL International.
[c] Soffban®, orthopaedic wool padding bandage, Smith and Nephew.
[d] Softexe®, orthopaedic wool padding bandage, SSL International.
[e] Velband®, orthopaedic wool padding bandage, Johnson & Johnson Ltd.
[f] Soffcrepe®, cotton crêpe bandage, Smith and Nephew.
[g] Setocrepe®, cotton crêpe bandage; SSL International.
[h] Litepress®, class 3A elastomeric compression bandage, Smith and Nephew.
[i] Elset®, class 3A elastomeric compression bandage, SSL International.
[j] Co-Plus®, cohesive, elastomeric compression bandage, Smith and Nephew.
[k] Coban®, cohesive, elastomeric compression bandage, 3M.

There are different widths of SSBs available. The nurses were advised to choose a narrower bandage, 6 or 8 cm, for narrow legs, 10 cm for the majority of legs and 12 cm for larger limbs.

One previous trial had reported significant slippage of the SSB system when it was applied in a spiral technique.[43] Slippage was reduced by training nurses in the use of the modified Putter technique, where bandage layers are anchored above the knee. In the event of bandage slippage, however, the protocol allowed an additional, cohesive bandaging layer (Coban, 3M) over the short-stretch system.

The SSB was removed by unwinding and, wherever possible, was washed by the patient and reused.

Nurse training

Workshops were held at all the recruiting sites in order to introduce the background to the trial, trial documentation and coordination team and for training in the trial bandages (supported by a nurse representative from Beiersdorf UK) (Appendix 6). A training cascade was used, where the nurses who attended the workshops were provided with bandages and training materials (leaflets, contact information) to allow them to train colleagues. This approach reflects standard practice when new bandages or dressings are introduced. It also reflects the pragmatic nature of this trial.

The timetable for trial training is presented in Appendix 6.

Follow-up assessments

A dressing log was used to record the date of each visit for leg ulcer care, regardless of setting (see Appendix 4). The nurse also recorded, on the dressing log, the following:

- the reason for the visit (e.g. planned or unplanned visit)
- the number of new bandages used at each visit
- the use of wound cleansers (such as tap water, sterile saline)
- the number and size of primary and secondary dressings
- use of skin preparations (treatments for eczema, emollients).

There was also a free text section for the nurse to record reasons for any changes in treatment.

At the first visit, a simple, low-adherent knitted viscose primary dressing was applied to the ulcer, with secondary dressings as necessary to absorb exudate. Nurses were permitted to use other primary dressings only if there were clinical indications, such as ulcer pain or maceration of the periulcer skin.

The nurse responsible for the care of the trial patient decided upon the remainder of the plan of care, such as the frequency of dressing and bandage changes. General measures such as the provision of nutritional advice were permitted within the protocol.

Clinical follow-up

The nurses responsible for each patient were asked to complete a reassessment form every 4 weeks until healing. This form asked whether there had been any adverse events and prompted the nurse to trace all the ulcers on the trial leg. *Table 3* describes the progress of patients throughout the trial with reference to the assessments during that period. Follow-up of patients continued from randomisation until December 2001.

Adverse events

An adverse event can be defined as "any undesirable clinical occurrence in a subject, whether it is considered to be device related or not".[45] Both device-related and unrelated adverse effects were reported to the trial office on the monthly assessment form. The reporting clinician indicated whether the event was related to the bandage or the trial or not. We established a list of possible bandage-related adverse events *a priori*, based on reports in the literature, as follows.

Pressure damage

Excessively high levels of compression or the inappropriate application of compression can lead to pressure damage and, in a small number of cases, amputation,[46] although frequently these adverse outcomes are not well described in research reports. Pressure damage presents either on pressure areas (areas of small radius and/or little padding) such as the malleoli, Achilles tendon or the front of the foot; pressure damage is indicated by non-blanching erythema. Bands of high pressure on the leg can result in lines of skin damage along the lines of the bandage. Assessment of the skin of the leg after each bandage removal is a fundamental part of leg ulcer management.

TABLE 3 *Points during a patient's trial career at which data were collected*

Month in trial	Ulcer tracing[a] and clinical assessment	Resource use questionnaire[b]	HRQoL questionnaire[b]
0	×	×	×
1, 2	×	×	
3	×	×	×
4, 5	×	×	
6	×	×	×
7, 8	×	×	
9	×	×	×
10, 11	×	×	
12	×	×	×
13, 14, 15, 16, 17	×	×	
18	×	×	×
19, 20, 21, 22, 23	×	×	
24	×	×	×
25, 26, 27, 28, 29	×	×	
30	×	×	×

[a] Every month, while the ulcer is open only.
[b] Whether the ulcer was open or healed.

Maceration, excoriation and infection

Compression bandages may keep wound exudate in contact with the skin surrounding the ulcer, leading to maceration of the peri-ulcer skin. Occlusion of the ulcer and the skin provides a moist environment, which may encourage fungal and bacterial infections of the peri-ulcer skin or the ulcer itself. Maceration presents as swollen, white, soggy skin. Excoriation is the appearance of red, inflamed skin around the ulcer, thought to be due to wound exudate which contains enzymes. Infection usually presents with a combination of any or all of inflammation, pain, odour, heat and purulent discharge. Nurses were discouraged from routinely swabbing ulcers as this is a notoriously unreliable and costly method of ascertaining infection.

Pain

The nature of pain associated with leg ulceration is poorly understood. Until 10–15 years ago, the absence of pain was said to be diagnostic of a venous pathology, whereas painful ulcers were assumed to be arterial. Research investigating the impact of a leg ulcer on QoL has demonstrated that pain is one of the most troublesome aspects of having a venous leg ulcer.[17] Roe and colleagues reported that 23% of leg ulcer patients said they sometimes removed 'uncomfortable' compression stockings or bandages as they were too loose, too tight or too hot.[17] If two compression systems were equally effective at healing leg ulcers but one was associated with less pain, then that would be the preferred system. In order to determine whether there were any differences in the tolerance of the compression systems, any adverse event reports of pain were recorded and compared.

Ulcer deterioration

Assessment of the progress of ulcer healing is complex and includes assessment of the colour of the wound bed, e.g. pink or red indicates epithelialising or granulation tissue, whereas yellow slough or green/blue/black colours indicate the presence of infection. Ulcer area is also assessed, although the trajectory of venous ulcer healing is not necessarily linear, and therefore assessment of progress can be difficult. If an ulcer has necrotic tissue edges then the autolysis of this dead matter, under compression, may lead to an **apparent** increase in the area of the ulcer. Ulcer deterioration included increase in ulcer area, apparent infection, malodour, apparent allergy and ulcer bleeding.

Nurses were requested to report all adverse events on the monthly assessment form and state whether they considered them to be related to the trial bandage. Nurses were asked to report serious adverse events, such as admission to hospital, to the Trial Coordination Office by telephone. The Trial Coordinator followed up all adverse events so that information on eventual outcomes was recorded.

Withdrawals

Patients were considered as withdrawn from the trial if they requested to leave the trial, if they were lost to follow-up or if they died with the ulcer not having healed.

Patients were considered as withdrawals from the allocated treatment if they no longer received the compression system originally allocated. Nurses were asked to keep the patient in the original bandage system unless there were objective measures of deterioration such as increased pain or increase in ulcer area at two consecutive monthly assessments. Patients were also considered withdrawals from the trial bandage if they were admitted to hospital or if they commenced a non-trial leg ulcer treatment (e.g. therapeutic ultrasound, intermittent pneumatic compression).

Withdrawals from the trial and from allocated treatment were included in the analysis by intention-to-treat (ITT).

Measurement and verification of primary and secondary outcome measures

The primary end-point was time to healing of all ulcers on the trial leg. Secondary outcomes were the proportion of patients healed at 12 and 24 weeks, the rate of epithelialisation of the reference ulcer, costs of leg ulcer treatment and QoL.

Determination of ulcer healing

The definition of a healed ulcer was 'complete epithelial cover in the absence of a scab'. The nurse treating the patient (and the Trial Coordinator) was able to monitor the response of the ulcer through reduction in ulcer area. At the point of healing, the nurse responsible for the patient's care took a Polaroid photograph of the healed ulcer and sent this to the Trial Coordination Office. An investigator unaware of the bandage allocation confirmed ulcer healing. This partially masked outcome assessment as the clinician only took a photograph when he/she had already decided the ulcer was healed.

Ulcer area

Ulcer area was monitored until healing by monthly tracing of the ulcer on to acetate film and a dated Polaroid photograph both at baseline and at healing. The tracings were made using a fine indelible marker on to conformable acetate film with a preprinted grid. Standard methods of ulcer tracing were used throughout the study centres to reduce systematic error. Tracings were sent to the Trial Coordination Office at the University of York. Baseline wound area was measured using computerised planimetry, which is a simple method of area measurement using the mouse of a personal computer to trace the ulcer outline. A computer program, 'Mouseyes', calculates the ulcer area.[52] Serial tracings of ulcers were used to corroborate the primary end point and to identify ulcer deterioration (see the section Adverse events, p. 11). Data relating to the rate of epithelialisation as a secondary endpoint will be reported separately.

Neither the patients nor the nurses administering the bandages and giving the associated care could be blinded to the allocated treatment at any time, as the two bandage systems were very different in appearance. The nurse providing the regular leg ulcer care was responsible for documenting the assessments of ulcer progress every 4 weeks, including tracing the ulcer outline. These outcome assessors were therefore not blinded. The ulcer tracing was sent to the Trial Coordination Office where the ulcer area was determined by computerised planimetry by a researcher masked to bandage allocation.

The nurse usually responsible for care of the leg ulcer patient was also responsible for identifying the point at which the ulcer was healed. In order to confirm the end-point, a Polaroid photograph of the healed ulcer was taken by the nurse and sent to the Trial Coordination Office, where healing was confirmed by a researcher blinded to the bandage allocation (CONSORT Statement 11).

Collection of resource use data

At recruitment and monthly intervals thereafter, patients were asked to complete a questionnaire on health and social care resource use during the previous month. This was designed to be completed by the patient and returned to the Trial Coordination Office using a reply-paid envelope. Patients indicated how many times in the previous month they had used health services (seen a doctor or a nurse, being at hospital), for reasons related and unrelated to their leg ulcer treatment, and where these encounters had taken place (home, hospital).

Clinical analysis

All clinical trial documentation was scanned and the data were entered into a database (Microsoft Access) throughout the trial in order to generate trial follow-up. Data were analysed using SPSS for Windows Version 10.0.

Trial CONSORT chart and demographic characteristics

A CONSORT chart for the trial was constructed. Patients were classified as lost to follow-up when for reasons unknown to their nurses and the Trial Coordination Office contact was lost. When the patients discontinued their allocated treatment but had not withdrawn from the trial, they were followed up and classified as having discontinued the intervention. Trial violators were defined as those patients who did not fulfil all the trial inclusion criteria but were inadvertently recruited to the study.

A descriptive analysis of the individuals in both bandage groups was conducted according to the following baseline clinical and demographic characteristics:

- sex
- duration of ulcer disease on the reference leg (i.e. time since first ulceration)
- number of ulcer episodes
- level of mobility
- level of ankle mobility
- height
- weight
- ankle circumference
- duration of reference ulcer
- ulcer appearance
- skin condition
- area of reference ulcer
- age
- ABPI measurement
- scores on Hyland questionnaire
- scores on EQ-5D
- scores on SF-12.

Secondary outcome measures

Secondary outcomes were the proportion of patients healed at 12 and 24 weeks, total number of adverse events, recurrence rates, costs and QoL.

The primary analysis was by ITT and compared the time to complete healing of all ulcers on the trial leg, between the individuals randomised into the two bandage groups. Time to censoring was defined as the point in time when the follow-up of a patient ceased without the ulcer healing. There were several reasons for censoring, including end of study period, patient's death, loss to follow-up for reasons unrelated to the treatment. Kaplan–Meier survival curves were constructed for the two bandage groups. The statistical significance of the difference between the Kaplan–Meier curves of the two bandage groups was tested using the log-rank test.

To investigate the effects of previously identified prognostic factors for ulcer healing, a Cox regression model was fitted to the time to complete healing data. Potential prognostic factors considered were centre, ulcer area, ulcer duration, ulcer episode, age, weight, mobility, ankle mobility and ABPI. The identification of the relevant variables which best described the hazard of healing of individuals with leg ulcers was performed using a procedure described by Collet,[71] in which the difference between the statistic –2log(likelihood) associated with the models being compared is used as the criterion of best model fitting. The assumption of proportionality of hazards between treatment groups was checked using the log cumulative hazard plots, i.e. $\log\{-\log[S(t)]\}$ plotted against $\log t$, where $S(t)$ are the Kaplan–Meier estimates of the cumulative distribution of healing times.

Missing data from the demographic and clinical variables considered in the Cox model were imputed using the mean/mode per trial arm associated with the variables to be imputed.

Proportions of ulcers healed at 12 and 24 weeks

Proportions of ulcers healed at 12 and 24 weeks were compared using the Kaplan–Meier estimates of the cumulative probability of healing in each bandage group at each of these two points in time.[53]

Adverse events

We described the type and frequency of adverse events (AEs) reported by nurses, both those considered by the clinical nurse to be 'related to the bandage' (treatment-related AEs) and those unrelated to the bandage (treatment-unrelated AEs). The numbers of both related and unrelated AEs were examined by bandage group.

Recurrence rates

Nurses were asked to complete a recurrence slip with the exact date of an ulcer's recurrence reported by the patient. Recurrence was defined as a break of the skin on the trial's reference leg. Time to ulcer recurrence was measured as the

difference in days between patient's healing and recurrence dates. These data were analysed in an ITT survival analysis. Time to censoring was defined as the point in time when the follow-up of a patient ceased without any notification of an ulcer having recurred on the trial leg. Kaplan–Meier survival curves were constructed for the two bandage groups. The statistical significance of the difference between the Kaplan–Meier curves of the two bandage groups was tested using the log-rank test.

Health related quality of life

Patients were asked to complete a survey describing their QoL during the 3 months preceding recruitment and at quarterly intervals thereafter. The survey was designed to be completed by the patient and returned to the Trial Coordination Office using a prepaid envelope. Patients were asked to complete three different HRQoL instruments: two generic (EuroQol and SF-12) and one leg ulcer-specific questionnaire (Hyland).[21]

EuroQol

The EQ-5D is a generic measure of health status, where health is characterised on five dimensions (mobility, self-care, ability to undertake usual activities, pain, anxiety/depression).[54] Patients are asked to describe their level of health on each dimension using one of three levels: no problems, moderate problems and severe problems. Each response locates a person into one of 245 mutually exclusive health states, each of which has previously been valued on the 0 (equivalent to dead) to 1 (equivalent to good health) 'utility' scale based on interviews with a sample of 3395 members of the UK public.[55] The utility values for the EQ-5D range from –0.57 to 1, where negative utility values represent health states that the general public has considered to be worse than dead.

Utility scores for each patient were calculated at baseline and every 3 months afterwards during the first year of follow up and 6-monthly thereafter. Mean scores for each trial arm at each time point were estimated together with 95% CIs for the differences between bandage groups.

SF-12

The SF-12 is derived from a health profile and measures physical and mental components of HRQoL.[56] In a pilot study of our health outcome measurement instruments we identified that the original 'stem and leaf' layout of the SF-12 presented some difficulties for our elderly population. Consequently, we modified the layout of the SF-12 and used this new version throughout the follow-up period.[57]

The scores for the physical and mental components of the SF-12, and also the scores for its eight individual health dimensions, were calculated at baseline and every subsequent 3 months for the first year of follow-up. Mean scores for each time point were calculated. To facilitate the interpretation and comparison of our results with those from other studies, all scores were base-norm to the average mean values of the general US population, that is, scores were transformed to be distributed with a mean of 50 and a standard deviation (SD) of 10. Consequently, any values below/above 50 indicate that the physical or mental components of the population under study are below/above the average of the general US population.

Hyland leg and foot ulcer questionnaire

The Hyland QoL scale for leg ulcer patients has good face validity and has been constructed using a reasonably sound psychometric methodology.[21] However, the sample size for the factor analysis in the original study was extremely small given the number of items that comprise the scale. This trial provided an opportunity to validate this scale in a larger sample to determine the factorial structure of this scale and check the reliability and concurrent validity.

The original paper presents evidence for a one factor solution using principle components analysis.[21] The data collected in the VenUS study were factor analysed using principal-axis factoring in SPSS 10. Examination of the scree plot[58] indicated a two-factor solution. The scree plot was used as an indication of number of factors both here and in the original scale construction, as opposed to the criterion of those with an eigenvalue >1 since the scree plot provides a more conservative estimate of the number of factors and produces less shared variance. Principal-axis factoring using a Varimax orthogonal rotation was used as this form of factor analysis seeks the least number of factors to account for the common variance of a set of variables. This is a more conservative analysis than the principal components analysis used in the original scale construction. An exclusion criterion of 0.3 was employed.

A simple scoring system of adding one point for every 'yes' response to a negative attribute was used to score the instrument. Consequently,

higher scores indicate a poorer state of HRQoL. Mean scores for the practical and mental factors identified on the Hyland questionnaire were calculated at baseline and every 3 months thereafter during the first year of follow-up.

Economic analysis

Both a cost-effectiveness analysis and a cost–utility analysis were performed using patient-level data collected alongside the VenUS Leg Ulcer trial. The perspective for the economic analysis was that of the UK NHS and Personal Social Service.[59] The time horizon for the analysis was 1 year after recruitment.

Resource use (data collection)

During visits for the primary purpose of leg ulcer care, nurses were asked to complete a dressing log form describing the reason for the visit, total number of new bandages used, wound cleanser used, number and size of primary and secondary dressing and the use of any skin preparation (Appendix 4). Dressing logs were returned to the Trial Coordination Office on a monthly basis using a reply-paid envelope.

At recruitment and monthly intervals thereafter, patients were asked to complete a questionnaire on health and social care resource use during the previous month (Appendix 4). This was designed to be completed by the patient and returned to the Trial Coordination Office using a reply-paid envelope. Patients indicated how many times in the previous month they had used health services (for example, had seen a doctor or nurse or had they received care in hospital, outpatients, community clinic or their own home).

Volume of resources used

Four different types of resource use were included in the estimation of costs: number of nurse visits, number of doctor visits, number of hospital visits and number of bandages used. Information regarding wound cleansers, number and size of primary and secondary dressings and the use of skin preparations was not included in the economic analysis since they are common to both compression systems, hence their effect will be expected to cancel out in the incremental analysis of costs.[60]

Unit cost

All costs were measured using 2001 prices. Costs of nurse and doctor visits were estimated using the unit cost of community-based healthcare staff.[61] In the base case analysis it was considered that a nurse visit for leg ulcer care took 22 minutes in a clinic and 40 minutes at home.[61] The estimates were in agreement with the results from a survey of the times taken for nurses to see a patient and apply each of the trial bandage (see Appendix 7). Visits to hospital were costed based on average outpatient costs per day visits costs to value the resource use measured in trial.[61] Acquisition costs of the different bandage systems were taken from the retail prices quoted in the *British National Formulary*.[62] The time horizon for the economic analysis was no longer than 1 year, therefore costs did not need to be discounted.

Health benefits

Health benefits were measured in two ways in the economic analysis. First, Kaplan–Meier estimates of mean time to healing over a 12-month horizon in each trial arm were considered. These in turn were used to estimate the difference in ulcer free days. In the second, quality-adjusted life-years (QALYs) were used.

Kaplan–Meier estimates of mean time to healing over 12 months per trial arm were estimated using the information from the primary clinical analysis by ITT.

QALYs were estimated using the responses to the EuroQol questionnaire included in the patient's quarterly QoL survey (Appendix 4). EuroQol scores at baseline and every 3 months thereafter during the first year of follow-up were estimated, that is, each patient could have a utility value at up to five time points. QALYs were calculated for each patient using the area under the curve defined by his or her EuroQol scores over time. Given that the analysis was concerned with a single year, our two measures of health benefit, mean time to healing and QALYs, were left undiscounted. QALYs were adjusted by the Kaplan–Maier estimates of patients' survival over 1 year.

The two compression systems were then compared in terms of both the costs and the health benefits associated with the technologies, using economic evaluation analysis. The exact form that an economic evaluation takes depends mainly on the way in which health benefits associated with the technology are measured, so that the measurement is both clinically and economically relevant.[63] As described above, in this trial the health benefits associated with the SSB and the four-layer compression system were measured in terms of both a natural unit (ulcer-free days) and changes in QoL (QALYs). In turn, this allowed us

to conduct two different types of analyses, a cost-effectiveness analysis where health benefits are measured in natural units, and a cost–utility analysis were health benefit measurement is adjusted by changes in QoL.

The decision regarding which of the two technologies is more cost-effective is based on the incremental cost-effectiveness ratio (ICER). The ICER is defined by the ratio of the difference in costs relative to the difference in health benefit associated with the technology under evaluation:

$$\text{ICER} = \frac{c_1 - c_0}{B_1 - B_0}$$

where c_1 = mean cost associated with the technology under evaluation (SSB); c_0 = mean cost associated with the technology of comparison (4LB); B_1 = mean health benefit associated with the technology under evaluation (SSB); and B_0 = mean health benefit associated with the technology of comparison (4LB)

Possible values of the mean ICER can be represented in a Cartesian plane, better known as the cost-effectiveness plane (see *Figure 2*). Incremental analysis (such as that described above) is justified in a situation of absence of dominance, that is, where neither technology under evaluation is dominant (associated with lower costs and greater health benefit than the comparator). In other words, an incremental analysis is justified when the ICER does not fall on the second or fourth quadrant of the cost-effectiveness plane (see *Figure 2*). When the mean ICER is on either the first or third quadrant of the cost-effectiveness plane, a decision rule is needed. In this case, if the ICER associated with the technology is smaller than the decision-makers' maximum threshold value for an extra unit of health benefit, then the technology under evaluation can be deemed to be potentially cost-effective.

Statistical analysis

The economic analysis was conducted using Stata 7 (StataCorp 2000 Stata Statistical Software: Release 7.0; Stata Corporation, College Station, TX, USA). The volume of resources used per month was summarised using simple descriptive statistics. Given the censored nature of cost data (information regarding patient's resource use may be truncated at any point in time before the end of the study because of closure of the ulcer, loss to follow-up, patients' own request, etc.), the Lin method was used to estimate mean total treatment cost per trial arm.[64] The total minimum follow-up period (1 year) was divided into monthly periods, and mean total costs per period were then estimated and adjusted by the Kaplan–Meier estimates of the probability of non-healing per period. Mean total cost was then estimated as the sum of the adjusted mean total cost per period:

$$\textit{KMSA (Kaplan–Meier Sample Average)} = \sum_{i=1}^{n} \bar{c}_i S_i$$

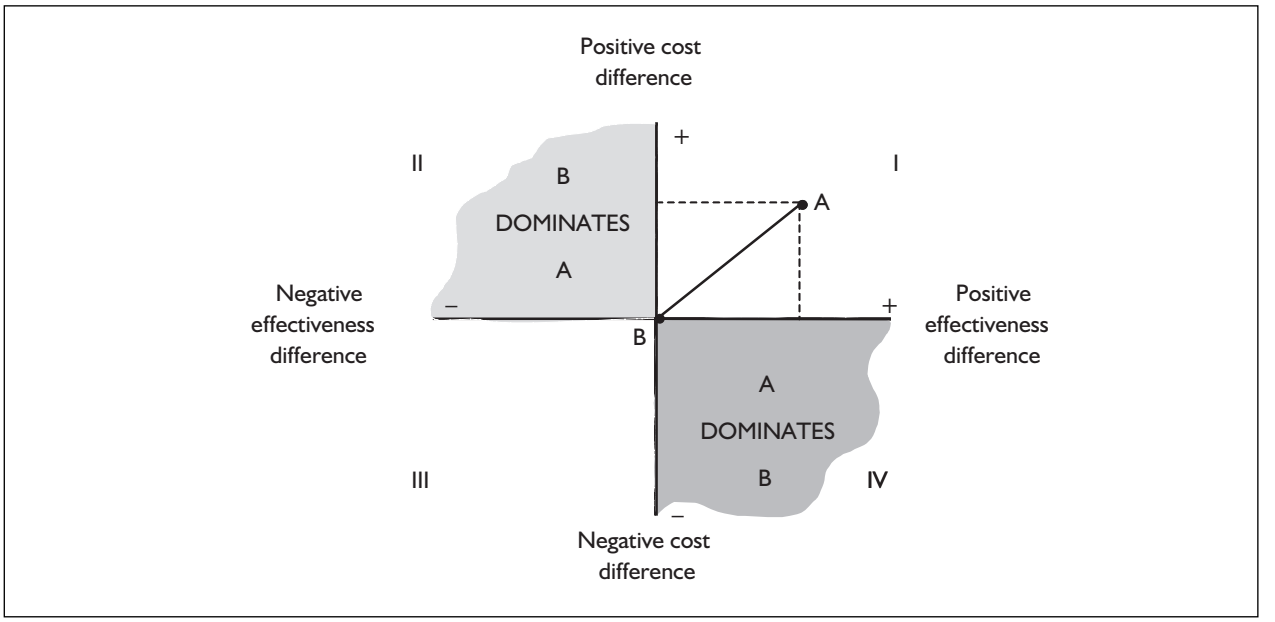

FIGURE 2 *Cost-effectiveness plane*

where $\bar{c}_i$ = mean average cost in period i, S_i = Kaplan–Meier estimate of the probability of non-healing at the beginning of period i and n = total number of periods.

To account for the skewed nature of cost data, 95% CIs for the adjusted total cost and the average mean cost difference between bandage treatments were estimated using non-parametric bootstrapping techniques (1000 replications). CIs are based on the bias corrected and accelerated estimates.[65]

Non-parametric bootstrapping techniques were also used to estimate the CI around the estimated mean difference in ulcer-free days and mean difference in QALYs. Linear multiple regression was used to adjust the differential QALY by any imbalances in the EuroQol score at baseline.

Sensitivity analysis

In our analysis, the total cost of compression therapy in the treatment of venous leg ulcers was mainly driven by three items: the difference in number of nurse visits required for patients in each bandage group, the setting where the leg ulcer care is delivered and the large number of SSBs that patients required. As the volume and setting of nurse visits required by a patient are issues mainly related to the way in which service provision is organised in the UK, no sensitivity analysis on these two parameters was justified. In order to explore the robustness of the results from our base case analysis, we used the scenario approach to sensitivity analysis.[66,67]

Scenario 1

In a first scenario, the total number of SSBs used per patient per month was modified in the following way. According to our data, the assumption of a once-weekly change of SSB was unrealistic, since the mean number of changes per month for SSB was six (range 1–29). Consequently, for all the patients allocated to the SSB group, the history of resources used per month was analysed individually. Each time a patient's SSBs were reported to have been replaced with new ones, the quantity of bandages reported was replaced with the patient's minimum number of bandages used over the whole period of treatment.

Scenario 2

The second scenario considered the possibility of acquiring the four-layer compression system as a 'kit'. Although the four-layer kit is not available on prescription in the UK, leg ulcer clinics commonly purchase them and supply them from stocks.

Scenario 3

In a third and final scenario, the two options described above were considered simultaneously.

Cost-effectiveness acceptability curves

The level of uncertainty associated with the cost-effectiveness of SSBs when compared with 4LBs was explored using cost-effectiveness acceptability curves. Acceptability curves represent the probability of an alternative being cost-effective for a range of willingness to pay values for an extra unit of health benefit associated with the alternative.[68] In this case, the cost-effectiveness acceptability curve for SSBs represented the probability of SSBs being cost-effective compared with 4LBs for a range of willingness to pay values associated with an ulcer-free day.

Chapter 3
Results

Recruitment results

A total of 387 people were recruited to the trial between April 1999 and December 2000; this represents 39% (387/988) of those approached and 97% of our target. Since the target assumed a 10% loss to follow-up and only one patient was lost to follow-up for the primary end-point, the study had 80% power to detect a difference in healing of 15%. A CONSORT flow diagram[69] showing the recruitment and outcome of all patients recruited into the trial is presented in *Figure 3*.

Most frequent reasons for exclusion from the trial were patients not suitable for compression, ABPI <0.8, diabetes mellitus and maximum ulcer length <1 cm. All patients received the allocated bandage at least once. One patient in the 4LB group failed to return to clinic after having entered into the study.

Discontinuation from the allocated treatment occurred in 46 and 66 patients in the 4LB and SSB groups, respectively. Similar numbers of patients in each bandage group were discontinued from the study at their own request. More patients were removed from the SSB as the result of a recommendation from the research nurse.

Three patients in the 4LB group were identified as potential trial violators. It became apparent that two patients had previously been treated unsuccessfully with the 4LB, and a third patient was subsequently diagnosed as having a malignant ulcer. Although these patients were not eligible for inclusion according to the protocol, by excluding them from the analysis we would have been losing valuable information. Therefore, we decided that since the conditions described above were unknown at the time of randomisation, and considering the pragmatic nature of the study, we included them in the ITT analysis.

Baseline demographics and clinical characteristics of patients by treatment

In total, 195 patients were allocated to the 4LB and 192 to the SSB. The distribution of these patients between the trial sites is shown in *Table 4*.

TABLE 4 *Recruitment at each of the trial sites by treatment group*

	4LB		SSB	
Centre	**No.**	**%**	**No.**	**%**
Cumbria	35	18	35	18
Leeds	54	28	52	27
West London	18	9	20	10
North Yorkshire	53	27	55	29
Other	35	18	30	16
Falkirk	9	5	6	3
Calderdale	4	2	5	3
East London	7	4	2	1
Newmarket	4	2	4	2
Southport	11	6	13	7
Total	195		192	

For the purposes of randomisation, the five smaller trial centres that entered the trial after it began were grouped together in order to have one stratification centre, labelled 'Other'. Stratification of the randomisation was successful in ensuring that a similar number of patients in each site were allocated to each treatment.

The demographic and clinical characteristics of patients in each treatment group are shown in *Table 5*. Patients in the two treatment groups were well matched for demographic variables, clinical history and leg ulcer characteristics (see *Table 5*). The two study groups were also compared with respect to patient characteristics, leg ulcer characteristics and stratification variables (see *Table 5*). Patients were similar in these two groups.

Baseline demographics and clinical characteristics of patients by trial centre

The baseline demographic variables, medical history and leg ulcer characteristics are presented by trial centre in *Table 6*.

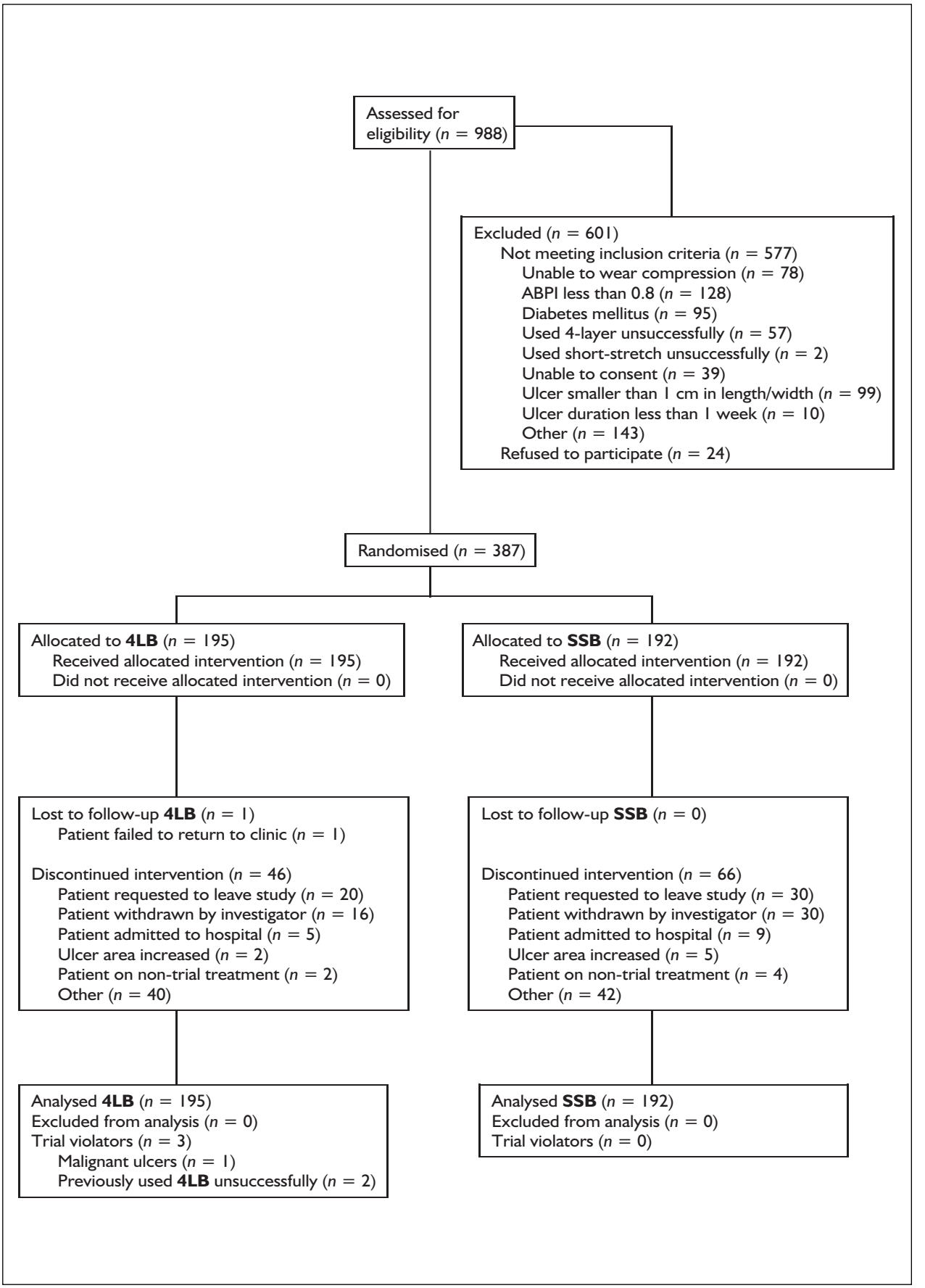

FIGURE 3 *VenUS trial CONSORT flow diagram*

TABLE 5 *Baseline demographic variables, medical history and leg ulcer characteristics*

	4LB		SSB	
Continuous variables	***n***	**Mean (SD) [range]**	***n***	**Mean (SD) [range]**
Patients' characteristics				
Age (years)	195	71.9 (12.29) [25–97]	192	71.3 (14.10) [23–96]
Height (m)	192	1.7 (0.11) [1.5–2.0]		1.7 (0.11) [1.4–2.0]
Weight (kg)	192	80.6 (19.35) [33.1–139.71]	185	79.0 (20.29) [38.1–142.4]
History of ulceration				
Duration (years since onset)	190	3[a] [0–60]	182	4[a] [0–75]
Episodes (since onset)	190	2[a] [0–50]	185	2[a] [0–64]
Leg and ulcer characteristics				
Ankle circumference (cm)	193	23.8 (2.91) [16.2–34.0]	187	23.9 (2.89) [16–32.3]
Duration (months)	193	3[a] [0–456]	184	3[a] [0–768]
Area (cm^2)	194	3.8[a] [0.2–254.6]	192	3.8[a] [0.4–143.9]
ABPI	187	1.1 (0.15) [0.8–1.9]	186	1.0 (0.14) [0.8–1.6]
	4LB		**SSB**	
Categorical variables	***n***	**%**	***n***	**%**
Patients' characteristics				
Male	79	41	80	42
Female	116	60	112	58
Ulcerated right leg	88	45	82	43
Ulcerated left leg	107	55	108	56
Fully mobile	123	63	115	60
Walks with assistance	72	37	70	37
Immobile	0	0	3	2
Ankle mobility (full motion)	131	67	128	67
Ankle mobility (reduced motion)	59	30	58	30
Ankle mobility (fixed)	3	2	2	1
Leg or ulcer characteristics				
Sloughy ulcer	130	67	108	56
Granulating ulcer	127	65	115	60
Epithelialising ulcer	27	14	25	13
Eczematous skin	59	30	49	26
Macerated skin	31	16	26	14
Cellulitis skin	15	8	15	8
Lipodermatosclerosis skin	88	45	86	45
Stratifying variables				
Ulcerated area ≤ 10 cm^2	158	81	158	82
Ulcerated area >10 cm^2	37	19	34	18
Had previous ulcer on the trial leg	115	59	114	59
First episode of ulceration on trial leg	80	41	78	41
Ulcer duration ≤ 6 months	138	71	143	75
Ulcer duration >6 months	57	29	49	26

[a] For highly skewed distributions, medians are shown.

TABLE 6 *Demographic variables, medical history and ulcer characteristic by trial centre*

	Cumbria		Leeds		London		North Yorkshire		Other	
Variable	***n***	**Mean (SD) [range]**	***n***	**Mean (SD) [range]**	***n***	**Mean (SD) [range]**	***n***	**Mean (SD) [range]**	***n***	**Mean (SD) [range]**
Patients' characteristics										
Age (years)	70	69.5 (12.35) [38–87]	106	72.0 (13.40) [29–97]	38	64.7 (16.39) [23–89]	108	74.3 (11.68) [39–96]	65	72.8 (12.77) [24–92]
Height (m)	70	1.7 (0.10) [1.5–2.0]	105	1.7 (0.10) [1.4–1.9]	37	1.7 (0.12) [1.5–2.0]	104	1.7 (0.11) [1.5–2.0]	63	1.7 (0.09) [1.6–2.0]
Weight (kg)	70	79.9 (17.67) [50.8–130.2]	103	79.7 (20.97) [33.1–139.7]	36	83.6 (17.09) [44.5–120.7]	105	80.4 (21.27) [38.1–137.9]	63	76.9 (19.20) [44.5–142.4]
History of ulceration										
Duration (years since onset)	69	6.0 (10.13) [0–50]	102	9.2 (13.61) [0–64]	35	9.7 (14.33) [0–65]	103	10.1 (15.00) [0–75]	63	12.4 (15.98) [0–60]
Episodes (since onset)	69	2.0 (1.85) [0–10]	105	3.7 (8.58) [0–64]	35	2.0 (1.58) [0–8]	103	3.7 (6.34) [0–50]	63	4.6 (7.41) [0–50]
Ulcer and leg characteristics										
Ankle circumference (cm)	70	24.1 (2.48) [18–29.14]	105	24.2 (3.22) [16–34]	35	24.8 (2.56) [19–29]	106	23.9 (3.12) [16.2–32.3]	64	23.1 (2.37) [18–30.5]
Duration of this ulcer (months)	69	5.4 (16.74) [0–120]	104	14.8 (76.59) [0–768]	34	29.9 (102.38) [1–456]	106	16.6 (47.25) [0–360]	64	13.6 (32.02) [0–180]
Area (cm^2)	69	4.6 (8.81) [0.7–73.7]	106	11.0 (20.86) [0.4–156.8]	38	13.3 (28.05) [0.2–143.9]	108	11.9 (31.45) [0.4–254.6]	65	10.4 (17.27) [0.8–131.3]
ABPI	70	1.3 (0.07) [0.8–1.3]	186	1.0 (0.16) [0.8–1.5]	38	1.1 (0.17) [0.9–1.7]	106	1.0(0.12) [0.8–1.6]	62	1.1 (0.16) [0.9–1.9]

Age
Patients ranged in age from 23 to 97 years at trial entry, with a mean age of 71 years. Overall, patients in West London were slightly younger (mean age 64 years), than those in the other centres, where the mean ages ranged from 69 to 74 years.

Duration of ulcer disease
The duration of ulcer disease, defined as the number of years since the onset of the first leg ulcer, ranged from 0 to 75 years, with a mean of 9 years. Patients recruited from the five additional trial sites, combined to form the 'Other' site, had a longer duration of ulcer disease at 12 years, and Cumbria had a shorter duration, at 6 years, than North Yorkshire, Leeds or West London (*Table 6*). The median durations of ulcer disease in 4LB and SSB arms were 3 and 4 years respectively (see *Table 5*).

Number of previous ulcer episodes
The number of previous ulcer episodes ranged from 0 to 64 with a mean of 3.38. Patients in Cumbria reported fewer previous episodes of ulceration, an average of 1.96 (range 0–10) less than the other three original trial sites. Patients in the trial sites grouped as 'Other' reported more previous ulcer episodes than any other site, an average of 4.63 (*Table 6*). These data are skewed; 40% of patients had no previous episodes of ulceration. Accurate recall of the exact number of previous episodes of ulceration is less likely when a patient has had a large number of ulcer episodes. Hence the median number of ulcer episodes in each trial setting is a more useful measure of the chronicity of ulceration in the population recruited to the trial. The median number of episodes of ulceration in both trial arms was 2 (see *Table 5*)

Ankle circumference
The ankle circumference at trial entry was similar across the five centres, with a mean of 24 cm.

Duration of reference ulcer
The duration of the reference ulcer was ≤ 6 months for 72.6% of patients recruited to the trial. The majority of patients had ulcers of short duration but as the trial recruited people with both existing ulcers and incident ulcers, the upper range varied from 120 months (in Cumbria) to 768 months (64 years) in Leeds. When the mean values for 'duration of reference ulcer' are inspected, there appears to be fewer long-standing ulcers in Cumbria (mean duration 5.4 months) than the other four centres (13–29 months) (see *Table 6*). Median duration of the reference ulcer is 3 months in both treatment groups (see *Table 5*).

Area of reference ulcer
The area of the largest ulcer on the trial leg was used as a stratifying variable as increased ulcer area is a predictor for delayed healing.[9,10,47] The majority of patients in this trial (82%; 316/387) had a reference ulcer with an area of ≤ 10 cm^2. A few ulcers were very large, ranging up to 255 cm^2 (almost 16 by 16 cm square) (*Table 6*). There was no minimum ulcer area in the trial, as the only size requirement for entry was a minimum dimension on any axis of 1 cm. The median baseline ulcer areas were 3.81 cm^2 and 3.82 cm^2 for the 4LB and SSB groups, respectively (see *Table 5*).

Analysis of primary outcome

Unadjusted analysis
The analysis of the primary outcome, time to complete healing of all ulcers on the trial leg, included all patients randomised into the study. Patients' time to complete healing in days was used to estimate the Kaplan–Meier curves for the individuals in the two bandage groups (see *Figure 4*). The numbers of patients failing to heal or lost to follow-up until December 2001 (censored cases) were 38 and 45 for the 4LB and the SSB groups, respectively.

Kaplan–Meier estimates of the proportion of ulcers healed over time show that within the first 12 weeks of treatment about the same proportion of individuals in either bandage group was healed (see *Figure 4*). Beyond 12 weeks (84 days) a slightly higher proportion of people healed in the 4LB group than the SSB group.

To test the difference over time of the Kaplan–Meier curves for the two bandage groups, the distributions of the cumulative times to healing of individuals in the two trial groups were compared using the log-rank test. The difference in the distributions of cumulative healing times between the individuals in the two groups was not statistically significant at the 5% level [log-rank = 2.46, $p = 0.12$ (see *Table 7*)].

The total proportions of ulcers healed in the 4LB and SSB groups were 80.5 and 76.5%, respectively; this difference was not statistically significant at the 5% level (95% CI –4 to 15%). The median time to healing for the two bandage arms is shown in *Table 7*. A difference of 34 days in the median time to healing between groups was observed.

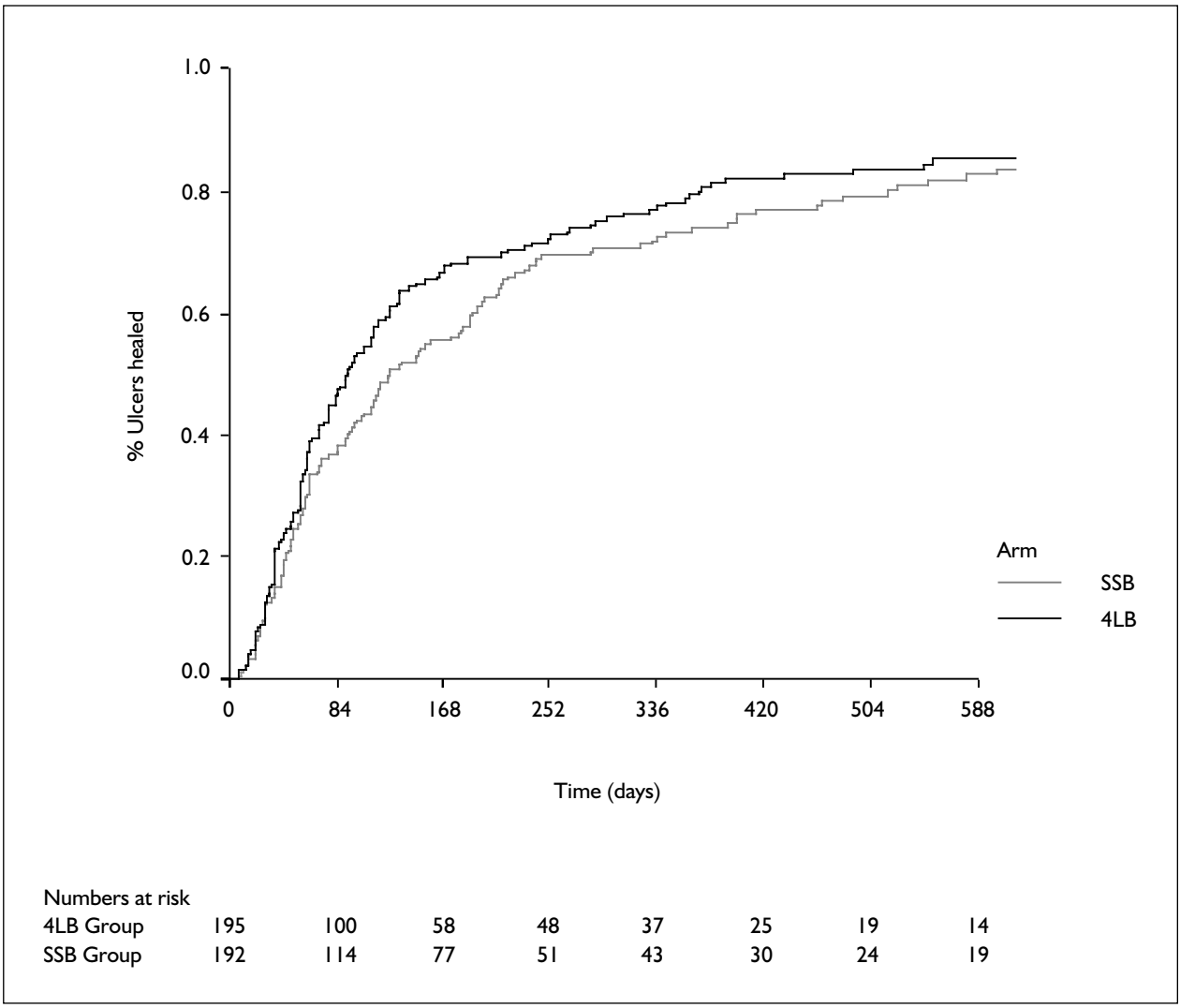

FIGURE 4 *Kaplan–Meier curves per bandage treatment*

TABLE 7 *Unadjusted analysis of time to healing*

Variable	4LB (*n* = 195)	SSB (*n* = 192)
No. of ulcers healed	157	147
No. of censored cases	38	45
Median time to heal	92 days	126 days
[95% CI]	[71–113]	[95–157]
Log-rank test	2.46	
Statistical significance	0.12 (*p*-value)	

To allow the comparison of the results from this study with those from previous studies in which the proportions of ulcers healed at 12 and 24 weeks are usually reported,[31] we explored the differences between the two treatments in terms of the Kaplan–Meier estimates of the proportion of ulcers healed at 12 and 24 weeks. After 12 weeks of treatment, 46 and 37% of ulcers had completely healed in the 4LB and SSB group, respectively. This absolute difference of 9% was not statistically significant at the 5% level (95% CI –20 to 0%). At 24 weeks, the absolute difference in the proportion of ulcers healed was 13% (68 and 55% of individuals had their ulcers fully healed in the 4LB and the SSB group, respectively). This difference is statistically significant at the 5% level (95% CI 2 to 22%). Testing the difference in effect between the two bandage treatments at specific points in time will usually be misleading, since the results from such analysis will depend heavily on the time point chosen for the comparison. As shown above, two different results are observed when the survival experiences of the individuals in the two bandage groups are compared at 12 and 24 weeks.

Adjusted analysis

In order to explore the effect of a number of prognostic factors on the distribution of times to

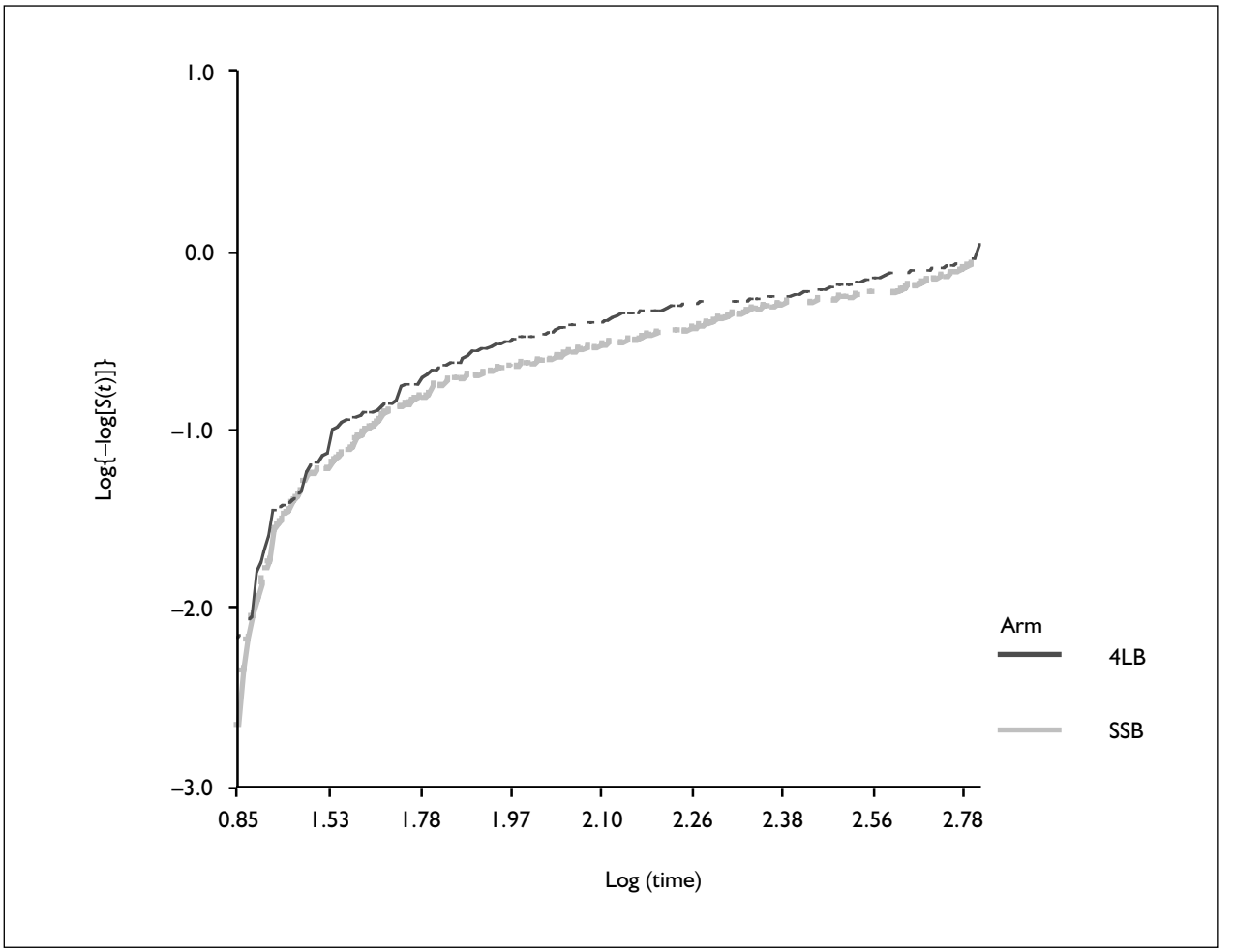

FIGURE 5 *Cumulative hazard plots for the two treatment groups*

healing of the two bandage groups, we fitted a Cox proportional hazards model to our data. Adjustment of the hazard of healing [i.e. the probability of an ulcer healing at any point in time (t) given non-healing up to that point] for covariates is necessary as stratification alone does not always ensure a perfect balance of the clinical and demographic characteristics of the individuals across both treatment groups. Ulcer area, for example, was stratified using a cut-off point of 10 cm^2. If a larger number of really large ulcers, say >100 cm^2, was recruited into one trial arm, then the unadjusted analysis would not take this into account and therefore may be biased against the treatment arm containing the very large ulcers. The following variables were considered as potential covariates (prognostic factors for ulcer healing) for the Cox proportional hazards model:[8–10,47,70]

- number of episodes of ulceration
- duration of current ulcers in months
- total area of ulceration at baseline
- centre
- patient's age
- patient's weight
- patient's mobility
- patient's ankle mobility.

The Cox regression model assumes that there is proportionality of hazards between the treatment groups, i.e. that the treatment effects do not change over time. The proportionality of hazards between treatment groups was checked using the log(cumulative hazard) plots, that is, $\log\{-\log[S(t)]\}$ plotted against $\log t$, where $S(t)$ are the Kaplan–Meier estimates of the cumulative distribution of healing times. *Figure 5* shows how the $\log\{-\log[S(t)]\}$ curves for each trial arm do not cross each other, that is, they are fairly parallel, thus supporting the adequacy of the proportionality of hazards assumption.

In order to identify the covariates that best explained the variability in the healing rate, we followed a procedure described by Collet[71] in

TABLE 8 *Unadjusted Cox model*

Variables in model	–2log*L*	Difference	*p*-Value
First stage			
Null model	3186.98		
Null model + arm	3184.54	2.43	0.12

which the difference between the statistic –2log(likelihood) (–2log*L*) associated with the models being compared is used as a criterion of a model's goodness of fit. Decisions as to whether to include or omit a covariate were made using a 5% level of significance.

We began by defining a null model, that is, a Cox model with no covariates. This model was then used to investigate the treatment effect by including into the null model a dichotomous variable (treatment arm, which took the value of one for individuals allocated to the SSB and zero for individuals allocated to the 4LB). This analysis is equivalent to testing the hypothesis of the difference between the Kaplan–Meier curves for the two bandage groups. The difference in the –2log*L* statistic was not statistically significant ($p = 0.12$), indicating that there was no statistically significant treatment effect (see *Table 8*). This result is in agreement with the results from the log-rank test (reported in *Table 7*) as expected. According to the null model, the HR of healing associated with patients in the SSB group compared with those in the 4LB group was 0.84 (95% CI 0.67 to 1.05), suggesting that the individuals in the SSB group had a smaller probability of healing than those in the 4LB group.

In order to adjust for any potential confounding/bias that may be affecting the data on time to healing, we compared the null model with models that contained the prognostic factors for healing, one at a time. *Table 9* shows the stepwise procedure that we followed in order to select the model that best described our data. The differences in the –2log*L* statistic between the null model and each of the models with a single covariate were then checked to determine the variables that on their own significantly reduced the value of the statistic. In a second stage of the analysis, all the variables that individually significantly reduced the –2log*L* statistic were used to define a new reference model. The independent explanatory value of each of the variables in this reference model was tested by computing the changes in the –2log*L* statistic when each of the variables was omitted from the model one at a time. A new model was then defined, retaining all the variables that significantly increased the value of the –2log*L* statistic when they were omitted from the initial reference model.

Some covariates may cease to be, or become important, in the presence of other variables, therefore all the covariates that were discarded in previous steps were included in the last reference model one at a time. Having carefully examined the contribution of each of the potential covariates to explain our data, the model that best described the hazard of healing at any point in time (t) was:

$$h(t) = \exp[\beta_1 episodes + \beta_2 weight + \beta_3 area + \beta_4 duration + \beta_5 ankle\ mobility + \beta_6 centre]h_0(t)$$

where $h(t)$ = hazard of healing at time t, $h_0(t)$ = baseline hazard function, *episodes* = ulceration episodes since disease onset, *weight* = patient weight (kg), *area* = area of ulceration at baseline, *duration* = months current ulcer is being opened, *ankle mobility* = indicator variable (0,1), 1 if ankle has full range of motion and 0 if impaired mobility, and *centre* = matrix of eight indicator variables with North Yorkshire taken as the reference centre.

At this point, the linearity of continuous covariates (*area*, *episodes*, *duration*, *weight*) was tested; the logarithmic transformation of *area* was the only transformation that significantly improved the goodness of fit of our model, hence the rest of the covariates remained in their original form.

We then explored the treatment effect in this adjusted model by including a dichotomous variable (*arm*, which took the value of 1 for individuals allocated to the SSB group and zero for individuals allocated to the 4LB group). Our adjusted model for the hazard of healing at any point in time including the treatment effect was:

$$h(t) = \exp[\beta_0 arm + \beta_1 episodes + \beta_2 weight + \beta_3 \ln(area) + \beta_4 duration + \beta_5 ankle\ mobility + \beta_6 centre]h_0(t)$$

where *arm* = indicator variable (0, 1), 1 if bandage treatment = SSB and 0 if bandage treatment = 4LB, and ln(*area*) = natural logarithm of area of ulceration at baseline.

When the treatment effect was included into the model, the –2log*L* statistic was reduced by 7.57, indicating a statistically significant treatment effect

TABLE 9 *Model selection (stepwise procedure)*

Variables in model	–2log*L*	Difference	*p*-Value
First stage			
None	3186.98		
Duration, months (Dur)	3127.87	59.11	0.00
Area (Are)	3150.04	36.94	0.00
Centre (Cen)	3151.47	35.50	0.00
Ankle (Ank)	3162.78	24.19	0.00
Mobility (Mob)	3168.57	18.41	0.00
Episodes (Epi)	3171.32	15.66	0.00
Weight (Wei)	3181.70	5.27	0.02
Age	3184.44	2.53	0.11
ABPI	3186.83	0.15	0.70
Second stage			
Dur + Are + Cen + Ank + Mob + Epi	3066.44		
Are + Cen + Ank + Mob + Epi	3093.98	27.55	0.00
Dur + Cen + Ank + Mob + Epi	3077.72	11.29	0.00
Dur + Are + Ank + Mob + Epi	3088.33	21.90	0.01
Dur + Are + Cen + Mob + Epi	3071.62	5.18	0.02
Dur + Are + Cen + Ank + Epi	3066.81	0.38	0.54
Dur + Are + Cen + Ank + Mob	3074.23	7.79	0.01
Third stage			
Dur + Are + Cen + Ank + Epi	3066.81		
Are + Cen + Ank + Epi	3095.31	28.50	0.00
Dur + Cen + Ank + Epi	3078.21	11.40	0.00
Dur + Are + Ank + Epi	3089.41	22.59	0.00
Dur + Are + Cen + Epi	3076.12	9.30	0.00
Dur + Are + Cen + Ank	3074.71	7.89	0.01
Fourth stage			
Dur + Are + Cen + Ank + Epi	3066.81		
Dur + Are + Cen + Ank + Epi + Age	3066.81	0	1
Dur + Are + Cen + Ank + Epi + Wei	3059.19	7.62	0.01
Dur + Are + Cen + Ank + Epi + ABPI	3066.22	0.59	0.45
Final model			
Dur + Are + Cen + Ank + Epi + Wei	3059.19		

($p = 0.01$). Estimated coefficients for each of the explanatory covariates and for the overall adjusted treatment effect are given in *Table 10*.

The results indicate that after having adjusted the hazard of healing at any point in time (t) for a number of explanatory variables (number of episodes of ulceration, ulcer size, current ulcer duration in months, patient's weight and centre), there was evidence of a statistically significant treatment effect.

The sign of each regression coefficient (β_i) gives us an indication of whether the hazard increases (positive sign) or decreases (negative sign) for subjects with higher values of that variable. For continuous covariates, the estimated regression coefficient refers to the increase in the log (hazard) for an increase of one in the value of the covariate.

By taking the exponential of the coefficient associated with a covariate, i.e. $\exp(\beta_i)$, we obtain the covariate's HR at time t; this transformation facilitates the interpretation of the estimated coefficients of categorical covariates. HR values >1 suggest that the ratio of the hazards at time t is greater for the individuals in that category, relative to the individuals in the category's reference group. Conversely, HR values <1 suggest that the ratio of the hazards at time t is smaller for the individuals in that category, relative to the individuals in the category's reference group. Therefore, the estimated coefficient associated with the indicator variable for bandage treatment, *arm* (0.72), suggested that the hazard of healing

TABLE 10 *Treatment effect adjusted for explanatory covariates*

Variable	β_i	SE(β_i)	Exp(β_i)	95% CI, exp(β_i)
Arm	–0.33	0.12	0.72	0.57 to 0.91
Episodes	–0.04	0.02	0.97	0.94 to 1.00
Weight	–0.01	0.00	0.99	0.99 to 1.00
Ln (area)	–0.30	0.06	0.74	0.66 to 0.83
Duration	–0.02	0.01	0.98	0.97 to 0.99
Ankle mobility	0.43	0.14	1.53	1.17 to 2.00
North Yorkshire			1	
Leeds	–0.00	0.16	0.10	0.73 to 1.37
Cumbria	0.70	0.17	2.00	1.43 to 2.82
West London	0.38	0.23	1.46	0.93 to 2.29
Southport	–0.10	0.25	0.90	0.55 to 1.47
Falkirk	–0.17	0.33	0.85	0.45 to 1.60
Calderdale	0.41	0.38	1.50	0.72 to 3.16
East London	–0.63	0.43	0.53	0.23 to 1.25
Newmarket	–0.13	0.52	0.88	0.32 to 2.43

for individuals in the SSB treatment group was smaller relative to that of individuals in the 4LB group; this result was statistically significant at the 5% level [95% CI for exp(β) 0.57 to 0.91].

Treatment interactions

Interactions occur when the treatment effect is affected by another variable. For example, it would be interesting and clinically important to know if the treatment effect was greater in people who have had ulcers for longer or have reduced ankle mobility. Therefore, we investigated the interactions between the bandage treatment and all previously identified relevant covariates. However, apart from the interaction between treatment and centre, none of the other interaction terms statistically significantly reduced our statistic for the goodness of fit of the model. By including an interaction term between treatment and centre, the $-2\log L$ statistic was reduced by 19.0; this difference was statistically significant ($p < 0.02$). In other words, it appeared that the treatment effect varied by centre. Consequently, our final best model for the hazard of healing was:

$$h(t) = \exp[\beta_0 arm + \beta_1 episodes + \beta_2 weight + \beta_3 \ln(area) + \beta_4 duration + \beta_5 ankle\ mobility + \beta_6 centre + \beta_1 (arm \times centre)]h_0(t)$$

where $h(t)$ = hazard of healing at time t, $h_0(t)$ = baseline hazard function, *arm* = indicator variable (0, 1), 1 if bandage treatment = SSB and 0 if bandage treatment = 4LB, *episodes* = ulceration episodes since disease onset, *weight* = patient weight (kg), ln(*area*) = natural logarithm of area of ulceration at baseline, *duration* = months current ulcer is being opened, *ankle mobility* = indicator variable (0, 1), 1 if ankle has full range of motion and 0 if impaired mobility, *centre* = matrix of eight indicator variables with North Yorkshire taken as the reference centre and *arm* × *centre* = matrix of indicator variables which represents an interaction between the different centres participating in the trial and the two bandage treatments.

Because of the interaction between treatment and centre, we no longer have a single treatment effect but one associated with each participating centre. The treatment coefficients for each centre are presented in *Table 11*.

The hazard of healing for patients in the SSB group relative to those in the 4LB group becomes statistically significant at the 5% level for patients in North Yorkshire, West London and Falkirk (see *Table 11*). Interestingly, the direction of the treatment effect is not consistent between centres. Whereas in some centres the hazard ratio favours the 4LB (North Yorkshire, Leeds, Cumbria, and West London), in other centres the opposite result is true (Southport, Falkirk, Calderdale, East London, Newmarket). In Falkirk (15 patients), for example, the hazard of healing for patients in the SSB group is higher relative to patients in the 4LB group.

As can be seen in *Table 11*, the results vary by centre (heterogeneity). The heterogeneity of the treatment effect across the different centres was explored using a L'Abbé plot (see *Figure 6*). The size of a rectangle is proportional to the number of participants in that centre. If a rectangle is transversally crossed by the 45° line it means that

TABLE 11 *Treatment effect coefficients per participant centre (final model)*

N	Centre	β_i	SE(β_i)	Exp(β_i)	95% CI, exp(β_i)
108	North Yorkshire	–0.65	0.23	0.52	0.33 to 0.82
106	Leeds	–0.40	0.22	0.67	0.43 to 1.04
70	Cumbria	–0.35	0.25	0.70	0.43 to 1.15
38	West London	–0.96	0.41	0.38	0.18 to 0.83
24	Southport	0.43	0.46	1.54	0.65 to 3.66
15	Falkirk	1.47	0.66	4.33	1.31 to 14.35
9	Calderdale	0.27	0.84	1.31	0.31 to 5.62
9	East London	0.98	0.92	2.67	0.49 to 14.69
8	Newmarket	0.77	1.12	2.16	0.30 to 15.50

in that centre the event rate (number of ulcers healed) is the same in the two groups (4LB and SSB). If a rectangle lies below the line, the event rate was lower in bandage group 1 (SSB). Conversely when a rectangle lies above the line, the event rate was higher in group 1 (SSB).

The heterogeneity of the trial results between centres is apparent in *Figure 6*. The results from four of the larger centres indicate that the number of ulcers healed in the 4LB group is greater than that in the SSB group. In two of the centres the number of healed ulcers in the bandage groups is almost the same, and in three rather small centres the number of healed ulcers is higher in the SSB group. The number of ulcers healed across centres is very different in the two bandage groups, ranging from 50 to 97%.

The smaller centres participating in VenUS produced the most heterogeneous results for the treatment effect. However, given the small numbers of patients in these centres, it is likely that the heterogeneity in the results is due to chance rather than a real centre effect. Bearing this in mind, we conducted an analysis of the

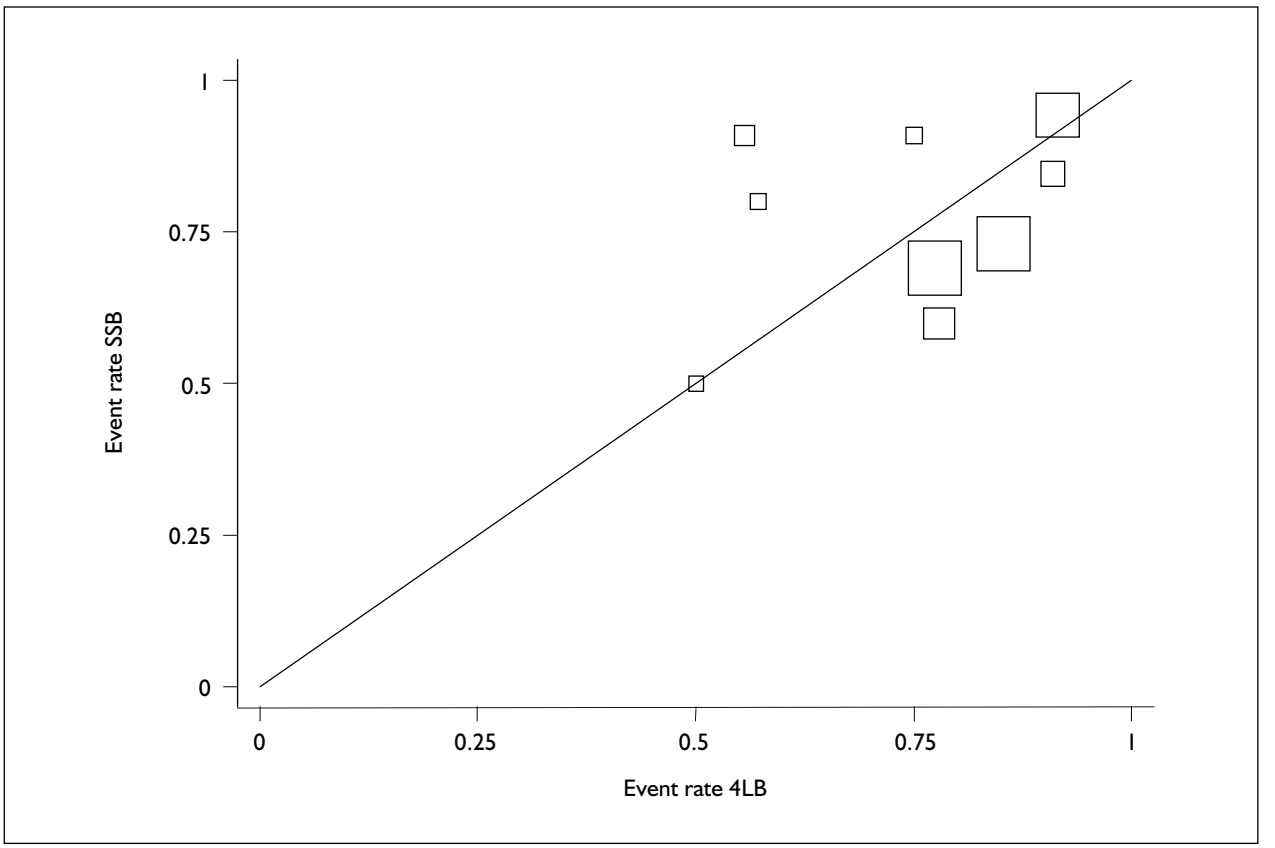

FIGURE 6 *L'Abbé plot of results by centre*

treatment effect using only the information from the four original participating centres, that is, North Yorkshire, Leeds, Cumbria and West London. The results from this model still suggested the presence of a statistically significant treatment effect; the 15.06 difference in the $-2\log L$ statistic was statistically significant at 5% level ($p = 0.00$). However, when the interaction between treatment effect and centre was tested in this model, the 2.05 difference in the $-2\log L$ statistic was not statistically significant $p = 0.98$, which indicated that there was not a statistically significant interaction between centre and treatment.

Table 12 presents the coefficients for the model of the hazard of healing for the original four centres. The coefficient associated with the treatment effect indicates that the hazard of healing of individuals in the SSB group is smaller than that for individuals in the 4LB group, that is, the result of this analysis goes in the same direction as the model which included all data but without interaction terms. The main discrepancy between the results of these two analyses refers to the size of the overall estimated treatment effect; in the first analysis the HR of the treatment effect was 0.72 (95% CI 0.57 to 0.91) and in the latter analysis the HR decreased to 0.61 (95% CI 0.47 to 0.78). In order to estimate rigorously an overall treatment effect taking into account the potential interaction or random effect between centre and treatment, we will have to fit a frailty model to our data.[72] This analysis will be conducted at some later stage.

Adverse events

Both bandage-related and bandage-unrelated events are reported. The proportion of patients experiencing bandage-unrelated adverse events was similar between the two bandage arms (see *Table 13*).

Those adverse events described by the reporting nurse as being related to, or potentially related to, the bandage being used are shown in *Table 14*.

For the adverse event 'deterioration of ulcer' there is a higher number of adverse events reported in the SSB arm than the 4LB arm. The higher

TABLE 12 *Treatment effect including only four initial centres*

Variable	β_i	SE(β_i)	Exp(β_i)	95% CI, exp(β_i)
Arm	–0.50	0.13	0.61	0.47 to 0.78
Episodes	–0.03	0.02	0.97	0.93 to 1.01
Weight	–0.01	0.00	0.99	0.98 to 1.00
Ln (area)	–0.32	0.06	0.73	0.64 to 0.82
Duration	–0.02	0.01	0.98	0.97 to 0.99
Ankle mobility	0.42	0.14	1.52	1.15 to 2.01
North Yorkshire			1	
Leeds	–0.04	0.16	0.96	0.70 to 1.32
Cumbria	0.67	0.18	1.93	1.37 to 2.72
West London	0.39	0.23	1.47	0.94 to 2.32

TABLE 13 *Adverse events unrelated to compression treatment*

Adverse event	4LB	SSB	Total
Total number of patients with adverse events	33	39	72
General health problems	25	33	58
Non leg ulcer related surgical interventions	3	2	5
Death	15	20	35
Temporary patient absence	1	6	7
Skin damage relating to non bandage products	1	2	3
Patient leaves trial	3	5	8
Change of diagnosis/aetiology	8	9	17
Reduced mobility		2	2
Total No. of adverse events	56	79	135

TABLE 14 *Adverse events potentially related to compression treatment*

Adverse event	4LB	SSB	Total
Total number of patients with adverse events	76	91	167
Maceration	18	17	35
Excoriation	10	14	24
Skin damage	49	55	104
Bandage failure	37	36	73
Ulcer deterioration	91	166	257
Skin deterioration	30	27	57
Surgical intervention to leg	4	5	9
Dryness	2	1	3
Non-surgical hospitalisation related to leg ulceration	2	0	2
Occurrence of new ulcer	11	13	24
Medical event relating to leg	1	3	4
Total No. of adverse events	255	337	592

number of events in the SSB arm may be a function of the greater length of time that patients in this group were treated, as the longer healing time means that patients were at risk of suffering an adverse event for longer (patients in the SSB arm healed in a median of 126 days, compared with patients in the 4LB arm who healed in 92 days); hence people in the SSB group were at risk of an adverse event for an additional 31 days.

Recurrence

Time to an ulcer recurrence on the trial leg was used to estimate the Kaplan–Meier curves for the individuals in the two bandage groups (see *Figure 7*). More than 70% of patients who had healed in both bandage groups remained so after the first year of follow-up.

Kaplan–Meier estimates of the proportion of ulcers recurring over time show that within the first 90 days after healing a slightly higher number of ulcers re-opened in the 4LB group. This initial trend was reversed after 3 months of follow-up, when a higher number of individuals in the SSB experienced a recurrence (see *Figure 7*).

Kaplan–Meier curves for the two bandage groups were compared using the log-rank test. The difference in the distribution of cumulative ulcers recurrence between the individuals in the two groups was not statistically significant at the 5% level [log rank = 1.51, $p = 0.22$ (see *Table 15*)].

The total proportions of recurring ulcers in the 4LB and SSB groups were 36.2 and 39.1%, respectively. This 2.9% difference was not statistically significant at the 5% level (95% CI 20 to 26%). Given the low numbers of recurrence events observed in both bandage groups, no median time to ulcer recurrence could be estimated.

To allow the comparison of the results from this study with those from previous studies in which the proportions of ulcers reoccurring after 12 months were reported,[73] we explored the differences between the two treatments in terms of the Kaplan–Meier estimates of the proportion of ulcers healed at 12 months. After 12 months of treatment, 13.1 and 25.4% of ulcers had reoccurred in the 4LB group and the SSB group, respectively. This absolute difference of 12.3% was statistically significant at the 5% level (95% CI 2 to 23%). As mentioned previously, testing the difference in effect between rate of recurrence in the two bandage treatments at specific points in time may be misleading, since the results from such analysis will depend heavily on the time point chosen for the comparison

HRQoL

Response rates for the three HRQoL questionnaires gradually fell to 50% as the trial progressed. A subgroup analysis of the available data suggested that the proportion of missing responses may be associated with healing status, which itself is associated with bandage treatment. This suggests our data are unlikely to be missing completely at random, thus rendering inadequate some of the most frequently used methods of imputation. Therefore, we decided to take a conservative approach for the analysis and only present a descriptive analysis of the HRQoL data.

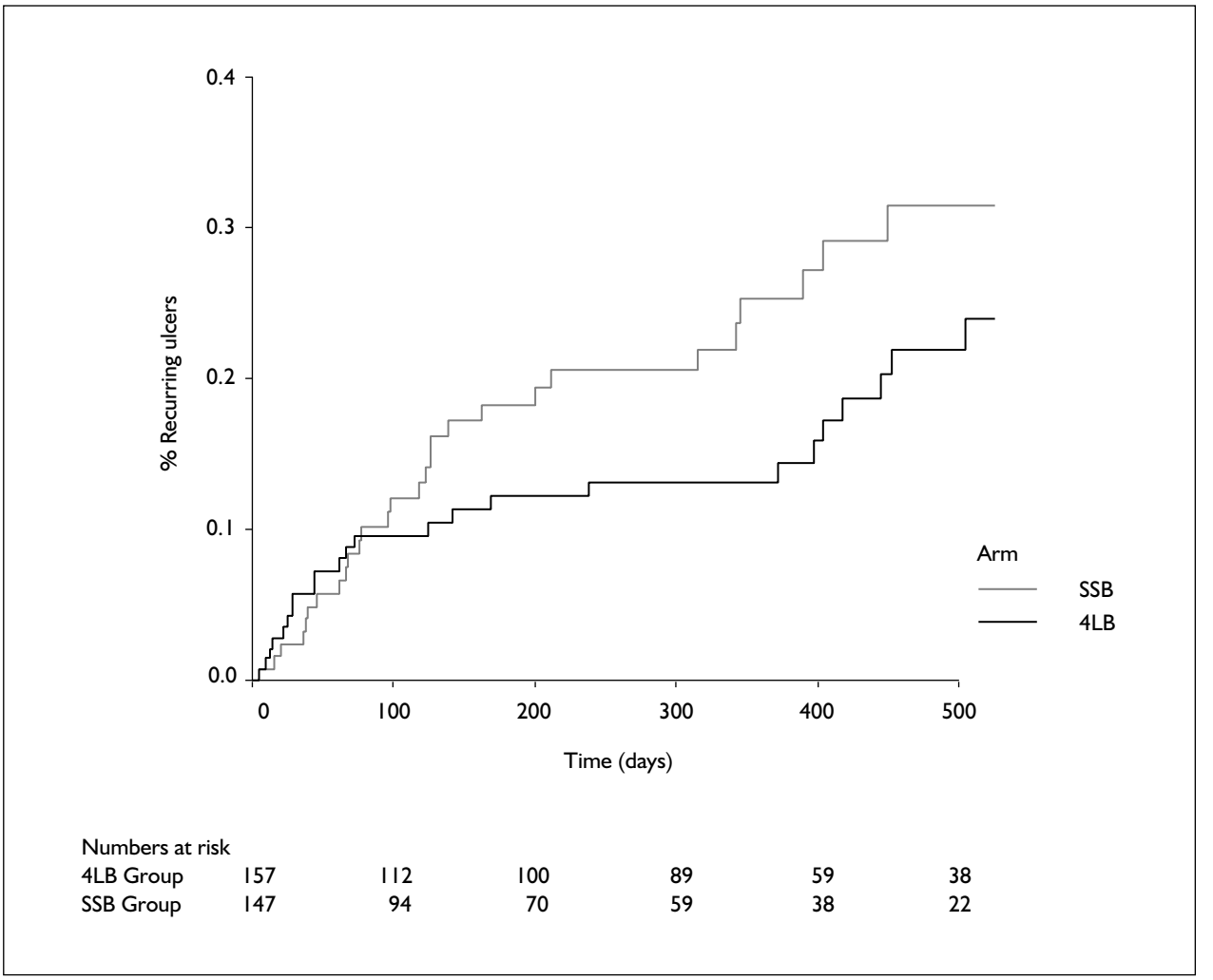

FIGURE 7 *Kaplan–Meier curves per bandage treatment (recurrence)*

TABLE 15 *Analysis of time to recurrence*

Variable	4LB (*n* = 157)	SSB (*n* = 147)
No. of recurring ulcers	27	29
No. of censored cases	130	118
Log rank test	1.51	
Statistical significance	0.22 (*p*-value)	

SF-12

Descriptive statistics of all health dimensions of the SF-12 including the physical component (PSC) and mental component (MSC) at baseline are described in *Tables 16* and *17*, respectively. Whereas the score for the mental component is similar in the two bandage groups (approximately 48.5), there is slight imbalance between bandage groups in PSC score (36.1 for the 4LB group and 35.6 for the SSB group). Whereas quarterly differences between bandage groups for the SF-12 MSC became more significant during the first year of follow-up, the same differences between bandage groups for the PSC remained more or less at the same level observed at baseline (see *Table 16*).

All health components of the SF-12 for our study population are below the average mean value (50) of the general US population, implying that, on average, the HRQoL of the individuals in the VenUS study was poorer than that of an average member of the US population. However, when we compared our baseline PCS and MCS scores with those of an average US individual aged ≥ 75 years (the mean age of our study population was 71 years), the differences between the scores were less apparent (see *Tables 18* and *19*).[74] In fact, the large difference between the PCS of our population and that of the general US population was no longer observed. The difference between

TABLE 16 *Quarterly physical component summary SF-12*

Period	Physical component (PCS)	
	4-LB (*n* = 195)	**SSB (*n* = 192)**
Baseline		
Mean (SD)	36.1 (8.30)	35.6 (7.62)
Median (min.–max.)	36.1 (4.75–55.27)	36.0 (18.29–52.37)
Missing (%)	19 (10%)	29 (16%)
1st quarter		
Mean (SD)	35.1 (7.93)	34.8 (7.10)
Median (min.–max.)	36.1 (15.23–53.41)	34.8 (14.13–49.12)
Missing (%)	60 (31%)	61 (33%)
2nd quarter		
Mean (SD)	35.1 (7.54)	34.4 (7.96)
Median (min.–max.)	36.0 (9.34–51.14)	35.5 (10.17–51.32)
Missing (%)	68 (35%)	84 (45%)
3rd quarter		
Mean (SD)	35.5 (7.51)	34.8 (7.85)
Median (min.–max.)	36.1 (14.12–49.99)	35.0 (11.45–49.33)
Missing (%)	80 (43%)	92 (49%)
4th quarter		
Mean (SD)	35.0 (8.03)	34.2 (7.60)
Median (min.–max.)	35.5 (12.27–47.48)	33.2 (14.42–47.49)
Missing (%)	78 (40%)	97 (51%)

TABLE 17 *Quarterly mental component summary SF-12*

Period	Mental component (MCS)	
	4LB (*n* = 195)	**SSB (*n* = 192)**
Baseline		
Mean (SD)	48.6 (12.34)	48.4 (12.28)
Median (min.–max.)	50.8 (13.11–70.07)	48.2 (16.85–68.43)
Missing (%)	19 (10%)	29 (16%)
1st quarter		
Mean (SD)	51.5 (11.86)	49.5 (11.28)
Median (min.–max.)	52.7 (19.68–69.82)	49.1 (17.02–68.01)
Missing (%)	60 (31%)	61 (33%)
2nd quarter		
Mean (SD)	52.3 (12.07)	48.1 (12.48)
Median (min.–max.)	55.2 (17.47–70.5)	50.5 (12.43–66.4)
Missing (%)	68 (35%)	84 (45%)
3rd quarter		
Mean (SD)	52.3 (12.35)	49.4 (12.28)
Median (min.–max.)	57.5 (21.77–38.37)	50.7 (17.98–69.83)
Missing (%)	80 (43%)	92 (49%)
4th quarter		
Mean (SD)	51.7 (11.76)	49.1 (11.43)
Median (min.–max.)	55.1 (10.1–70.39)	52.0 (20.43–68.40)
Missing (%)	78 (40%)	97 (51%)

TABLE 18 *Comparison with norm-base scores for individuals aged ≥ 75 years*

	Physical component (PCS)	
Period	**4LB**	**SSB**
VenUS study population		
Mean (SD)	36.1 (8.30)	35.6 (7.62)
Range	(4.8–55.3)	(18.3–52.4)
US general population		
Mean (SD)	37.9 (11.16)	37.9 (11.16)
Range	(13–59)	(13–59)
Difference	–1.8	–2.3

TABLE 19 *Comparison with norm-base scores for individuals aged ≥ 75 years*

	Mental component (MCS)	
Period	**4LB**	**SSB**
VenUS study population		
Mean (SD)	48.6 (12.34)	48.4 (12.28)
Range	(13.1–70.1)	(16.9–68.4)
US general population		
Mean (SD)	50.4 (11.66)	50.4 (11.66)
Range	(18–71)	(18–71)
Difference	–1.9	–2.0

the mean PCS and MCS in our population and that of an average 75-year-old American individual was approximately 1.88 and 2.01 for the PCS and MSC for the two bandage groups (see *Tables 18* and *19*).

Our data suggest that the detriment to the QoL of the individuals in our study population was associated with both physical and mental components of health (see *Figure 8*). Looking at the individual dimensions on the SF-12 we observed that bodily pain, of the eight different dimensions, had the lowest scores. Interestingly, bodily pain was also the only dimension that showed a negative trend over the whole study period, that is, reported levels of pain actually increased with respect to those observed at baseline (see *Figure 11*). Conversely, the role of emotional and mental health and social functioning (all dimensions mainly related to

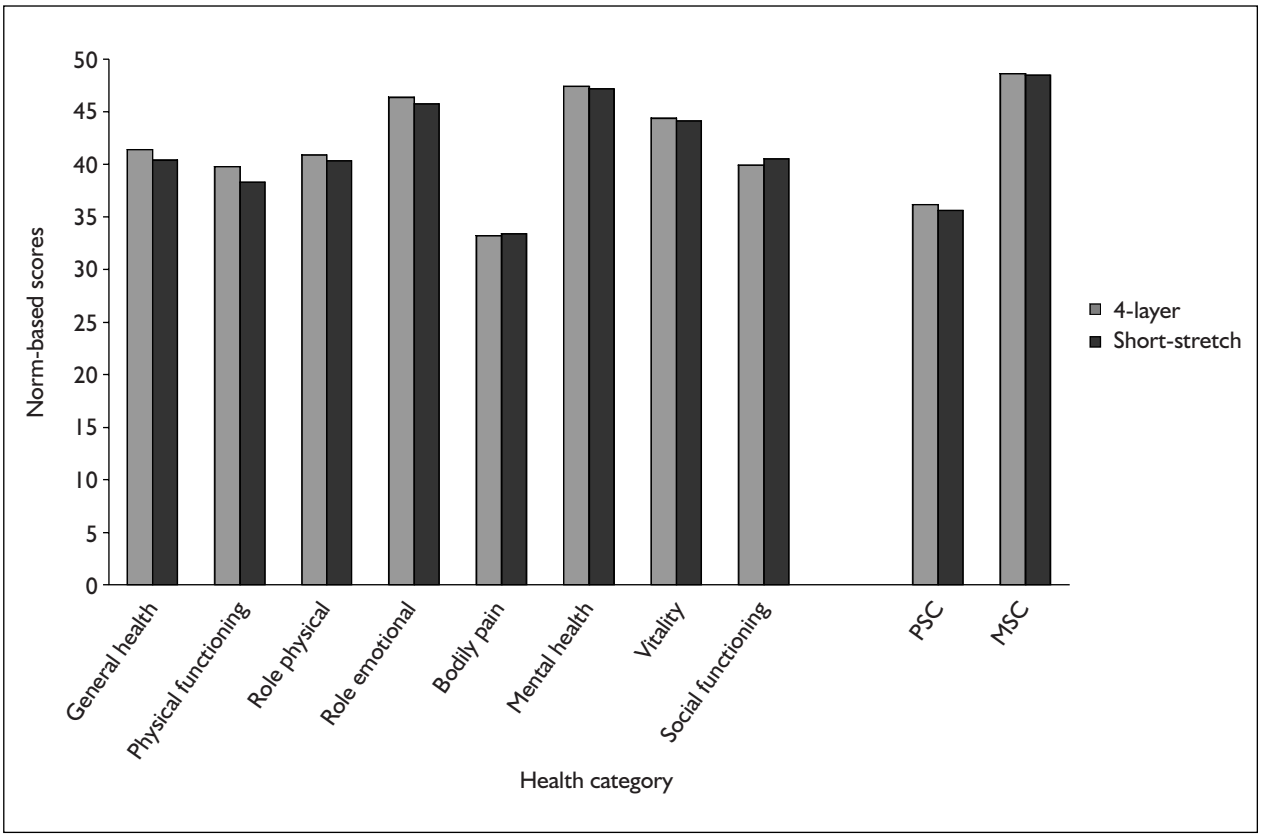

FIGURE 8 *Mean baseline SF-12 scores*

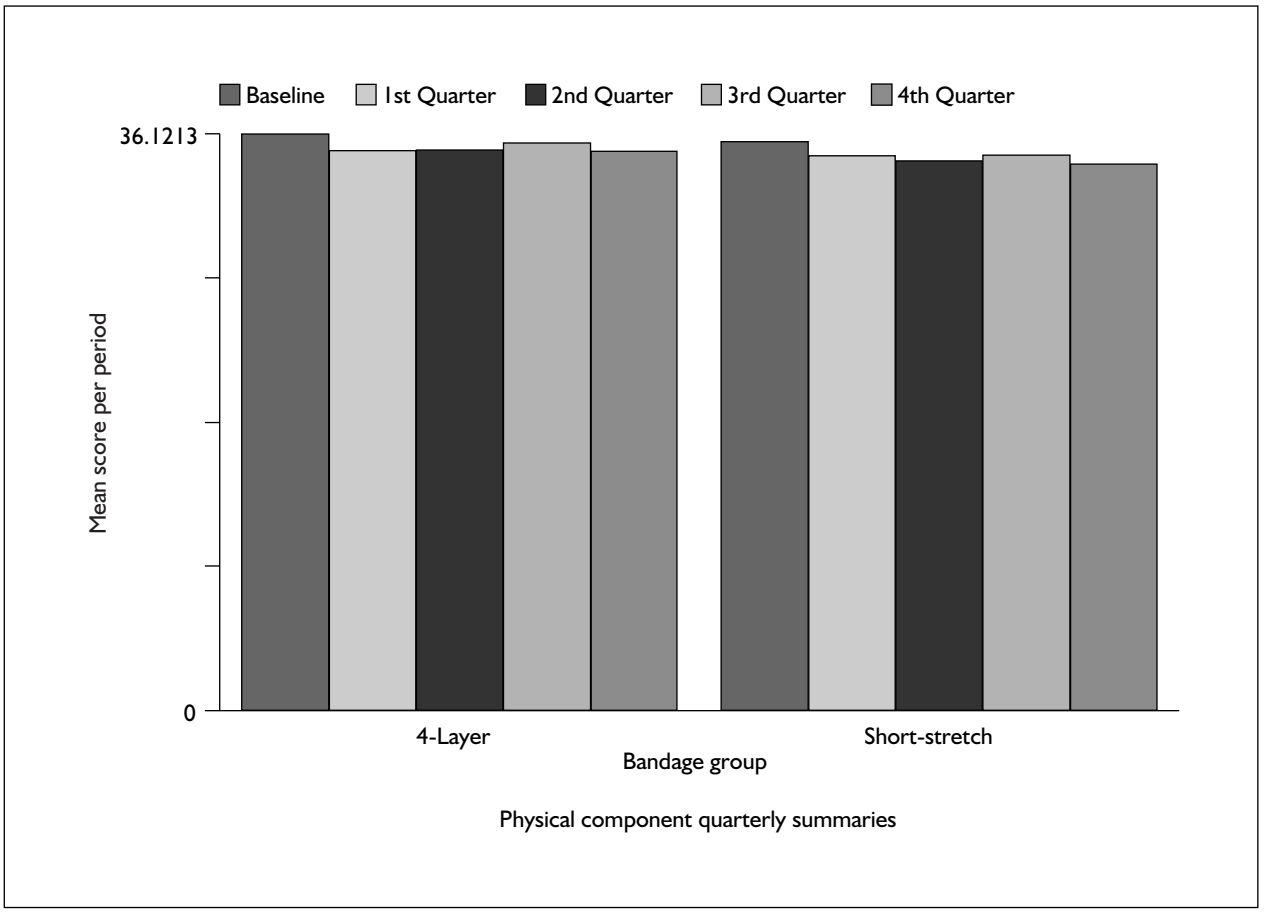

FIGURE 9 *SF-12 physical component*

mental health) showed a constant increment over time (*Figure 11*). Furthermore, whereas at baseline the MSC scores for our population were slightly below average, the scores significantly improved over time (see *Figure 10*). In contrast, the PSC scores did not follow a constant pattern over time (*Figure 9*).

Hyland

An initial two-factor extraction was employed. The three highest loading items on each factor can be seen in *Table 20*. Factor 1 accounted for 28.94% of the variance and factor two for a further 5.21%. In total, the scale accounts for 34.15% of the variance. Two items failed to load on either factor: item 14, "Because of my ulcer I try to keep away from cats, etc." and item 19, "I think my ulcer will not get better". These items were removed from further analysis.

Several items also double loaded on factors. In most cases these items were sufficiently different in their loadings on the two factors for it to be apparent where they belonged. In three cases, however, the items were very closely loaded. There would be an argument for discarding these items as the loadings on each factor were so close, but for the purposes of this study it was decided to retain them to keep the structure of the original scale. These three items are shown in *Table 21*. These items were included in Factor 2.

The factors proved to be reliable using the coefficient α to establish this. Factor 1 and 2 had coefficients α of 0.82 and 0.79, respectively. Factor 1 appeared to be measuring some of the more practical perceptions of limitations and Factor 2 more emotional responses to the ulcer.

Since the original scale had described the scale as one-dimensional, a one-factor solution was also examined; 27 of the 28 items loaded with the exception of item 19: "I think my ulcer will not get better". The factor explained 28.75% of the variance and had an internal reliability of 0.88. Although the reliability was high in this solution, more variance can be explained using the two-factor solution with the added benefit of being able to identify perception of practical limitations and also emotional issues which would seem to be

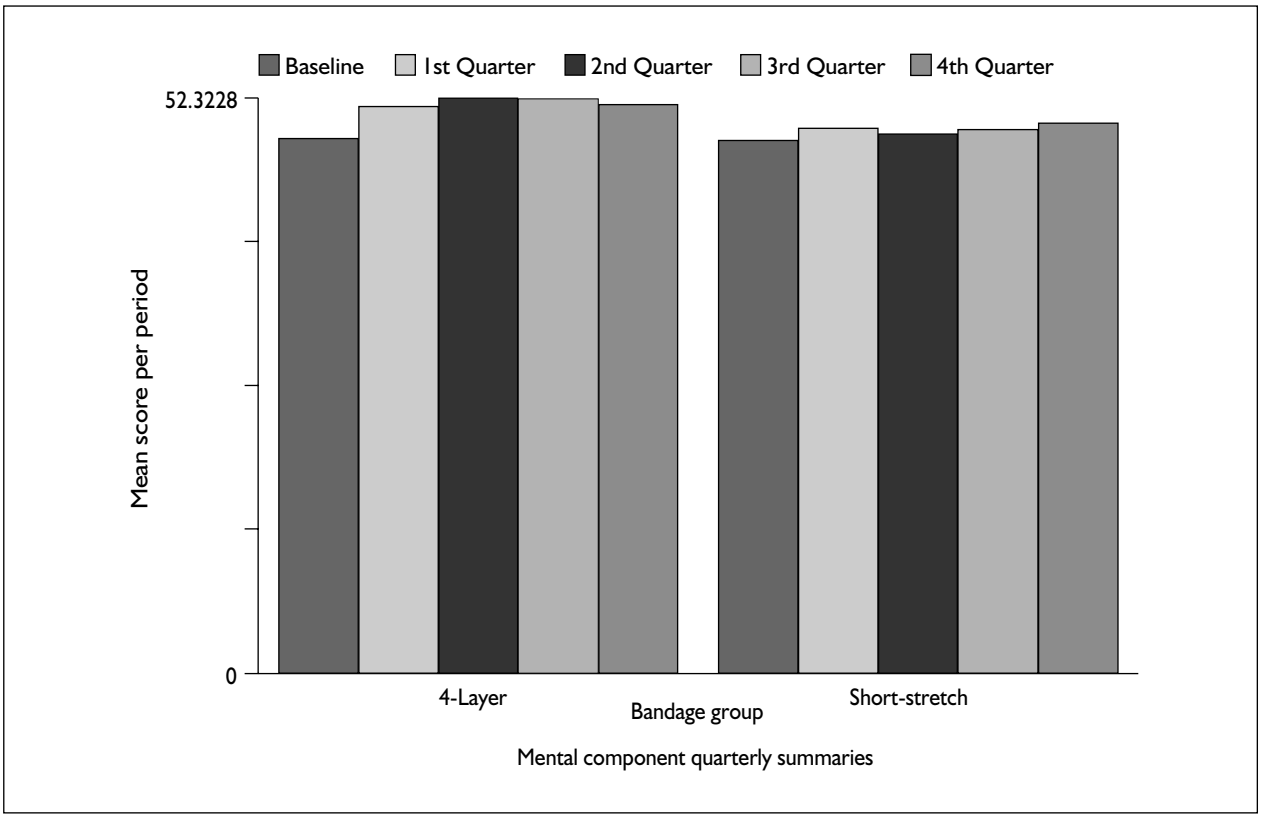

FIGURE 10 *SF-12 mental component*

TABLE 20 *Three highest loading items on each factor*

Item	Description	Factor	Loading
11	My ulcer makes getting on or off a bus difficult	1	0.735
18	My ulcer restricts where I can travel to, e.g. restricting holidays or business trips	1	0.708
9	My ulcer stops me from shopping in crowded places	1	0.678
24	My ulcer makes me ask myself, 'Why me?'	2	0.655
23	My ulcer makes me feel depressed	2	0.654
25	Because of my ulcer it feels as though my legs/feet dominate my body	2	0.630

TABLE 21 *Double loaded items*

Item	Description	Factor 1 loading	Factor 2 loading
21	Because of my ulcer I can't be bothered to do anything	0.419	0.446
20	My ulcer gets in the way of personal relationships	0.332	0.367
16	My ulcer prevents me from wearing the type of shoes I prefer	0.337	0.365

important. Hence the scale was scored using two factors; a practical and an emotional one.

Quarterly practical and mental scores for the individuals in the two bandage groups are described in *Tables 22* and *23*, respectively. No pronounced differences between bandage groups were observed at baseline for either the practical or the emotional factors: 0.6 and 0.2, respectively. Over the whole follow-up period a difference of approximately one point was observed in the practical and emotional components between bandage groups (see *Figures 12* and *13*).

Both the practical and emotional components of health measured by the Hyland questionnaire

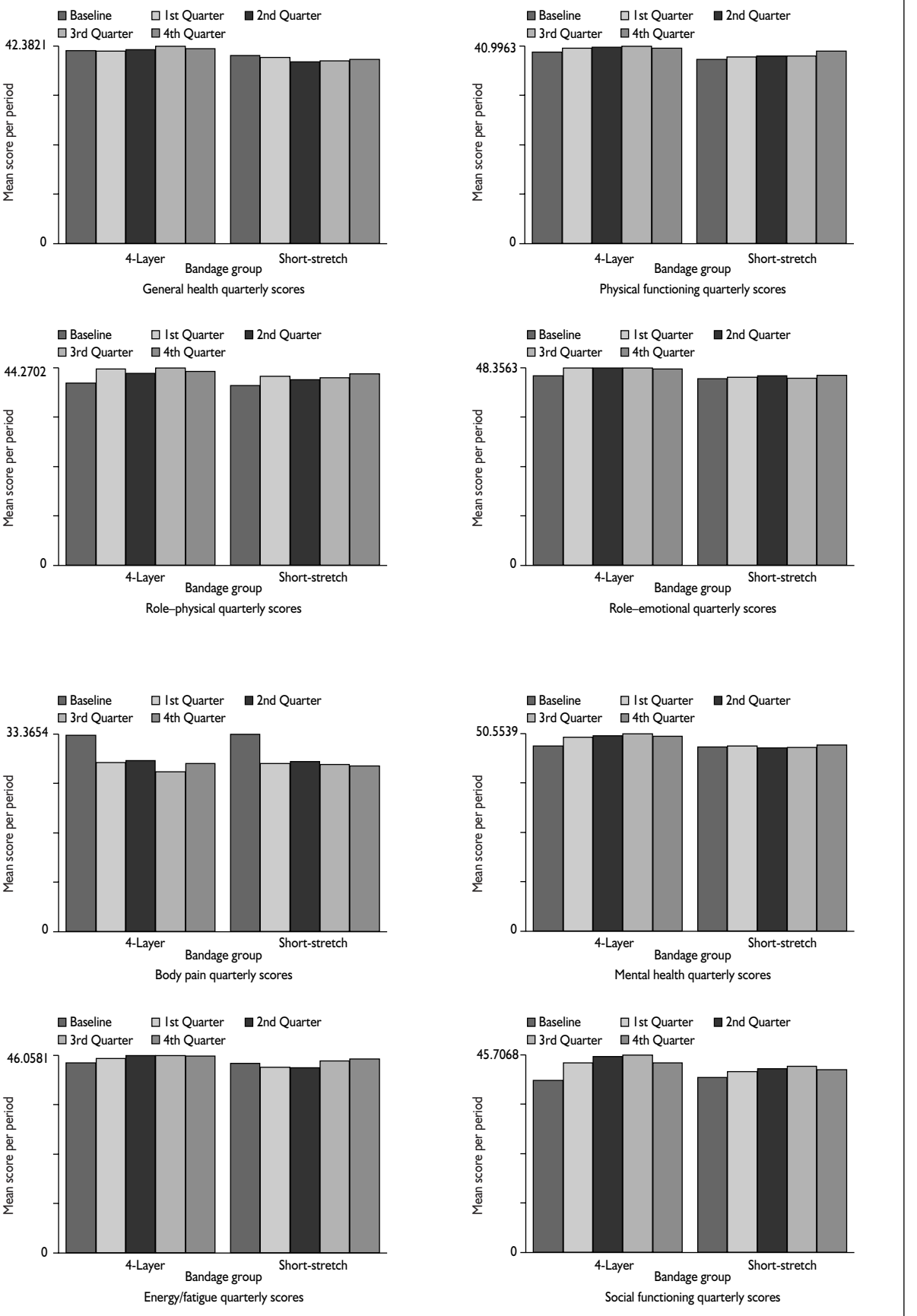

FIGURE 11 *Quarterly scores per health dimension*

TABLE 22 *Quarterly practical factor summary Hyland*

	Practical factor	
Period	**4LB**	**SSB**
Baseline		
Mean (SD)	5.3 (3.75)	5.9 (4.07)
Median (min.–max.)	5 (0–12)	6 (0–12)
1st quarter		
Mean (SD)	4.7 (3.82)	5.9 (4.02)
Median (min.–max.)	4 (0–12)	6 (0–12)
2nd quarter		
Mean (sd)	5.9 (3.6)	6.6 (4.35)
Median (min.–max.)	6 (0–12)	7 (0–12)
3rd quarter		
Mean (sd)	5.7 (4.43)	6.5 (4.44)
Median (min.–max.)	5 (0–12)	7 (0–12)
4th quarter		
Mean (SD)	6.3 (3.99)	5.1 (3.84)
Median (min.–max.)	8 (0–12)	5 (0–12)

TABLE 23 *Quarterly emotional factor summary Hyland*

	Emotional component	
Period	**4LB**	**SSB**
Baseline		
Mean (SD)	5.0 (3.54)	5.2 (3.67)
Median (min.–max.)	4 (0–14)	5 (0–13)
1st quarter		
Mean (SD)	4.6 (3.37)	5.8 (3.66)
Median (min.–max.)	3 (0–14)	5 (0–13)
2nd quarter		
Mean (SD)	6.0 (3.33)	5.6 (3.30)
Median (min.–max.)	6 (0–14)	6 (0–12)
3rd quarter		
Mean (SD)	4.8 (2.66)	5.4 (4.24)
Median (min.–max.)	5 (0–13)	4 (0–14)
4th quarter		
Mean (SD)	5.3 (3.66)	4.9 (2.24)
Median (min.–max.)	4 (0–14)	5 (0–12)

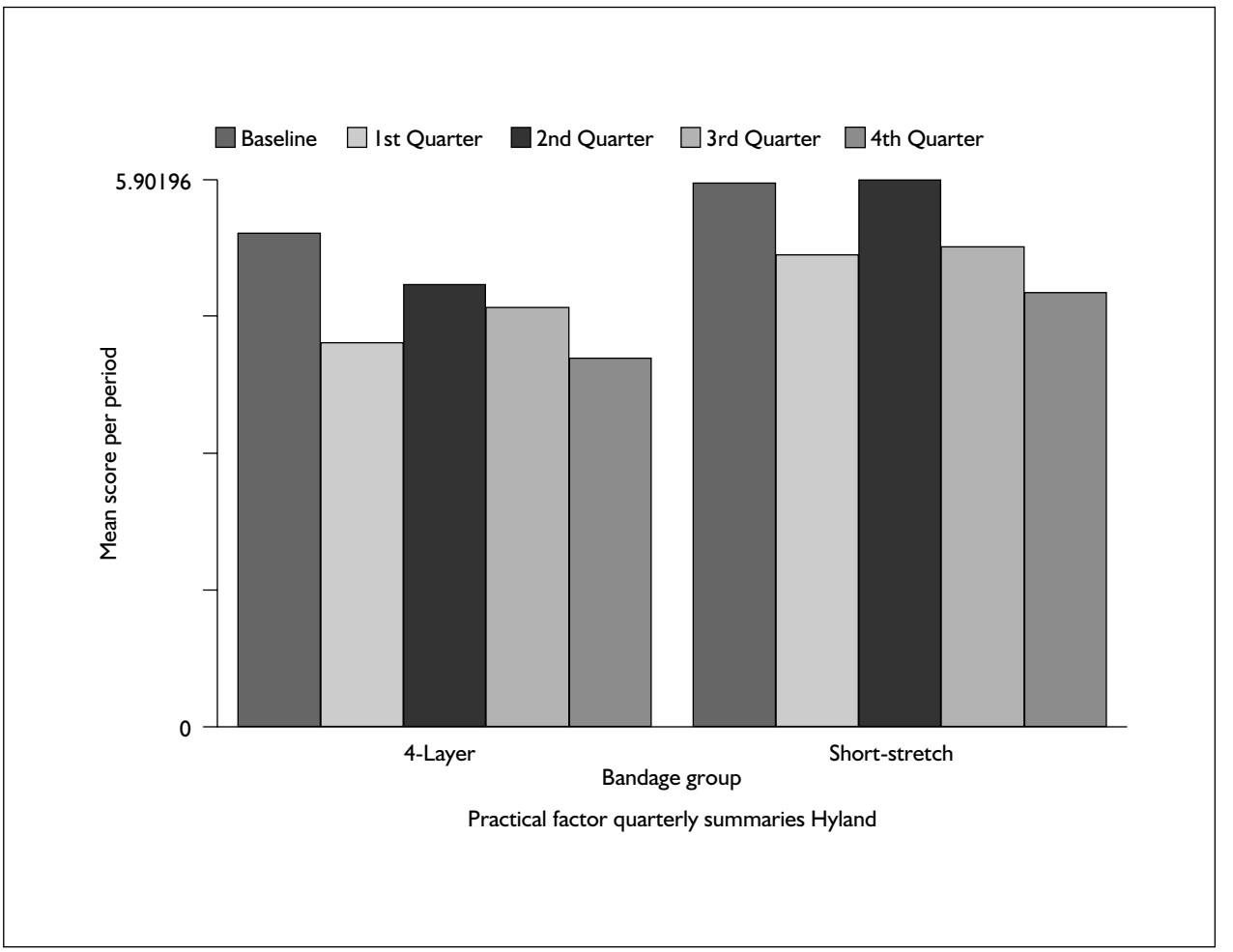

FIGURE 12 *Summary scores practical factor*

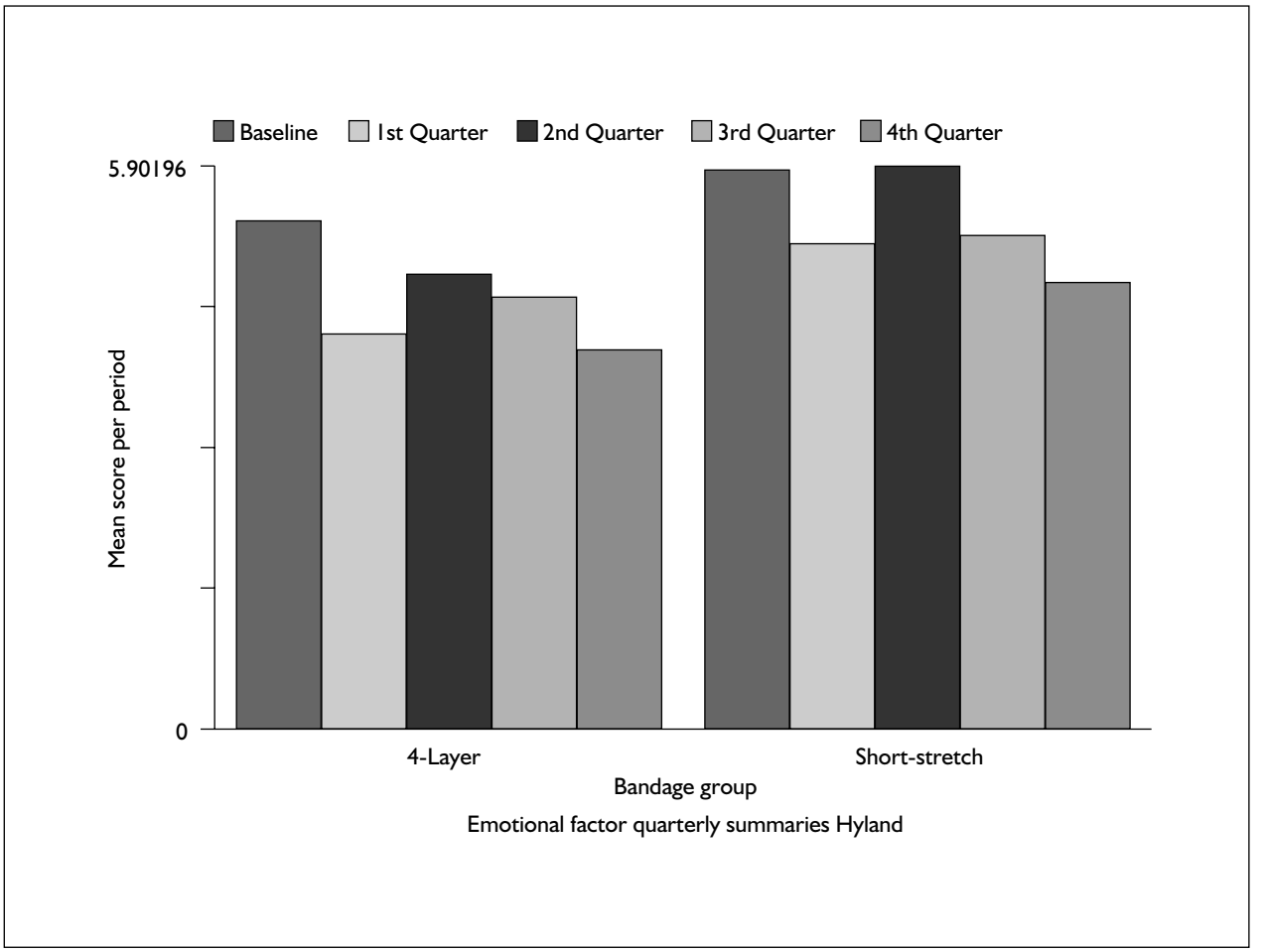

FIGURE 13 *Summary scores emotional factor*

remained fairly constant over time. The practical score was estimated at approximately 6 ± 1 point and the mental component at approximately 5 ± 1 point (see *Tables 22* and *23*).

Summary of results

- Individuals in both bandage groups were similar in terms of their clinical and demographic characteristics.
- Kaplan–Meier estimates of the probability of healing (the unadjusted analysis) showed no statistically significant difference in time to healing between the bandage groups, log-rank test 2.46 ($p = 0.12$).
- Using a Cox proportional hazards model to adjust for the effects of other variables which may influence healing (centre, baseline ulcer area, duration, episodes, ankle mobility, weight), a statistically significant treatment effect in favour of the 4LB group was identified. The HR for individuals in the SSB treatment arm (0.721) is significantly lower than that for people in the 4LB arm [95% CI for exp(β) 0.575 to 0.910].
- There was evidence of heterogeneity of the treatment effect between centres.
- A frailty model will be fitted to the times to healing in order to investigate formally the heterogeneity of the results, to explore what factors at the centre level may explain the variation in treatment effect.
- Kaplan–Meier estimates of the probability of having a recurrence showed no statistically significant difference in time to recurrence between the bandage groups, log-rank test 1.51 ($p = 0.22$).

Chapter 4
Economic analysis

Base case analysis

Information from 387 patients was included in the analysis, 197 allocated to the 4LB group and 195 to the SSB group. Descriptive statistics of monthly volume of resources used in both bandage groups are described in *Table 24*. Between one and two extra nurse visits per month were received by patients in the SSB arm. No marked differences between the monthly volume of resources used in either arm of the study were observed for other resource items. Interestingly, the number of SSBs reported to have been used per patient per month was significantly higher than that recommended by the manufacturers (the manufacturer's recommendation is based on the effect of laundering on bandage performance). According to nurse reports, the higher usage of SSBs was mainly explained by the characteristics of our study population: elderly patients often found it difficult to wash the bandages, and nurses preferred not to re-use the bandages of patients with sloughy, exuding ulcers. Details of the key unit costs, together with their sources, are presented in *Table 25*.

A summary of the unadjusted total mean monthly costs estimated for both treatments is presented in *Tables 26* and *27*. However, given the differences in duration of patient follow-up and the censored nature of cost data, these unadjusted estimates of monthly cost are prone to bias. Therefore, to make a more accurate estimate of the mean difference in the costs of healing between bandage treatments over a year, we used the Kaplan–Meier estimates of time to healing to adjust the monthly mean costs over a 1-year period. The results of the base case analysis in *Table 28* show a statistically significant result in favour of 4LB. Treatment with the 4LB cost, on average, £227.32 less per patient per year (95% bias corrected and accelerated CI £16.53 to £448.30).

Health benefit associated with either bandage treatment was first measured as the difference in mean time to healing between bandage treatments over a year. The difference in the Kaplan–Meier estimates of the mean time to healing over a year was in favour of the 4LB; on average, patients in the 4LB group healed 10.9 days before those in the SSB group. However, this difference was not statistically significant (95% bias corrected and accelerated CI of the difference was from –6.76 to 29.06 days) (see *Table 29*)

Quarterly utility scores per patient by trial arm are presented in *Table 30*. A slight imbalance in the utility scores at baseline between bandage groups was identified. Therefore, we adjusted our

TABLE 24 *Monthly resources used per trial arm (first year of follow-up)*

Resource use	4LB	SSB
Nurse visits		
Mean (SD)	5.1 (3.26)	6.0 (4.09)
Median (min.–max.)	4 (0–21)	5 (1–29)
Doctor visits		
Mean (SD)	0.2 (2.17)	0.3 (1.44)
Median (min.–max.)	0 (0–62)	0 (0–14)
Hospital visits		
Mean (SD)	0.4 (1.04)	0.3 (1.10)
Median (min.–max.)	0 (0–7)	0 (0–15)
Wool bandages		
Mean (SD)	4.9 (3.55)	5.9 (5.61)
Median (min.–max.)	4 (0–22)	4 (0–54)
Crêpe bandages		
Mean (SD)	3.3 (2.83)	0.8 (2.30)
Median (min.–max.)	3 (0–18)	0 (0–20)
Elset bandages		
Mean (SD)	3.6 (2.94)	0.6 (1.86)
Median (min.–max.)	4 (0–20)	0 (0–17)
Coban bandages		
Mean (SD)	4.1 (3.02)	0.8 (2.22)
Median (min.–max.)	4 (0–20)	0 (0–16)
Comprilan 12 bandages		
Mean (SD)	0.0 (0.14)	0.5 (2.31)
Median (min.–max.)	0 (0–3)	0 (0–25)
Comprilan 10 bandages		
Mean (SD)	0.1 (0.92)	2.7 (4.88)
Median (min.–max.)	0 (0–16)	0 (0–52)
Comprilan 8 bandages		
Mean (SD)	0.0 (0.19)	0.6 (1.86)
Median (min.–max.)	0 (0–4)	0 (0–18)
Other bandages		
Mean (SD)	0.0 (0.30)	0.0 (0.41)
Median (min.–max.)	0 (0–5)	0 (0–9)

TABLE 25 *Unit costs and sources*

Item	Unit cost (£)[a]	Source
Nurse visit		
Home (40 minutes)	37	Netten & Curtis[61]
Clinic (22 minutes)	15	Netten & Curtis[61]
Doctor visit		
Home (13.2 minutes)	59	Netten & Curtis[61]
Clinic (12.6 minutes)	26	Netten & Curtis[61]
Hospital visit (outpatient)		
Other reasons	74	Netten & Curtis[61]
4LB system		
Softban	0.61	*British National Formulary*
Softexe	0.60	
Velband/Softband	0.72	
Soffcrepe	1.18	*British National Formulary*
Setocrepe	1.12	
Crepe	0.87	
Litopress	3.44	*British National Formulary*
Elset	2.46	
Co-plus	2.85	*British National Formulary*
Coban	3.01	
4LB system (kits)	8.88	Smith and Nephew
SSB system		
Comprilan/Rosidal K 12	4.08	*British National Formulary*
Comprilan/Rosidal K 10	3.43	*British National Formulary*
Comprilan/Rosidal K 12	3.08	*British National Formulary*
Softban	0.61	*British National Formulary*
Softexe	0.60	
Velband	0.72	
Other bandages		
Setopress	3.29	*British National Formulary*
Tensopress	3.24	
Surepress	3.18	
Tubigrip	9.00	Internet

*Year of pricing 2001[a].

TABLE 26 *Monthly patient costs (unadjusted)*

	Unadjusted costs per month during first year of follow-up (£)	
Resource used	**4LB**	**SSB**
Nurse visits		
Mean (SD)	166.0 (129.90)	188.5 (154.220)
Median (min.–max.)	148 (0–777)	0 (15–1073)
Doctor visits		
Mean (SD)	9.8 (124.58)	10.1 (40.91)
Median (min.–max.)	0 (0–3658)	0 (0–364)
Hospital visits		
Mean (SD)	29.7 (81.35)	24.3 (81.35)
Median (min.–max.)	0 (0–518)	0 (0–1110)
Bandages		
Mean (SD)	29.2 (20.08)	22.0 (24.04)
Median (min.–max.)	29.8 (0–132.8)	15 (0–195)
Total costs (unadjusted)		
Mean (SD)	236.8 (208.7988)	244.5 (193.02)
Median (min.–max.)	180.4 (16.2–4072.3)	188.2 (15.64–1808.7)

TABLE 27 *Unadjusted costs per month*

Period	Unadjusted monthly costs (£)	
	4LB	**SSB**
1st month (*n*)[a]	165	170
Mean (SD)	188.9 (143.44)	197.1 (143.94)
Median (min.–max.)	155.5 (16.2–763.7)	165.0 (22.2–684.4)
2nd month (*n*)	146	150
Mean (SD)	280.1 (355.91)	241.8 (203.60)
Median (min.–max.)	214.3 (21.4–4072.3)	191.0 (30.6–1542.1)
3rd month (*n*)	105	114
Mean (SD)	239.2 (152.71)	251.4 (197.27)
Median (min.–max.)	180.4 (37–856.3)	177.9 (15.6–1100.7)
4th month (*n*)	70	94
Mean (SD)	238.1 (146.71)	256.7 (236.98)
Median (min.–max.)	207.4 (44.5–777)	196.6 (15.6–1808.74)
5th month (*n*)	56	74
Mean (SD)	220.4 (150.25)	264.2 (181.40)
Median (min.–max.)	188.9 (37–777)	213.2 (37.6–797.3)
6th month (*n*)	46	61
Mean (SD)	222.3 (146.04)	266.5 (211.79)
Median (min.–max.)	187.5 (20.1–629)	188.2 (15.6–993.7)
7th month (*n*)	39	51
Mean (SD)	264.3 (169.67)	275.0 (204.71)
Median (min.–max.)	217.0 (40.6–740)	219.3 (43.8–958.7)
8th month (*n*)	33	45
Mean (SD)	242.6 (147.60)	280.6 (207.67)
Median (min.–max.)	208.7 (44.5–703)	222.3 (34.7–1091.1)
9th month (*n*)	29	39
Mean (SD)	255.0 (171.61)	266.2 (196.03)
Median (min.–max.)	178.4 (22.5–711.2)	263.5 (21.4–911.0)
10th month (*n*)	23	36
Mean (SD)	245.7 (162.29)	248.1 (178.40)
Median (min.–max.)	213.6 (38.7–703)	222.5 (37–763.0)
11th month (*n*)	20	36
Mean (SD)	260.1 (150.11)	251.1 (209.61)
Median (min.–max.)	235.4 (89.8–777)	184.0 (37–1031.7)
12th month (*n*)	19	33
Mean (SD)	257.3 (163.60)	224.2 (125.88)
Median (min.–max.)	236.8 (63–703)	214.4 (22.5–507.3)

[a] *n* = Sample size per month.

TABLE 28 *Mean adjusted annual cost*

	Mean (£)	95% bias-corrected and accelerated CI (£)
4LB	1298.41	1187.83 to 1471.89
SSB	1525.73	1373.92 to 1716.66
Difference	227.32	16.53 to 448.30

TABLE 29 *Mean adjusted annual time to healing*

	Mean (days)	95% bias-corrected and accelerated CI
4LB	96.72	85.31 to 111.59
SSB	107.62	95.88 to 122.25
Difference	–10.90	–29.06 to 6.76

TABLE 30 *Quarterly unadjusted utility scores*

Period	Unadjusted quarterly EuroQol scores	
	4LB (*n* = 195)	**SSB (*n* = 192)**
Baseline		
Mean (SD)	0.6 (0.28)	0.6 (0.29)
Median (min.–max.)	0.7 (–0.18 to 1)	0.7 (–0.24 to 1)
Missing (%)	30 (15%)	29 (15%)
1st Quarter		
Mean (SD)	0.7 (0.26)	0.7 (0.29)
Median (min.–max.)	0.7 (–0.08 to 1)	0.7 (–0.43 to 1)
Missing (%)	60 (31%)	66 (34%)
2nd Quarter		
Mean (SD)	0.7 (0.30)	0.7 (0.28)
Median (min.–max.)	0.8 (–0.14 to 1)	0.7 (–0.24 to 1)
Missing (%)	65 (33%)	83 (43%)
3rd Quarter		
Mean (SD)	0.7 (0.2)	0.7 (0.28)
Median (min.–max.)	0.7 (–0.18 to 1)	0.7 (–0.18 to 1)
Missing (%)	81 (42%)	85 (44%)
4th Quarter		
Mean (SD)	0.7 (0.26)	0.7 (0.26)
Median (min.–max.)	0.6 (–0.18 to 1)	100 (0.02 to 1)
Missing (%)	79 (41%)	100 (52%)

estimate of QALYs using multivariate regression analysis. Mean average QALYs gained per bandage group are presented in *Table 31*. The results showed that after having adjusted for any original imbalances in utility scores at baseline and censoring, individuals in the 4LB group had, on average, a better QoL than individuals in the SSB group (the annual difference in QALYs was –0.02; see *Table 32*). However, this difference was not statistically significant at conventional levels of significance (95% bias corrected and accelerated CI for the difference was –0.08 to 0.04 QALYs; see *Table 32*).

Our base case analysis showed that 4LB treatment is a dominant strategy, that is, it is associated with a greater health benefit and lower costs than SSB treatment, although the differences are not statistically significant. In these circumstances, an incremental analysis is not justified, so we did not combine our estimates of differential costs and health benefits.

To represent the sampling uncertainty of the mean difference in costs and health benefits between bandage treatments, we used the incremental cost-effectiveness plane, where we graphically plotted the results for the 1000 replicates of the non-parametric bootstrap of the mean difference in cost and benefits. As *Figure 14* shows, in the majority of the replicates the point estimates fall in the first and second quadrants of the plane, suggesting that the SSB treatment is associated with greater costs than the 4LB treatment. There is more uncertainty associated with the relative clinical effectiveness of the bandages; whereas in a large proportion of the simulations our point estimate suggested a better performance of the current treatment (4LB), in a non-negligible proportion of cases the results favour the SSB system. This uncertainty was explored using sensitivity analysis.

Sensitivity analysis

Careful analysis of the volume of resources used showed that the difference in costs between compression systems was mainly driven by three parameters: the difference in number of nurse visits required for patients in each bandage group, the care setting (domiciliary visits, clinics), and the higher than expected number of SSBs that patients required. As *Table 24* shows, on average patients in the SSB group required one more visit per month than patients in the 4LB group. Across all centres the majority of care was delivered via domiciliary nurse visits. This, combined with the

TABLE 31 *Quarterly unadjusted QALYs*

Period	Unadjusted quarterly QALYs[a]	
	4LB (*n* = 195)	**SSB (*n* = 192)**
1st quarter		
Mean (SD)	0.2 (0.06)	0.2 (0.06)
Median (min.–max.)	0.2 (–0.02 to 0.25)	0.2 (–0.04 to 0.25)
Missing (%)	72 (37%)	73 (38%)
2nd quarter		
Mean (SD)	0.2 (0.06)	0.2 (0.06)
Median (min.–max.)	0.2 (–0.02 to 0.25)	0.2 (–0.02 to 0.25)
Missing (%)	81 (42%)	96 (50%)
3rd quarter		
Mean (SD)	0.2 (0.07)	0.2 (0.06)
Median (min.–max.)	0.20 (–0.03 to 0.25)	0.17 (–0.05 to 0.25)
Missing (%)	90 (46%)	101 (53%)
4th quarter		
Mean (SD)	0.2 (0.06)	0.2 (0.06)
Median (min.–max.)	0.2 (–0.03 to 0.25)	0.2 (0.01 to 0.25)
Missing (%)	93 (48%)	108 (56%)
Annual		
Mean (SD)	0.7 (0.24)	0.7 (0.22)
Median (min.–max.)	0.8 (–0.06 to 1)	0.7 (–0.06 to 1)
Missing (%)	111 (57%)	123 (64%)

[a] QALYs were calculated as the area under the curve (AUC) defined by the quarterly EQ-5D scores, i.e. the QALY for the 2nd quarter is based on the AUC from 3 months to 6 months, etc.

TABLE 32 *Mean adjusted QALY*

	Mean (QALYs)[a]	95% bias-corrected and accelerated CI
4LB	0.69	0.66 to 0.74
SSB	0.67	0.63 to 0.72
Difference	0.02	–0.08 to 0.04

[a] QALYs were adjusted for any imbalances in the EQ-5D scores between the bandage groups at baseline.

TABLE 33 *Mean adjusted annual cost (first scenario)*

	Mean (£)	95% bias-corrected and accelerated CI (£)
4LB	1298.41	1187.83 to 1471.90
SSB	1486.47	1339.77 to 1668.03
Difference	188.06	–15.36 to 410.00

TABLE 34 *Mean adjusted annual cost (second scenario)*

	Mean (£)	95% bias-corrected and accelerated CI (£)
4LB	1385.92	1270.11 to 1565.79
SSB	1525.73	1373.91 to 1716.66
Difference	139.81	–62.11 to 369.09

TABLE 35 *Mean adjusted annual cost (third scenario)*

	Mean (£)	95% bias-corrected and accelerated CI (£)
4LB	1385.92	1270.11 to 1565.79
SSB	1486.47	1339.77 to 1668.03
Difference	100.55	–105.13 to 321.62

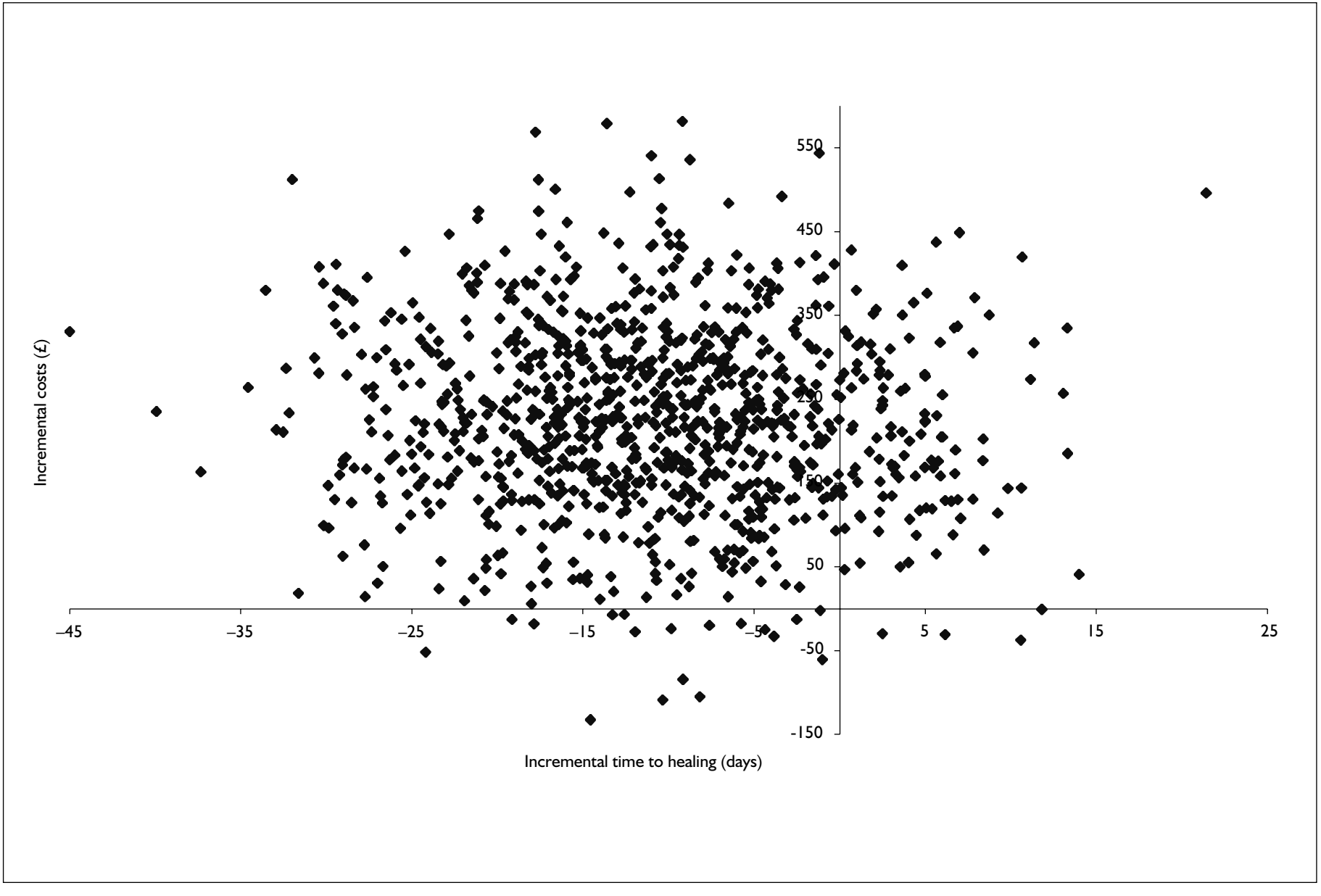

FIGURE 14 *Cost-effectiveness plane, base case analysis*

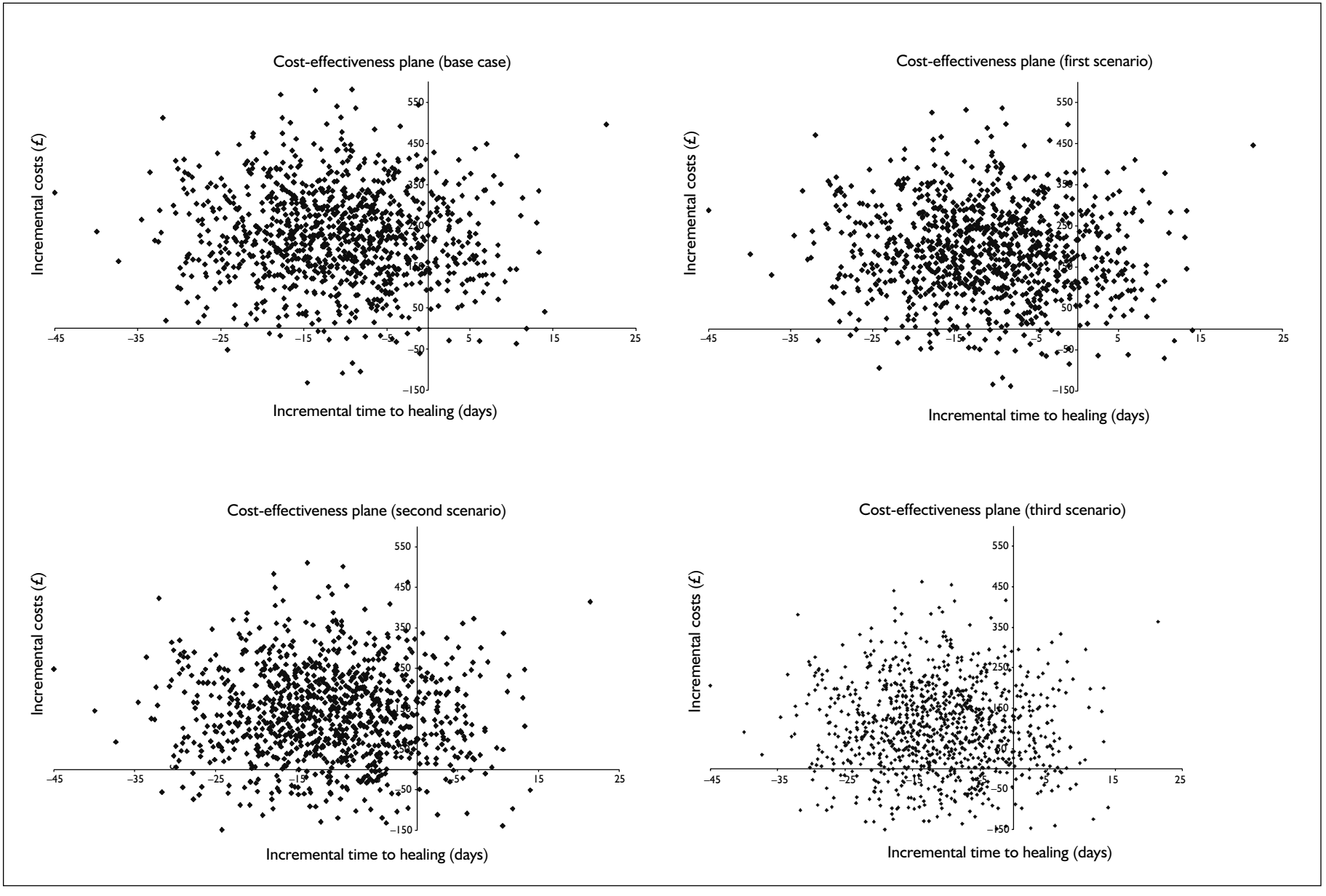

FIGURE 15 *Cost-effectiveness plane, sensitivity analyses*

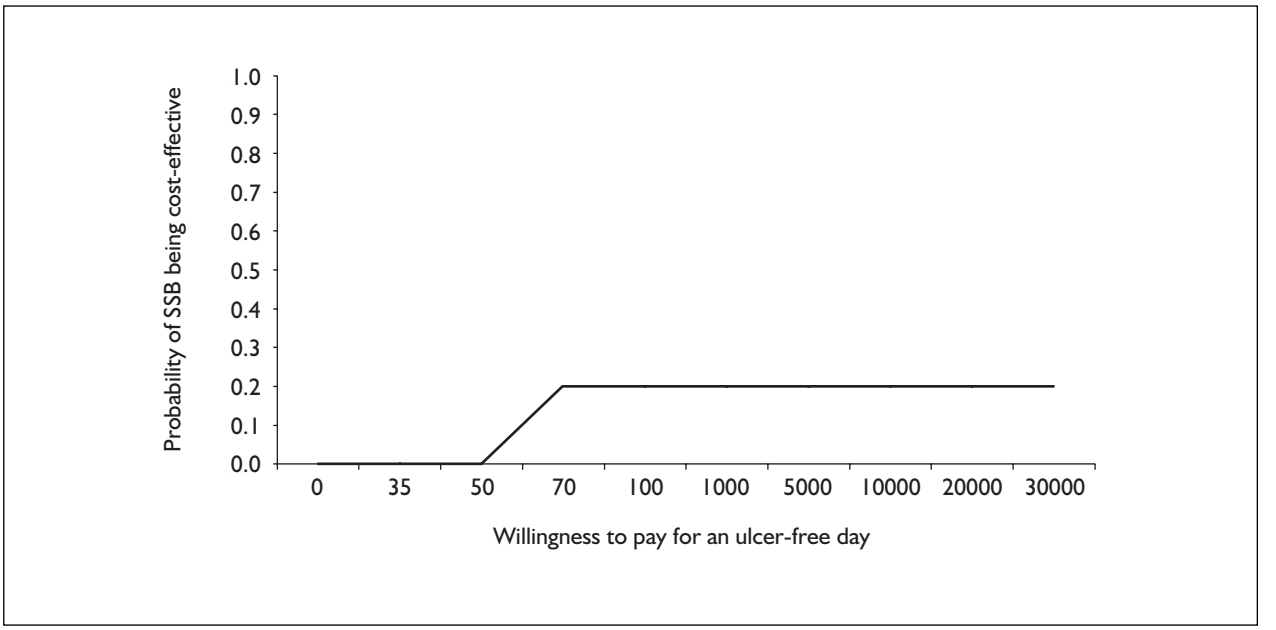

FIGURE 16 *Cost-effectiveness acceptability curve (short-stretch)*

significant difference between the cost of clinic care (£15) and a home visit (£37) (a difference of £22, see *Table 25*) means that even slight imbalances in the number of visits between the groups results in a significant increase in the total costs of the treatment.

Point estimates of the difference in costs between these compression bandages under the three sensitivity analysis scenarios are shown in *Tables 33–35*. In all three scenarios the difference in total treatment cost over a year was smaller than that estimated in the base case scenario (£227). The mean differential costs in the first, second and third sensitivity analyses were £188.06, £140 and £100.55, respectively. In none of the three scenarios considered for the sensitivity analysis was the difference in costs statistically significant at conventional levels of significance (see *Tables 33–35*).

Cost-effectiveness planes for the three sensitivity analysis scenarios and the base case analysis are presented in *Figure 15*, where it can be seen that the main effect of considering feasible variations of the volume of bandages used and the unit costs of the compression systems is to shift the distribution of the mean difference in costs and effects towards the third quadrant. In other words, when lower rates of SSB use are used and the price of the 4LB is at its highest possible level, this results in a shift of the mean average cost-effectiveness ratio towards the third quadrant. However, it is worth noticing that in the third scenario most of the point estimates of the cost-effectiveness ratio still fall in the second quadrant, suggesting that even under three conditions the 4LB is more likely to be a dominant strategy than the SSB.

The likelihood of the SSB being cost-effective was explored in a cost-effectiveness acceptability curve. This curve for SSBs in *Figure 16* suggests that even for considerably high willingness to pay values for an ulcer-free day the SSB is associated with only a 20% probability of being cost-effective.

Chapter 5
Discussion

Most previous randomised trials of wound care treatments (e.g. dressings and other devices for venous ulcers, diabetic foot ulcers and pressure ulcers) have been too small and/or were susceptible to a range of biases. These include selection bias (e.g. lack of allocation concealment), performance bias (e.g. different clinicians treating patients in intervention and control groups) and attrition bias (due to differential withdrawal from the trial in the intervention groups). These problems mean that estimates of treatment effects were either relatively imprecise, owing to the small sample sizes, or prone to bias. In contrast, VenUS is a very large RCT of pressure bandaging. Indeed, it is the largest RCT of a leg ulcer intervention, and with the longest follow-up, of any wound healing trial that we have been able to identify. Through VenUS we have demonstrated that large, multicentre RCTs in wound care can answer questions of relevance to patients, clinicians and healthcare managers.

This discussion will consider the clinical and economic analyses in turn, first of VenUS and then in context of the previously published trials.[31] Finally, issues concerning the internal and external validity of the study findings will be discussed.

Clinical effectiveness

Ulcer healing

In this trial, patients with venous ulcers treated with the 4LB achieved an ulcer-free limb an average of 34 days earlier than people treated with the SSB (median time to healing 92 days with 4LB compared with 126 days with SSB). Whereas the unadjusted analysis (Kaplan–Meier) found no significant difference in healing time between the two bandages, a Cox proportional hazards model, in which the probability to heal at any point in time (hazard) was adjusted by a number of baseline risk factors, found a statistically significantly greater chance of healing associated with the 4LB and a significantly reduced hazard of healing with the SSB (HR 0.72, 95% CI 0.57 to 0.91). It is worth emphasising, however, that the adjusted and unadjusted analyses are fundamentally the same, although the adjusted estimate is more precise, hence reaching conventional levels of statistical significance. Both analyses are based on total numbers of ulcers healed; the adjustment merely corrects for small differences in patient characteristics at baseline.

A number of patient characteristics were statistically significantly associated with healing in our model. The number of previous ulcer episodes, weight, baseline area and duration of reference ulcer were all inversely related to the risk of healing, whereas ankle mobility was directly related. In addition, there was an interaction between bandage and centre, indicating that the probability of healing with each bandage depended on where the patient was treated. These data should be treated with caution, however, as the treatment–centre interaction was not an a priori hypothesis, and patient numbers in several centres were extremely small. In fact, when we excluded the information from the four smaller centres in a sensitivity analysis, the centre effect disappeared. In order to have a clearer insight into the existence of a centre effect, we plan to undertake further analysis in the future using frailty models.

Adverse effects

The SSB was associated with more frequent reporting of ulcer deterioration (166) than the 4LB (91). The descriptor 'ulcer deterioration' encompassed several ulcer states including signs of infection and increased ulcer area. The apparent increase in the rate of deterioration under SSB was mainly as a result of reporting of increased infections. This increase has three plausible explanations: a real increase in the incidence of infection; the longer healing time exposing SSB patients to increased risk of deterioration; and detection bias (the lack of blinding of nurses coupled with their unfamiliarity with short-stretch bandaging technique in most centres increasing their perception of ulcer deterioration). There is a lack of consensus as to how infection in chronic wounds is best detected and the stage at which bacterial burden impedes healing. All chronic wounds are colonised by bacteria, but in modest numbers (usually quoted as less than 10^6 colony-forming units per gram of tissue).[75] Colonising

bacteria do not generally cause clinical infection (denoted by the cardinal signs and symptoms of pain, swelling, redness and pus). Microbiological analysis of chronic wounds has indicated that the number of bacteria may not be the only contributing factor. For example, Trengove and colleagues found that the number of bacteria in a wound **and** the number of colonising species determined outcome.[76]

Diagnosis of infection is normally made by the combination of clinical signs and symptoms (such as increased wound exudate, ulcer area, pain, inflammation). The diagnosis of infection in this trial was almost entirely subjective, and the increase in reported infection associated with SSB should be treated with caution. Although detection bias could be minimised by using microbiological sampling and the criterion of 10^6 bacteria per gram of tissue, the reliability of wound swabs for quantitative microbiological analysis is unclear.

Furthermore, the detection of anaerobes is difficult, as they require specific culture media and rapid transport to the laboratory, and therefore a false-negative result is possible. Tissue biopsy is more reliable but is invasive (increasing the wound volume) and therefore unlikely to be widely used. There was no increase in the rate of hospitalisation for serious infection in the SSB group.

There was, however, a significantly higher number of nurse-initiated withdrawals from the allocated treatment in the SSB group (30 compared with 16 in the 4LB group). The extent to which the lack of blinding of nurses and patients to treatment may have had an impact on the decisions to withdraw from treatment is not clear. Hence it is impossible to be sure of the true incidence of infection in this study; however, wound infection is likely to affect the primary end-point of ulcer healing, and thus any important differences in infection rates will be captured in the difference in clinical effect of the bandages.

HRQoL

Changes in HRQoL over the study period were investigated using three different instruments, one generic measure, the SF-12, one utility measure, the EuroQol, and a disease specific measure, the Hyland. The results from the analysis using these three instruments were all in the same direction, suggesting that the QoL of the individuals in the 4LB group was better than that of the individuals in the SSB group.

Interestingly, both the results from the SF-12 and those from the Hyland suggested that over time the greatest improvements on the QoL of patients with venous leg ulcers was associated with a mental/emotional component of QoL rather than with a physical/practical one. This suggests, therefore, that the utility loss due to leg ulcers is due primarily to an effect on mental well-being rather than on physical functioning.

In accordance with previous studies, the results from the SF-12 indicated that patients with venous leg ulcers manifested increased levels of pain (see the section 'Impact of ulceration on quality of life', p. 2). However, when looking at the quarterly progress of the bodily pain dimension on the SF-12, we observed that after a small change during the first quarter, levels of reported pain remained constant for the duration of the trial. This may be an indication that changes in the condition of the ulcer did not have an impact on the levels of pain reported by the patients.

Consequently, the pain reported by patients may be associated with other health conditions common to this population group. Venous leg ulcers are most frequently present in elderly people who are more likely to be affected by several health problems simultaneously. Future studies should explore the feasibility and effect of disentangling ulcer-related pain from other pain.

Cost-effectiveness

The cost-effectiveness of the two bandages was investigated in two ways. A cost–effectiveness and a cost-utility analysis were conducted using the patient-level economic data collected within the VenUS study. The two different economic analyses showed that the SSB was a dominated alternative, that is, the SSB was associated with smaller health benefits and greater costs than the 4LB.

In the cost-effectiveness analysis, health benefit was measured as the differential in mean time to healing between bandage treatments over a year. On average, patients in the 4LB group healed 10.9 days before those in the SSB group; however, this difference was not statistically significant at conventional levels of significance. The mean difference in total cost between compression systems was £227.32 per patient per year; this difference in favour of the 4LB was statistically significant at the 5% level of significance.

QALYs associated with the two compression systems were used as the unit of health benefit measure for the cost–utility analysis. The mean average difference in QALYs between compression systems in favour of the 4LB was –0.02; however this is not statistically significant at the 5% level of significance. This may be a function of the relative insensitivity of the EuroQol to detect modest, but important, differences, in QoL. This shows the need to include disease specific and general measures of health status in addition to utility measures.

The robustness of our results was tested using a scenario approach to sensitivity analysis. The main sources of uncertainty explored were the number of SSBs that a patient required and the actual costs of the 4LB system. The rationale for this was that the other factors identified as potential drivers of compression treatment costs, that is number of nurse visits and visits setting, are issues mainly related to the way in which service provision is organised in the UK and were not part of this evaluation, so no sensitivity analysis on these parameters was justified.

Sensitivity analysis indicated that even if the volume of SSBs involved in the treatment of a patient was lower than that reported in this trial, and the acquisition price of the 4LB was at its maximum level, on average the SSB is still a dominated alternative. Consequently, our results are relatively robust to plausible changes in assumptions.

Consideration of the mechanisms and exploration of key findings

Centre effect

Both compression bandage systems work in a similar manner, that is, they apply external compression to the limb in order to counteract the raised venous pressure that is implicated in venous ulceration. In both systems a layer of padding smoothes out high compression over bony prominences and aids absorption of exudate. There has been much discussion in the literature of the differences between the elastomeric compression systems and the inelastic compression systems. It has been suggested that inelastic systems (such as the SSB) confer particular advantages over elastic systems, such as greater safety, ease of application, reusability and patients are able to wear their usual footwear.[77–79] On the other hand, elastic systems, such as the 4LB, are said to stay on longer without the need for reapplication, thus reducing the cost of treatment.[80] In the three trials identified in a previous review,[81] only two[40,44] reported the frequency of bandage application, one[43] reported the incidence of pressure damage and none reported any data on footwear problems.

The majority of these suggested differences between the bandage systems, therefore, appear to be unsupported by data from RCTs. We did, however, find that 4LBs were changed less frequently than the SSBs and this may reflect the ability of the 4LB system to stay in place for longer; alternatively, it may be that those nurses who were less familiar with the SSB arranged to see these patients more frequently as they were less confident about leaving the bandages in place for a week. Partsch and colleagues,[44] who undertook their study in places where the SSB is standard treatment, planned weekly visits in both arms. Although this trial reported similar intervals between bandage applications (median of 7 days), this is relatively uninformative since (1) the protocol recommended a once weekly visit and (2) it tells us nothing of the volume of resource used by 50% of patients (as these data are likely to be skewed). What is also needed, therefore, is information about the mean number of visits required, and this was not reported. Hence we cannot conclude from Partsch and colleagues' study whether the experience of nurses influenced the capacity of the bandages to stay in place, but this is clearly a research question for the future.

Since the clinical effectiveness of any compression system might be influenced by nurses' familiarity with it, we retrospectively ascertained patterns of bandage use in our centres both before the trial commenced and after completion of follow-up (see *Table 36*). We obtained this information by enquiring of the local trial coordinators during the analysis phase and it therefore must be treated with caution. Previous bandaging practice by centre can be only a crude proxy for actual bandage skill.

The 4LB only became prescribable within the community during 1999 (the same year that the trial commenced recruitment).[82] It is therefore likely that bandager experience of the 4LB at the start of the trial was variable, and the 4LB was certainly not universally used. All nine trial sites were to some extent familiar with the 4LB before the trial; however, only Falkirk and East London (centres recruited later in the trial) were using the SSB before the trial. This means that many of the nurses in all the trial sites were learning about

TABLE 36 *Choice of compression bandages used in the treatment of venous leg ulcers in the trial sites before and after the VenUS trial*

Centre	Bandages used before trial	Bandages used after trial
North Yorkshire	4LB Class 3c bandage systems	4LB SSB Class 3c bandage systems
Leeds	4LB (although not extensively) Class 3c bandage systems	4LB SSB Class 3c bandage systems
West Cumbria	4LB	4LB
West London	4LB	4LB
East London	4LB SSB	4LB SSB
Calderdale	4LB	4LB SSB
Southport	4LB Class 3c bandage systems Compression hosiery	4LB SSB Class 3c bandage systems Compression hosiery
Newmarket	4LB	4LB
Falkirk	4LB SSB	4LB SSB

both bandages during the trial. This, combined with a high staff turnover in some of the centres, may have led to a learning effect, where bandaging skill and other bandage-related decisions were not optimal at the start. Even if nurses were completely unfamiliar with both bandage techniques, a differential learning curve could underestimate the effectiveness of one of the bandage systems. The trial by Partsch and colleagues[44] provides an interesting comparison with ours. This trial also compared the 4LB and SSB and recruited patients from the outpatient clinics of major referral centres, where the SSB was the standard treatment prior to the trial. Experienced clinicians applied the bandages and 73% of patients in the SSB group healed by 16 weeks compared with 62% in the 4LB group. This difference was not significant, although the chance of a Type II error cannot be ignored since the trial was underpowered (112 participants). We intend to investigate the possible presence of a learning curve effect in future work; however, it is also important to emphasise that, for the reasons outlined earlier, the apparent centre effect should be viewed with caution, since we cannot reject the possibility of this being a chance finding.

Ankle mobility

We found no interaction between ankle mobility and healing rates in the two forms of bandages, an interaction that might have been expected if SSBs work better in people with good ankle mobility. We found that people with greater ankle mobility had a higher healing rate regardless of which bandage system was used.

Comparison of the findings with other published studies

Four-layer bandaging is the standard mode of compression in the UK, although a few centres use the SSB. In Austria, Germany, The Netherlands and Australia, the SSB is standard. A previous systematic review comparing the effectiveness of these systems found no difference in healing rates between the elastomeric (e.g. 4LB) and inelastic (e.g. SSB) multilayered bandages.[81] A subset of three of these previous RCTs compared the 4LB with the SSB in the UK, Austria and The Netherlands.[40,43,44] Individually, none of these trials found a statistically significant difference in healing rates between the bandages (although they were too small, at 43, 53 and 112 patients, respectively, to find anything other than a very large effect). The absolute healing rates in the trials are presented in *Table 37*. It is notable that Partsch and colleagues' study achieved much higher healing rates than the others, almost certainly explained by the small ulcer size at

TABLE 37 *Healing rates at various time points in trials comparing 4LB and SSB*

Trial	Proportion (%) of ulcers healed at specified time points (weeks)					
	SSB (12)	4LB (12)	SSB (16)	4LB (16)	SSB (52)	4LB (52)
Duby *et al.*[38–40 a]	40	44				
Scriven *et al.*[43 a]	41	34			56	53
Partsch *et al.*[44 b]			73	62		
VenUS[b]	37	46	45	55	72	78

[a] In these trials the legs of several patients with bilateral ulceration were randomised independently.
[b] Primary outcome in these trials was complete healing of all ulcers on trial leg (in the presence of multiple ulcers this would tend to underestimate the outcome of 'ulcer healing').

baseline in this study (median ulcer for 4LB patients in Partsch and colleagues' study 1.5 cm^2 compared with 3.81 cm^2 in VenUS).

Contribution of this trial to the evidence

In order to determine how this new large RCT affects our overall knowledge of how these bandages compare, we considered adding this trial to the original meta-analysis comparing the effectiveness of multilayered elastomeric compression systems (including 4LBs) with short-stretch compression systems. However, this approach would be inappropriate since this approach ignores the survival nature of the data. In VenUS, for example, there was no statistically significant difference in the proportion of ulcers healed at 12 weeks, but there was at 24 weeks. Hence choice of reporting time greatly influences the results. The trial of Partsch and colleagues[44] and VenUS are similar in design and analysis, and both used adjusted analyses that account for the uneven distribution of prognostic factors for healing across the two groups. One approach would be to pool the HRs from these two similar studies. Although this yields a pooled HR of 0.85 (95% CI 0.49 to 1.48) in favour of the 4LB, this statistic is relatively uninformative since we suspect that there is important heterogeneity between these two trials, particularly in terms of the bandaging skills and techniques.

Strengths and limitations of the study

Allocation concealment

In all wound care trials, it is possible to ensure that the person recruiting patients into the trial does not have foreknowledge of the treatment group to which a patient will be allocated. Such allocation concealment is important in reducing patient selection bias, and open allocation has been associated with inflated estimates of effect size.[83] We achieved allocation concealment by using a remote telephone randomisation service which only revealed the allocation after the recruiting nurse had provided unique patient enrolment data. In the 26 trials reviewed by Cullum and colleagues,[81] only six reported allocation concealment and three used obviously 'open' methods of allocation to intervention arms.

Blinding of outcome assessment

Ideally, the personnel measuring trial outcomes should be unaware of the allocation. In this trial, the patients were treated either in the home or at a leg ulcer clinic, and the blinding of outcome assessment would have required additional, blinded personnel to assess the state of the ulcer at each visit, after removal of bandages, and this was not possible for reasons of logistics and available resources. We considered other forms of blinded outcome assessment, such as digital photographs of the ulcer at each visit for assessment by a trial coordinator blinded to the allocation. Digital photography was in its infancy (and extremely costly) at the inception of this trial, but in future studies should probably be seriously considered as a means of verifying wound status on an ongoing basis. For this to be successful, however, the variable provision of information technology in the community nursing workplace would need to be addressed to enable the photographs to be emailed to the Trial Coordinator. For this trial we used a blinded remote observer to verify independently healing from photography. If at a treatment visit the nurse decided that the ulcers were nearly healed, they took a Polaroid camera to each subsequent visit and photographed the newly healed wound. This photograph was returned to the Trial Coordinator

for confirmation of healing. No false-positive photographs (i.e. unhealed ulcers described by the local nurse as healed) were received at the Trial Coordination Office; however, this procedure would not identify when healing occurred at a visit prior to the healing photograph being taken (e.g. if the wound healed unexpectedly). If this happened, then the nurses were instructed to complete a healing form on the day of healing and to send in a healing photograph with the actual date, even if this was days later.

Blinding patients and caregivers

Ideally, the patients receiving the interventions under evaluation and the clinicians treating them would all be blinded to the allocation. In trials evaluating medical devices (e.g. dressings, bandages and beds/mattresses), it is rarely possible to arrange for the patients and nurses treating the patients to be blinded to the interventions. This is because the majority of comparisons that need to be made are between different types of dressings/bandages. It is sometimes possible to blind the allocation when treatments being compared are within the same class, for example, different dressing types such as alginates/hydrogels/hydrocolloids, but even then practitioners may be able to detect small differences in the properties of the dressings. A small number of topical wound products are classified as pharmaceuticals, such as topically applied growth factors, and trials of these products have been able to include a placebo arm in which the vehicle is used as a comparator.

We were unable to blind either the patient or the healthcare personnel to the bandages. It is not clear what impact the lack of patient and nurse blinding would have on the direction or size of the effect observed in this trial.

Bandage application

A criticism of our study is that we did not record nurses' competence in bandage application at the beginning of the trial. There were several reasons for this. First, the trial was to determine how effective the bandages were **as currently used in UK clinical practice**, and not on their performance with perfect bandage application. Second, it is far from clear how bandager performance should be measured for the SSB, as there is no agreed pressure profile for the application of the SSB system.[84]

The only reliable and valid method for checking bandage application is by placing small pressure sensors at predefined points on the patient's limb and wrapping the bandage over it. The bandage normally needs to be removed for retrieval of the pressure sensors. The systematic checking of bandaging technique would have required enormous investment in personnel and may have resulted in fewer nurses agreeing to enrol their patients into the trial. Furthermore, as the method of care delivery in some centres included large teams of community nurses, then evaluation of bandaging techniques of all these staff, regularly over the period of the trial, would have been prohibitively expensive. The results of a trial in which bandage application technique had been assiduously monitored would not have been applicable to clinical practice, where there is a range of competence in compression bandaging.[85]

Previous work has demonstrated that nurses' bandaging technique is generally poor before training, with the majority applying them with greater pressures at the calf than at the ankle (which would tend to reduce rather than increase venous return).[85] Furthermore, training makes only a modest impact on the proportion of nurses applying the bandages with a reduction in pressure from the ankle towards the knee. One of us has previously evaluated the impact of training on the bandaging techniques of nurses using both 4LB and SSB system.[85,86] The proportion of community nurses applying a 4LB with graduated pressure higher at ankle than calf (just one element of 'appropriate' bandaging), increased from 32% to 55% after training. The proportion of nurses who applied graduated compression using an SSB also increased from 31% to 52% after training. For both bandage systems, therefore, in-service bandaging training decreased the proportion of bandages with higher pressure at the calf than the ankle but around 45% of nurses still applied a bandage with higher pressure at the calf, even after training. The impact of bandaging skill on patient outcomes, such as comfort, bandage slippage, pressure damage and ulcer healing, remains unknown. Further work will ascertain whether there was a learning curve with the bandages used in this evaluation. Future bandage trials should, as a minimum, collect baseline data on nurses' previous experience of the bandages under evaluation.

Diagnosis of ulceration

The nurses undertook the diagnosis of a leg ulcer for patients in VenUS using their clinical knowledge and judgement to decide whether an open area of skin on the leg was a venous leg ulcer rather than a traumatic wound, for example. There was no qualifying period for an open area

to be defined as an ulcer. Patients were considered for recruitment to the trial if their nurse felt that they had a leg ulcer, and that this was due to venous insufficiency, reflecting normal practice.

The lack of formal assessment of the functional characteristics or anatomy of the venous system in this trial means that we cannot guarantee that all the people in the trial had uncomplicated venous ulceration, or determine the impact of various patterns of venous insufficiency on healing rates, as others have done.[43] The rationale for this is that a pragmatic trial should mirror patient selection criteria seen in normal clinical practice. Current practice in the assessment of people with leg ulceration is directed towards diagnosis of venous insufficiency as evidenced by signs of venous insufficiency, such as varicose veins and lipodermatosclerosis, and elimination of the major contraindication to compression (diabetes, arterial insufficiency). During the trial, two patients were withdrawn as their ulcers were diagnosed as being of non-venous aetiology, and this small proportion of withdrawals, coupled with the high healing rates (78% of people achieved an ulcer-free leg), demonstrates the validity of this approach.

Attrition

Response rates for the resource use and QoL questionnaires reduced markedly as the trial progressed (for example, approximately 50% of the data were missing for QoL). It is difficult to compare the extent of lost data with that from other compression bandaging trials as the majority of trials (18/26) followed patients for only 3–6 months and rarely reported attrition. Attrition rates were similar between the two groups, which is reassuring that the attrition is less likely to lead to a biased result.

One factor possibly influencing attrition was the long duration of follow-up after healing. It became obvious after contact with patients that we had not made it sufficiently clear that data were still required after ulcer healing. Reminders for the patient and their nurses that we remained interested in their responses to the questionnaires even if the ulcer had healed did have some effect.

VenUS has the longest follow-up of any leg ulcer treatment study that we have identified, with a minimum follow-up of 52 weeks and a maximum of 140 weeks. In the future, consideration needs to be given to investing in more complete, higher quality data at fewer time points.

Generalisability of the results

The centres participating in this trial represent a range of methods of delivering venous leg ulcer care in the community. Specialist leg ulcer services, integrated vascular services and community nursing-led services were all represented, and therefore the findings of this study can be applied across the UK. However, when trying to extrapolate from these results to individual leg ulcer services in the UK, there are important considerations to be made, particularly with regard to existing skills and competencies in bandage application, since the relative clinical effectiveness of the compression systems is likely to be heavily influenced by this.

Conclusions

Implications for healthcare

This trial found a higher healing rate, a reduced median time to healing and lower costs associated with 4LB treatment compared with SSB application. The bandage costs were less important than the costs of treatment visits, and patients in SSBs required more treatment overall.

Generally, this trial supports the use of the 4LB in preference to the SSB.

For those centres where the SSB is currently used, we would suggest a careful audit of the frequency of district nurse visits and healing rates. If healing rates are acceptable but domiciliary visits for rebandaging are required more than once per week, then the care is not cost-effective. However, if healing rates are good, and patients and/or their carers are able to launder and reapply the bandage, then the treatment is likely to become cost-effective. One of us (EAN) is currently investigating the potential for self-management in patients with venous leg ulcers.

The SSB would be a reasonable alternative for those patients who like it and will not tolerate the 4LB.

Community nurses have to be adequately trained in the safe and effective application of a range of bandages, but particularly the 4LB.

Recommendations for further research

1. More research is needed to explore the relationship between bandager skill, application technique and healing. This work should include an exploration of the potential

for patients and/or their carers to apply bandages effectively and would involve sub-bandage pressure measurement.
2. The relative cost-effectiveness of community leg ulcer clinics should be re-examined using modelling (the only RCT, incorporating an economic evaluation, comparing home visits with clinic treatment was confounded by major differences in bandage provision).[87]
3. A study should be undertaken of nurse decision-making in venous ulcer management to understand better the influences on treatment choice and frequency of treatment visits (since the latter drives costs in the treatment of venous leg ulceration).

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Collaborators and contributions of the authors

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NAC was the principal investigator and coordinated the project. EAN was the clinical trial coordinator. CI was the data manager and health economist and conducted the clinical and economic analysis. NAC, EAN and DJT contributed to the study design.

Contribution of authors

Cynthia Iglesias was the health economics data manager and conducted the clinical and economic analyses. Andrea Nelson was the clinical trial coordinator, also contributing to the study design and the preparation of the paper. Nicky Cullum was the principal investigator, also coordinating the project, contributing to the study design and acting as guarantor for the paper. David Torgerson worked on the study design and contributed to the preparation of the paper.

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Appendix 1

Ethics approval

MREC approval was obtained from the Northern and Yorkshire MREC (MREC/98/3/1) on 18 June 1998. LRECs were also approached in each of the recruitment areas prior to recruitment. They gave approval at the following LREC meetings:

Cumbria (West Cumberland LREC) – October 1998
West London (Charing Cross LREC) – October 1998
York LREC (part of the North Yorkshire site) – September 1998
Scarborough LREC (part of the North Yorkshire site) – January 1999
Northallerton LRESC (part of the North Yorkshire site) – September 1999
Harrogate LREC (part of the North Yorkshire site) – October 1999
Hull LREC (part of the North Yorkshire site) – November 1999
Leeds Clinical Research (Ethics) Committee – September 1998
Bradford (part of the Leeds centre) – September 1999
Southport (North Sefton Local Research Ethics Committee) – September 1999
Falkirk (Forth Valley Health Board Ethics of Research Committee) – January 2000
East London (East London and The City Health Authority Research Ethics Committee) – March 2000
Newmarket (East Suffolk Local Research Ethics Committee) – May 2000
Calderdale (Halifax) – May 2000

Appendix 2

Study sites

Primary Care in North Yorkshire

Rural and urban centres in North Yorkshire: the community nursing service of York Health Services NHS Trust; the Priory Medical Consortium of GPs in York; and the community nursing services in Ryedale, Whitby, Scarborough, Hull, Northallerton, Harrogate and the East Riding of Yorkshire. Within the City of York patients were mainly managed by community nurses in their own homes, in generic nurse-led clinics (there are no leg ulcer clinics in York) or in GP practices. In rural settings where distances between patients can be large, patients received home visits from the district nursing team or were seen by the practice nurse in their GP surgery.

Before the trial commenced, nurses used a range of compression bandage systems. Prior to the trial, four-layer bandaging was only available through the hospital dermatology clinic and patients managed entirely in the community were treated with multilayer, class 3C compression bandage systems. Since the end of the trial patients being treated with compression bandages have received four-layer, short-stretch and class 3C multilayer compression systems. Specialist advice is available from vascular surgery or dermatology clinics in York or Scarborough.

Leeds Community Services

The Department of Vascular and Endovascular Surgery of St James's Hospital and Leeds Community and Mental Health Trust (LCMHT) collaborated in this study. GPs referred leg ulcer patients to the community nursing service (which included a clinical nurse specialist in tissue viability), vascular surgical service or dermatology. When the trial started there were no specialist leg ulcer clinics and hence patients were seen either in hospital outpatient departments or, more commonly, in their own homes.

Before the trial commenced, nurses used a range of compression bandage systems; patients in the community were treated with four-layer or class 3C compression bandage systems. Since the end of the trial, venous ulcer patients have received four-layer, short-stretch and class 3C compression bandage systems.

Specialist advice was available from a clinical nurse specialist in tissue viability and a nurse consultant in tissue viability from spring 2000, and also vascular surgery and dermatology services at Leeds United Teaching Hospitals.

West Cumbria

A leg ulcer specialist nurse (a member of the vascular team) coordinated the delivery of leg ulcer services across the area served by West Cumbria Healthcare NHS Trust. Patients were treated by the specialist nurse at the hospital clinic or by a community nurse in community leg ulcer clinics. Community nurses who had received in-house training in leg ulcer management visited patients unable to attend clinics.

Before the trial commenced, nurses used four-layer bandaging. Since the end of the trial, patients have been treated with four-layer compression bandages.

Links with vascular surgery allow the leg ulcer service to 'fast-track' patients for venous surgery or for hospital admission.

West London

Riverside Community Leg Ulcer Clinics and the Department of Surgery at Charing Cross Hospital (Imperial College of Science, Technology and Medicine) collaborated in this study.

GPs referred leg ulcer patients to the leg ulcer service and patients attended nurse-led clinics either in the community or in hospital. Patients unable to attend clinics were seen in their own home by the community nurse.

Before the trial commenced, nurses used four-layer bandaging. Since the end of the trial, patients being treated with compression bandages have received four-layer compression bandages.

Specialist advice was available from the Department of Surgery, Charing Cross Hospital.

Recruitment of 'Other' centres

In the first 6 months, the four initial sites had enrolled only 75% of the lower monthly target (four patients per centre, per month), and therefore there was already a short-fall in recruitment. An article describing the trial and promoting involvement by other centres generated enquiries from nine leg ulcer clinical specialists/clinics, of which five agreed to collaborate in the trial. These centres represented rural and urban settings, and had varying levels of experience with the two compression systems under evaluation. They are described below.

East London – Newham and Forest Gate

Newham Community Health Services NHS Trust collaborated in the trial. Patients were initially assessed by district nurses or practice nurses, and ongoing management was shared between community and practice nurses. Care was delivered in local clinics, or at home, if the patient was unable to attend the clinic.

Before the trial commenced, nurses used four-layer and short-stretch bandaging. Since the end of the trial, patients have been treated with four-layer and short-stretch bandaging.

Specialist advice was available from a clinical nurse specialist in tissue viability (consultant nurse post after April 2000) and the vascular surgical service in the local hospital.

Calderdale

Calderdale and Huddersfield NHS Trust collaborated in the trial. Patients were normally assessed by a community nurse with a qualification in leg ulcer management (the ENM N18 course), within the nurse-led leg ulcer community clinic. Ongoing management, such as dressings, was undertaken by community nurses in the patients' home.

Before the trial commenced, nurses used four-layer bandaging. Since the trial finished, patients have been treated with four-layer and short-stretch bandaging.

Specialist advice was available from four community-based, nurse-led clinics staffed by nurses with professional courses in tissue viability/leg ulcer care.

Southport

North Sefton and West Lancashire Community Trust collaborated in the trial. New patients were referred to the leg ulcer service and were assessed by the clinical nurse specialist in the leg ulcer clinic. Patients were treated by a leg ulcer service, comprising a clinical nurse specialist, community staff nurse and members of the community nursing service rotating into the leg ulcer team. Care was usually delivered in a community leg ulcer clinic, with immobile patients treated by the community nursing service at home.

Before the trial commenced, nurses used a range of compression bandage systems; four-layer or class 3C compression bandage systems or compression hosiery. Since the end of the trial, patients have received compression hosiery, four-layer, class 3C or short-stretch compression bandage systems.

Patients could be referred to the vascular clinic at the local hospital where a joint nurse/surgical clinic was held.

Newmarket

Community nurses based at the Rookery Medical Centre with a specialist qualification in leg ulcer management (ENB N18 course) ran the leg ulcer service. New patients were assessed by a member of this team at the leg ulcer clinic or, for immobile patients, at home. Community nurses with courses in leg ulcer management delivered ongoing treatment at clinics or, for patients unable to attend clinics, at home.

Before the trial commenced, nurses used four-layer bandaging. Since the trial, patients have been treated with four-layer bandaging.

Patients could also be referred to vascular and dermatology clinics at Addenbrooke's Hospital.

Falkirk

Falkirk and District Royal Infirmary collaborated in this project. Specialist nurses at a hospital-based leg ulcer clinic assessed patients with new leg ulcers. Ongoing treatment (dressing changes and bandaging) was delivered at home, for patients unable to make regular clinic visits, or at the hospital leg ulcer clinic.

Before the trial commenced, nurses used four-layer and short-stretch bandaging. Since the trial, patients have been treated with four-layer and short-stretch bandaging.

A consultant surgeon and orthotist also provided clinical support to the clinic.

Appendix 3

Information sheet for patients

Please read this document carefully

NB: Please ask if you do not understand anything in this information sheet, or if you would like further information.

We would like to invite you to take part in this study of bandages used in the treatment of venous leg ulcers.

Venous leg ulcers, sometimes called varicose ulcers, are caused by poor blood return from the legs to the heart. Bandages applied from the toes to the knee speed the healing of venous ulcers by helping the blood return. There are a number of bandages which can heal leg ulcers, and we are comparing a four-layer bandage system with a short-stretch bandage system. Both have been found to be effective in other studies but previous comparisons of the two bandages have proved inconclusive.

The purpose of the study is to find out which bandage system is most effective for healing leg ulcers. We are interested in how quickly the ulcers heal, and also in your opinion about the bandages. In order to compare two bandaging systems we need to treat 200 patients with the four-layer bandage system and another 200 with a short-stretch bandage system. In order to take part in the study you will be allocated either one of these bandages. The decision of which bandage you will receive will be made after you agree to take part. The choice of bandage will be determined at random, that is, we cannot predict which bandage you will receive. You will have an equal chance of receiving either bandage, in the same way that tossing a coin gives an equal chance of getting a 'heads' or 'tails'.

Your leg ulcer dressings will be carried out, as normal, by your community nurse or clinic staff. The ulcer will be traced and photographed at the start of the study and then regularly to see if your ulcer is reducing in size. This will continue until your ulcer heals. After your ulcer heals you will be given compression socks to help prevent the ulcer from recurring and we will check every 3 months that your ulcer has not recurred. We do not anticipate that you will have to see the nurse or attend your clinic more frequently than would normally be required and therefore we will not be able to pay any travel expenses incurred.

We do not anticipate that you will be harmed by being in this trial. Should this occur, however, normal NHS negligence procedures will apply.

In an emergency you should contact your community nurse or clinic nurse. The name of a contact nurse and the telephone number where they can be reached is provided below:

Remember: participation in this study is entirely voluntary

Your future care and treatment will not be influenced by your decision to take part or not.

If you do agree to take part in this study and decide at a later time to withdraw then you are free to do so at any time without influencing your future care or treatment.

Thank you for taking the time to read this information sheet.

Appendix 4

Data collection forms

1. Pre-trial screening form
2. Patient record form (trial entry and baseline data record)
3. Dressing log
4. Healing form
5. Monthly resource use patient questionnaire
6. Quarterly HRQoL patient questionnaire

VenUS Ulcer Study – Pre-trial Screening Form

Please use bold capitals when entering the data and make sure that the text is contained within the reponse boxes

Patient's Name: [ ]

Patient's DoB: [ ][ ] / [ ][ ] / [ ][ ][ ][ ] *dd/mm/yyyy*

Postcode [ ][ ][ ][ ] [ ][ ][ ][ ]

ANKLE/BRACHIAL PRESSURE INDEX ABPI (After at least 10 minutes rest)

	Right	Left
Arm artery pressure (record both arms) mmHg	[ ][ ][ ]	[ ][ ][ ]
Posterior tibial artery pressure (both legs) mmHg	[ ][ ][ ]	[ ][ ][ ]
Dorsalis pedis artery pressure (both legs) mmHg	[ ][ ][ ]	[ ][ ][ ]

Now calculate the ABPI $= \frac{\text{Higher leg pressure (DP or PT)}}{\text{Higher arm pressure (left or right)}}$

ABPI [ ] . [ ][ ]   [ ] . [ ][ ]

If ABPI is more than 0.8 then the patient is likely to be eligible to enter the trial, please give them the **Patient Information Sheet** and arrange to see them after 24 hours.

NB. you may wish to perform the ankle brachial pressure index measurement at this later appointment if this is convenient. Note that the ABPI for the trial leg MUST be completed before the patient is enrolled in the trial

Please now give the information sheet to the patient

Date information sheet given to patient [ ][ ] / [ ][ ] / [ ][ ][ ][ ] *dd/mm/yyyy*

Your signature [ ]

Name of caseload manager/senior nurse [ ]

If patient is **not** entered into the trial, please record the reason below
(place a cross in all the boxes that apply)

- Because the patient will not wear compression [ ]
- ABPI less than 0.8 [ ]
- Patient has diabetes mellitus [ ]
- Patient has previously used 4 layer bandage unsuccessfully [ ]
- Patient has previously used short stretch bandages unsuccessfully [ ]
- Patient unable to give consent to enter trial [ ]
- Reference ulcer smaller than 1 cm in any dimension (check in 1 week) [ ]
- Reference ulcer duration less than 1 week (reassess in 1 week) [ ]
- Other (specify below) [ ]

Pre-trial screening decision tree

Patient has a leg ulcer that might be due to venous disease (e.g. staining, eczema)

1. Has the patient been in the trial previously?
→ YES: Please complete and return this form
↓ NO

2. Has the patient used either of the trial bandages without success?
→ YES: Please complete and return this form
↓ NO

3. Is the patient diabetic?
→ YES: Please complete and return this form
↓ NO

4. Is the patient able to give informed consent
→ NO: Please complete and return this form
↓ YES

5. Is ulcer larger than 1 cm in length or width?
→ NO: Please complete and return this form
↓ YES

6. Has the ulcer been present for more than one week?
→ NO: Please complete and return this form
↓ YES

7. Measure ABPI: is reading 0.8 or more?
→ NO: Please complete and return this form
↓ YES

8. Give patient the information sheet (wait at least 24 hours)
↓

9. Is the patient willing to take part in the trial?
→ NO: Please complete and return screening form
↓ YES

10. Collect baseline information using record form and enrol patient in trial

Please return this form to:
Cynthia Iglesias, The VenUS Trial, Centre for Evidence Based Nursing,
Department of Health Studies, University of York, Heslington, York YO10 5DD

VenUS Ulcer Study – Patient Record Form

Dates

Date Today: ☐☐ / ☐☐ / ☐☐☐☐ *dd/mm/yyyy*

Date of ABPI measurement: ☐☐ / ☐☐ / ☐☐☐☐ *dd/mm/yyyy*

Date informed consent obtained ☐☐ / ☐☐ / ☐☐☐☐ *dd/mm/yyyy*

Date of first application of trial bandage ☐☐ / ☐☐ / ☐☐☐☐ *dd/mm/yyyy*

Personal Data

Patient's Name: ☐

Date of Birth ☐☐ / ☐☐ / ☐☐☐☐ *dd/mm/yyyy*

Postcode ☐☐☐☐ ☐☐☐☐

Sex Male ☐ 1 Female ☐ 2

Ulcer History and Initial Assessment

Leg being followed in the trial Right ☐ 1 Left ☐ 2

NB: The 'trial' leg will be the one with the largest ulcer. If the largest ulcer is on the right leg label that R1 and other ulcers on the same leg R2, R3 etc. If the largest ulcer is on the left leg, label that L1 and the other ulcers on the same leg L2, L3 etc)

Details of ulcer

How many years since **FIRST** leg ulcer on either leg? ☐☐
(one year = 01, two years = 02)

Total number of ulcer **EPISODES** since first onset? ☐☐
(first ulcer episode = 01, second ulcer episode = 02)

Mobility *(place a cross in one box)*

Patient walks freely ☐ 1

Patient walks with difficulty ☐ 2

Patient is immobile ☐ 3

Ankle mobility/trial leg *(place a cross in one box)*

Has full range of motion ☐ 1

Has reduced range of motion ☐ 2

Ankle is fixed ☐ 3

Height ☐ Feet ☐☐ Inches

Weight ☐☐ Stone ☐☐ Pounds

Ankle circumference (cm) ☐☐ . ☐ cm

Current Medication

	Medication	Daily dosage	Reason
1			
2			
3			
4			
5			
6			
7			
8			
9			

Description of reference ulcer

Duration of reference ulcer (months) ☐☐☐ Months

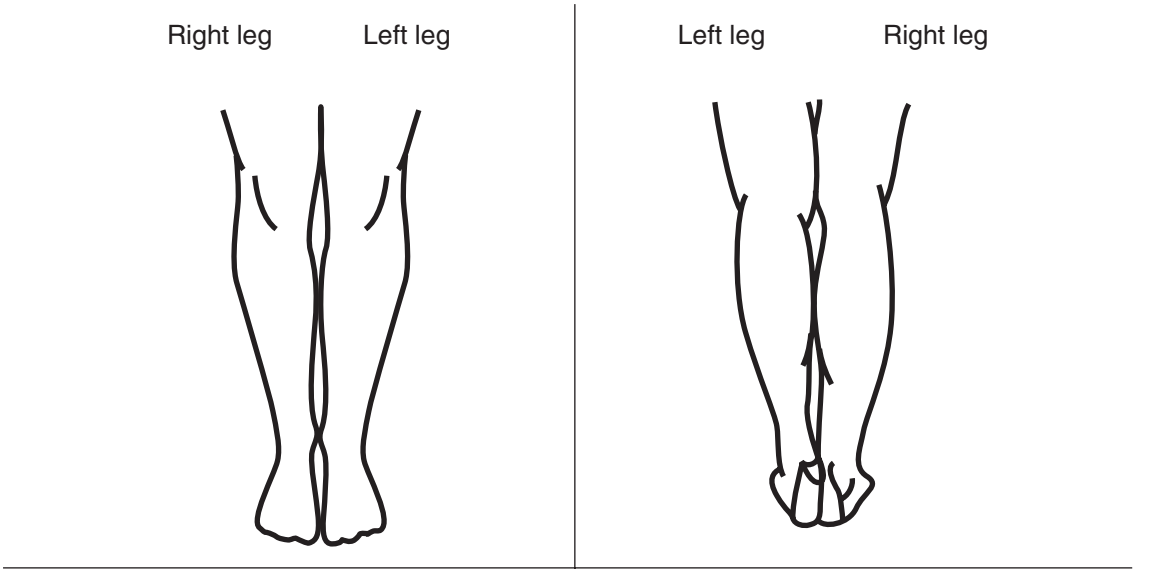
Ulcer appearance *(cross all boxes that apply)*

- Sloughy ☐ 1
- Granulating ☐ 2
- Epithelialising ☐ 3

Skin condition *(cross all boxes that apply)*

- Eczematous ☐ 1
- Macerated ☐ 2
- Cellulitis ☐ 3
- Lipodermatosclerosis ☐ 4
  (Brown staining and woody tissue in gaiter region)

Please draw the position of the ulcer below



Using the grids and pens provided, trace all ulcers on both legs. The trial ulcer will be the largest ulcer. If the largest ulcer is on the right leg label this R1 and other ulcers on that leg R2, R3 etc. Ulcers on the left leg should be labelled L1, L2, L3 etc.

Photograph

Please confirm that you have taken a Polaroid of the reference ulcer?

Yes ☐ 1 No ☐ 2

The photograph should be dated and labelled with the patient's name and trial number

Tracing

Please confirm that you have taken a tracing of all the ulcers on the reference leg?

Yes ☐ 1 No ☐ 2

The tracing should be dated and labelled with the patient's name and trial number

Please attach the tracing and photograph to the back of this record

Please use the following checklist to check whether the participant is eligible to enter the trial

	Yes	No
The patient has a leg ulcer	☐	■
ABPI greater than or equal to 0.8	☐	■
The patient has diabetes mellitus	■	☐
The patient previously used 4-layer bandages unsuccessfully	■	☐
The patient previously used short stretch bandages unsuccessfully	■	☐
The patient has given written consent to enter the trial	☐	■
The ulcer is greater than 1 cm in any dimension	☐	■
The ulcer duration is greater than 1 week	☐	■

If any of the responses fall into the grey boxes then the patient is NOT eligible for the trial

If all the responses are in the white boxes complete the randomisation form and follow the instructions for randomising the participant

VenUS Ulcer Study – Randomisation Form

Name of caseload holder:	
Patient's Forename:	
Patient's Surname:	
Patient's Address Line 1:	
Patient's Address Line 2:	
Patient's Address Line 3:	
Patient's Address Line 4:	
Patient's Postcode:	

Date Today: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Trial Centre

- North Yorkshire ☐ 1
- Leeds ☐ 2
- Cumbria ☐ 3
- London ☐ 4
- Other ☐ 5

Area of ulcer: count up squares on the tracing grid

- Less than or equal to 10 squares ☐ 1
- More than 10 squares ☐ 2

Ever had an ulcer on this leg before

- Yes ☐ 1
- No ☐ 2

Duration of reference ulcer

- Less than or equal to 6 months ☐ 1
- More than 6 months ☐ 2

Now please call the telephone randomisation service on 0800 0566682, between 8.30 am and 5.30 pm Monday to Friday, quoting the VenUS trial.

After randomisation please complete the details overleaf in the shaded box.

Patient Trial Number: ☐☐☐☐

Patient Assigned to:

4-Layer bandage ☐

Short stretch bandage ☐

Please get the patient to sign this form below.

Patient signature. _____

Please sign the form yourself

Your signature. _____

Please return this form in the stamped addressed envelope to:

Cynthia Iglesias
The VenUS Trial
Centre for Evidence Based Nursing
Department of Health Studies
University of York
Genesis 6
York Science Park
Heslington
York
YO10 5DQ

VenUS Ulcer Study – Dressing Log: Record of Leg Ulcer Treatment Visit

Patient's Name: _____ Patient Trial Number: ☐☐☐☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

- Planned visit to do dressing ☐ 1
- Unplanned visit to adjust bandage/dressing ☐ 2
- Other (specify below) ☐ 3

_____

NEW Materials used *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

- Planned visit to do dressing ☐ 1
- Unplanned visit to adjust bandage/dressing ☐ 2
- Other (specify below) ☐ 3

_____

NEW Materials used *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Patient's Name: _____ Patient Trial Number: ☐☐☐☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

Planned visit to do dressing ☐ 1

Unplanned visit to adjust bandage/dressing ☐ 2

Other (specify below) ☐ 3

_____

NEW Materials *(enter number used in box)*

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Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

Planned visit to do dressing ☐ 1

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Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Patient's Name: _____ Patient Trial Number: ☐☐☐☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

Planned visit to do dressing ☐ 1

Unplanned visit to adjust bandage/dressing ☐ 2

Other (specify below) ☐ 3

_____

NEW Materials used *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

Planned visit to do dressing ☐ 1

Unplanned visit to adjust bandage/dressing ☐ 2

Other (specify below) ☐ 3

_____

NEW Materials used *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Patient's Name: _____ Patient Trial Number: ☐☐☐☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

Planned visit to do dressing ☐ 1

Unplanned visit to adjust bandage/dressing ☐ 2

Other (specify below) ☐ 3

_____

NEW Materials used *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

Planned visit to do dressing ☐ 1

Unplanned visit to adjust bandage/dressing ☐ 2

Other (specify below) ☐ 3

_____

NEW Materials used *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Patient's Name: _____ Patient Trial Number: ☐☐☐☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

- Planned visit to do dressing ☐ 1
- Unplanned visit to adjust bandage/dressing ☐ 2
- Other (specify below) ☐ 3

_____

NEW Materials *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

Date of Visit: ☐☐ / ☐☐ / ☐☐☐☐
dd/mm/yyyy

Reason for visit *(cross one box only)*

- Planned visit to do dressing ☐ 1
- Unplanned visit to adjust bandage/dressing ☐ 2
- Other (specify below) ☐ 3

_____

NEW Materials *(enter number used in box)*

Orthopaedic wool	☐	Coban	☐	Comprilan 8 cm	☐
Crepe	☐	Comprilan 12 cm	☐	Other (specify below)	☐
Elset/Litepress	☐	Comprilan 10 cm	☐		

_____

Cleanser (water/saline) (please describe) ☐

Dressing (brand/size) (please describe) ☐

Cream/Ointment (please describe) ☐

If you have changed treatment, enter the reason in the box below

☐

VenUS Ulcer Study – Monthly Assessment

Patient Trial Number ☐☐☐☐ Assessment Date *dd/mm/yyyy* ☐☐ / ☐☐ / ☐☐☐☐

This assessment should be completed approximately 4 weeks (26–30 days) after the last trial assessment

Reference Leg: Left ☐ 1 Right ☐ 2

Assessment of trial leg:

Are there any ulcers on the trial leg? Yes ☐ 1 No ☐ 2

If **NO** please complete the Healing form

If **YES**, is the reference ulcer healed? Yes ☐ 1 No ☐ 2

If the original ulcer has divided, the larger portion becomes the reference ulcer.

If the reference ulcer has merged with another ulcer, the newly formed ulcer becomes the reference ulcer.

Adverse Events:

Has the patient suffered any adverse events in the past month? Yes ☐ 1 No ☐ 1

If Yes, describe the adverse event?

Description of the event	Date started/ended	Related to bandage/trial
☐	From ☐☐ / ☐☐ / ☐☐☐☐ To ☐☐ / ☐☐ / ☐☐☐☐	Probably ☐ 1 Possibly ☐ 2 No ☐ 3
☐	From ☐☐ / ☐☐ / ☐☐☐☐ To ☐☐ / ☐☐ / ☐☐☐☐	Probably ☐ 1 Possibly ☐ 2 No ☐ 3
☐	From ☐☐ / ☐☐ / ☐☐☐☐ To ☐☐ / ☐☐ / ☐☐☐☐	Probably ☐ 1 Possibly ☐ 2 No ☐ 3
☐	From ☐☐ / ☐☐ / ☐☐☐☐ To ☐☐ / ☐☐ / ☐☐☐☐	Probably ☐ 1 Possibly ☐ 2 No ☐ 3

Please confirm that you have taken a tracing of the reference ulcer? Yes ☐ 1 No ☐ 2

– tracing should be dated and labelled with patient name and trial number

Please send this form and ulcer tracing to Cynthia Iglesias at the Department of Health Studies, University of York, in the prepaid envelope provided

VenUS Ulcer Study – Healing Form

Patient Trial Number ☐☐☐☐ Healing Date *dd/mm/yyyy* ☐☐ / ☐☐ / ☐☐☐☐

All ulcers on the reference (trial) leg have healed Yes ☐ 1 No ☐ 2

If NO: please do not fill in this form
If YES: please fill in the form below

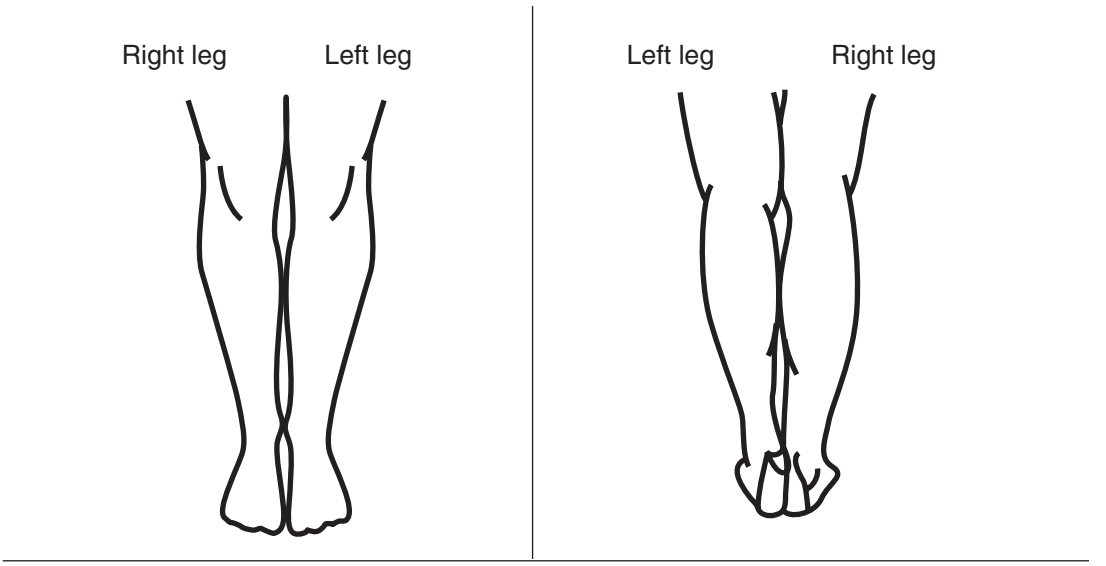
Appointment made for repeat assessment in 3 months Yes ☐ 1 No ☐ 2

Patient supplied with compression hosiery Yes ☐ 1 No ☐ 2

Record brand ☐ Class ☐ Size ☐

At date of reference leg healing, please photograph site of reference ulcer and mark position of healed reference ulcer on the diagram below

Please draw the position of all the ulcers on the reference leg below. If the reference leg has completely healed please place an X on the site of the healed ulcers and label R1, L1 etc. Do not take a tracing but PLEASE do take a photograph of the healed leg.



Photograph

Please confirm that you have taken a Polaroid of the reference ulcer?

Yes ☐ 1 No ☐ 2

The photograph should be dated and labelled with the patient's name and trial number

Please attach photograph to the back of this record

Now please send this form to Cynthia Iglesias at the Department of Health Studies, University of York in the prepaid envelope.

THE UNIVERSITY *of York*

dd/mm/yyyy

VenUS Ulcer Study

Monthly Questionnaire

We would like to find out a little about your use of health services so that we can estimate how much leg ulcers cost the NHS.

We would, therefore, be grateful if you could complete this questionnaire as fully as possible. This should take about 15 minutes. Some of the questions may not seem to be relevant to you but they do give us valuable information.

Your answers will be **CONFIDENTIAL** and will only be used as part of this study. Your name and address do not appear on this questionnaire and your patient identification number is known only to members of the study team.

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

Please enter the date you completed the survey ☐☐ / ☐☐ / ☐☐☐☐

dd/mm/yyyy

In order to accurately measure the cost of different leg ulcer treatments, we need to know the number of times you have seen a health professional (e.g. Doctor or Nurse) not as part of this study.

1. In the last month have you attended your **doctor's surgery** OR seen your doctor at home for any reason related to your health?
(place a cross in one box)

Yes ☐ 1

No ☐ 2

If yes, How many times?

Number of times you have been to the surgery ☐☐

Number of times the doctor has visited you at home ☐☐

Were any of these visits because of your leg ulcer?

Yes ☐ 1

No ☐ 2

If yes, How many times? Number of times ☐☐

2. In the last month have you seen a nurse at your **doctor's surgery** OR seen a nurse at home for any reason related to your health?
(place a cross in one box)

Yes ☐ 1

No ☐ 2

If yes, How many times?

Number of times you have been to the surgery to see a nurse ☐☐

Number of times a nurse has visited you at home ☐☐

Were any of these visits because of your leg ulcer?

Yes ☐ 1

No ☐ 2

If yes, How many times? Number of times ☐☐

3. In the last month have you been to hospital for any reason related to your health
(place a cross in one box)

Yes ☐ 1

No ☐ 2

Were any of these visits because of your leg ulcer? Yes ☐ 1

No ☐ 2

If yes, How many times? Number of times ☐☐

4. In the last month which of the following people have helped you around the house, to do the shopping etc.,?
(place a cross in the box for all those who have helped and then enter the number of hours per week they have helped you)

Home help ☐ 1 approximately how many hours per week? ☐☐☐

Relative ☐ 1 approximately how many hours per week? ☐☐☐

Friend/neighbour ☐ 1 approximately how many hours per week? ☐☐☐

Other (state relationship in box below) ☐ 1 approximately how many hours per week? ☐☐☐

☐

I have not needed any help ☐ 1

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☐☐☐☐

☐☐

☐☐ / ☐☐ / ☐☐☐☐

dd/mm/yyyy

THE UNIVERSITY of York

dd/mm/yyyy

VenUS Ulcer Study

Patient Survey

We would like to find out about your health in general and how your leg ulcer might affect your life.

We would, therefore, be grateful if you could complete this questionnaire as fully as possible. This should take about 30 minutes. Some of the questions may not seem to be relevant to you but they do give us valuable information about your leg ulcer.

Your answers will be treated as CONFIDENTIAL and will only be used as part of the study. Your name and address do not appear on this questionnaire and your patient identification number is known only to members of the study team.

THANK YOU FOR COMPLETING THIS QUESTIONNAIRE

This section asks about your health in general. By placing a cross in one box in each group below, please indicate which statement best describes your own health state today.

(Do not cross more than one box in each group)

Mobility
(please cross one box only)

I have no problems in walking about ☐ 1
I have some problems in walking about ☐ 2
I am confined to bed ☐ 3

Self-Care
(please cross one box only)

I have no problems with self-care ☐ 1
I have some problems washing or dressing myself ☐ 2
I am unable to wash or dress myself ☐ 3

Usual activities (eg. work, study, housework, family or leisure activities)
(please cross one box only)

I have no problems with performing my usual activities ☐ 1
I have some problems with performing my usual activities ☐ 2
I am unable to perform my usual activities ☐ 3

Pain/Discomfort
(please cross one box only)

I have no pain or discomfort ☐ 1
I have moderate pain or discomfort ☐ 2
I have extreme pain or discomfort ☐ 3

Anxiety/Depression
(please cross one box only)

I am not anxious or depressed ☐ 1
I am moderately anxious or depressed ☐ 2
I am extremely anxious or depressed ☐ 3

This section asks for your views about your health. This section will help us keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:
(please circle one number only)

Excellent	Very Good	Good	Fair	Poor
1	2	3	4	5

2. During a typical day does **your health** limit you in **moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf? If so, how much?
(please circle one number only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
1	2	3

3. During a typical day does **your health** limit you in climbing **several** flights of stairs? If so, how much?
(please circle one number only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
1	2	3

4. During the past **4 weeks**, how much time have you accomplished less than you would like in regular daily activities **as a result of your physical health**?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

5. During the past **4 weeks**, how much time have you been limited in performing any kind of work or other regular daily activities **as a result of your physical health**?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

6. During the past **4 weeks**, how much time have you accomplished less than you would have liked in your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

7. During the past **4 weeks**, how much time have you done work or other activities less carefully than usual **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

8. During the past **4 weeks**, how much did **pain** interfere with your normal work (both outside the home and housework)?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

9. This question is about how you feel and how things have been with you **during the last month**. Please give the one answer that comes closest to the way you have been feeling.
How much during the **last month** have you felt calm and peaceful?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

10. This question is about how you feel and how things have been with you **during the last month**. Please give the one answer that comes closest to the way you have been feeling.
How much during the **last month** did you have a lot of energy?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

11. This question is about how you feel and how things have been with you **during the last month**. Please give the one answer that comes closest to the way you have been feeling.
How much during the **last month** have you felt downhearted and low?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

12. During the past 4 weeks how much of the time has your physical health or emotional problems interfered with your social activities (like visiting fiends, relatives etc.)?
(please circle one number only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1	2	3	4	5

– Leg ulcers affect people in many different ways

– They can interfere with various aspects of life

– The purpose of these questions is to find out **in what ways your life is affected by your leg ulcer**

– **If your leg ulcer has completely healed**, please put a cross in the box below and return the questionnaire in the prepaid envelope.

Yes, my leg ulcer has completely healed ☐

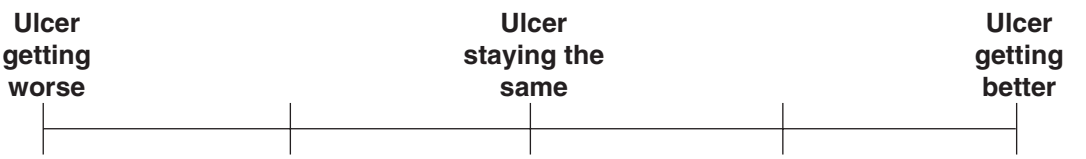
1. Have you ever stayed in hospital because of your ulcer? 1 ☐ Yes 2 ☐ No *(please cross one box)*

2. Would you say that you are largely housebound these days? 1 ☐ Yes 2 ☐ No *(please cross one box)*

If No, please go to question 3

2a. If yes, is this because of your leg ulcer? 1 ☐ Yes 2 ☐ No *(please cross one box)*

3. Just at the moment, would you say your ulcer is staying the same, getting better or getting worse? Please put a cross on the line where it applies to you.



for office use

The following questions ask about your leg ulcer **now**. Now means **within the last two weeks**. Please cross the answer which best applies to you.

4. At most, **how painful** is your leg ulcer?
(please cross one box)

- Don't notice it ☐ 1
- Uncomfortable rather than painful ☐ 2
- Hurts a little ☐ 3
- Painful ☐ 4
- Very painful ☐ 5
- Excrutiatingly painful ☐ 6
- More pain than than I can manage ☐ 7

5. Does you leg ulcer disturb your **sleep**?
(please cross one box)

- Doesn't disturb me ☐ 1
- Disturbs me only when going to sleep ☐ 2
- Sometimes wakes me up ☐ 3
- Keeps me awake a lot ☐ 4
- Keeps me awake most of the night ☐ 5

6. In total, how long do you spend **thinking about your leg ulcer** during the day?
(please cross one box)

- I don't think about my leg ulcer at all ☐ 1
- Less than 15 minutes ☐ 2
- About half an hour ☐ 3
- About an hour ☐ 4
- About an hour and a half ☐ 5
- About two hours ☐ 6
- About three hours ☐ 7
- About four hours ☐ 8
- Most of the day ☐ 9
- Most of the day and night ☐ 10

7. On average, how long per day do you spend trying to help your leg ulcer heal? **(such as ankle and leg exercises, raising your leg)**
(please cross one box)

- I don't spend any time at all trying to help my ulcer heal ☐ 1
- Less than 15 minutes ☐ 2
- About half an hour ☐ 3
- About an hour ☐ 4
- About an hour and a half ☐ 5
- About two hours ☐ 6
- Three or more hours ☐ 7
- Most of the day ☐ 8

Below is a list of statements which describe how people sometimes feel when they have leg ulcers. When you read a sentence that describes the way you feel, please circle the YES beside it. If the sentence does not describe you then please circle the NO beside it and go on to the next one.

PLEASE MAKE SURE YOU ANSWER ALL THE QUESTIONS

8.	My ulcer makes me afraid of having children on my knee	**YES**	**NO**
9.	My ulcer stops me from shopping in crowded places	**YES**	**NO**
10.	My ulcer makes me frightened of shopping trolleys or bags bumping into me	**YES**	**NO**
11.	My ulcer makes getting on or off a bus difficult	**YES**	**NO**
12.	My ulcer makes it difficult to walk	**YES**	**NO**
13.	Because of my ulcer I look at the floor when I walk	**YES**	**NO**
14.	Because of my ulcer I try to keep away from cats etc	**YES**	**NO**
15.	My ulcer stops me from visiting friends	**YES**	**NO**
16.	My ulcer prevents me from wearing the type of shoes I prefer	**YES**	**NO**
17	My ulcer makes it difficult to climb stairs	**YES**	**NO**
18.	My ulcer restricts where I can travel to, e.g. restricting holidays or business trips	**YES**	**NO**
19.	I think my ulcer will not get better	**YES**	**NO**
20.	My ulcer gets in the way of personal relationships	**YES**	**NO**
21.	Because of my ulcer I can't be bothered to do things	**YES**	**NO**
22.	I feel my ulcer will get the better of me	**YES**	**NO**
23.	My ulcer makes me feel depressed	**YES**	**NO**
24.	My ulcer makes me ask myself "Why me?"	**YES**	**NO**
25.	Because of my ulcer it feels as though my legs/feet dominate my body	**YES**	**NO**
26.	I think the worst thing about my ulcer is the way it goes on and on	**YES**	**NO**
27.	Even though I have an ulcer I find it easy to get out and about	**YES**	**NO**

28.	My ulcer makes me cry with frustration	**YES**	**NO**
29.	I have slowed down a lot because of my ulcer	**YES**	**NO**
30.	I feel unsure how to help my ulcer heal	**YES**	**NO**
31.	Because of my ulcer I am slower than I used to be	**YES**	**NO**
32.	I find the treatment for my ulcer easy to live with	**YES**	**NO**
33.	Because of my ulcer I have to hide my legs	**YES**	**NO**
34.	My ulcer makes me conscious of what I am wearing	**YES**	**NO**
35.	I take painkillers for my ulcer	**YES**	**NO**

36. **Compared to three months ago** how would you say your leg ulcer is **now**?
(please cross one box)

- Much better now than three months ago ☐ 1
- Somewhat better now than three months ago ☐ 2
- About the same as three months ago ☐ 3
- Somewhat worse now than three months ago ☐ 4
- Much worse now than three months ago ☐ 5

Thank you for completing this survey. We would be grateful if you could now send this back to us in the pre-paid envelope supplied

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☐☐☐☐ ☐☐ ☐☐ / ☐☐ / ☐☐☐☐

dd/mm/yyyy

Appendix 5

Bandage prescribing information

Four-layer bandaging

If your patient has been randomised to four-layer bandaging, please use one of the regimens in Table 38, *as these have very similar components. All components are available on FP10.*

For illustration only the components of the 'standard' kits have been listed. If a patient has an ankle circumference less than 18 cm, or more than 25 cm, please use the appropriate kit.

Short-stretch bandaging

If your patient has been randomised to short-stretch bandaging, please use Comprilan (Beiersdorf). Comprilan is available on FP10 (8, 10 and 12 cm).

Primary dressings

We suggest you use a knitted viscose dressing (e.g. NA, Silicone NA, Tricotex or those provided with a four-layer bandaging kit) unless there are clinical contraindications.

Additional gauze padding may be necessary if there is exudate.

A 3-m roll of stockinette is now available on FP10.

TABLE 38 *Four-layer bandage regimens*

1. Profore	2. System 4	3. Original[a]
Soffban £0.59	Softexe £0.59	Velband/Soffban £0.59
Soffcrepe £1.14	Setocrepe £1.12	Crêpe (10 cm) variable
Litepress £3.32	Elset (8.0) £3.10	Elset £3.10
Co-Plus £2.75	Coban £2.75	Coban £2.75

[a] Moffatt and colleagues.[50]

Appendix 6

Training days

Each trial training day covered the general pattern:

9:30–10:15	The need for the trial – lecture
10:15–10:40	Coffee break
10:40–11:15	The design of the trial and the outcomes being evaluated – lecture
11:15–12:15	Introduction to trial documentation – workshop
12:15–13:00	Recruiting a patient into the trial – case study
13:00–13:45	Lunch
13:45–14:00	Assessing leg ulcers (tracings and photography) – workshop
14:00–14:40	Introduction to compression bandages – lecture
14:40–16:00	Applying trial bandages – workshop
16:00–16:30	(Optional workshop on Doppler assessment of arterial supply)

Training days

These were held throughout the trial centres to allow the maximum number of local nurses to attend. Staff reimbursement costs were available for those nurses who could only attend the day if their replacement costs were covered. More than 150 nurses attended these training days.

Cumbria – March 1999

Leeds – March and May 1999

West London – April and June 1999

North Yorkshire – Scarborough – April 1999

North Yorkshire – York – May, July and September 1999

North Yorkshire – Hull – December 1999

North Yorkshire – Scarborough – December 1999

North Yorkshire – Northallerton – January 2000

Southport – February 2000

Falkirk – February 2000

Chorley – May 2000 (this group decided not to proceed with the trial)

Calderdale (Halifax) – June 2000

Newmarket – June 2000.

Appendix 7

Time required for nurse visits

Background

In order to inform the economic analysis, we undertook a small-scale survey of the times taken for nurses to see a patient and apply each of the trial bandages. We recorded both the bandage application time and the total time taken for a nurse consultation, that is, to make the patient comfortable and enquire about their leg, remove their existing dressings and bandages, cleanse the leg, apply emollients, reapply the dressing and bandage, and then to clear up, complete documentation and leave the patient with a follow-up appointment. The time taken to apply each of the trial bandages, both in a clinic setting and in the patient's home, was surveyed.

Methods

Nurses treating trial patients in three of the trial sites, Leeds, North Yorkshire and Southport, recorded data on the duration of treatment visits at 10 or 11 visits for each bandage and in each setting, that is, 4LB at home, 4LB at clinic, SSB at home and SSB at clinic. The times at which key events took place were recorded on a proforma, using a watch with a second hand. These times were used to calculate the duration of each aspect of the consultation. For the purpose of this survey, the start of the nurse consultation in a client's home was defined as the point at which the nurse entered the person's home, and the end was defined as the point at which the nurse left the home. For home visits, the following time points were recorded:

1. time of entering the house
2. time when bandage removal was started
3. time when bandage and dressing removal ended
4. time when ulcer cleansing started and finished
5. time when application of ointments/creams to skin started and finished
6. time when application of new dressing and bandage started
7. time when application of new dressing and bandage finished
8. time of leaving the house.

For clinic visits, the start of the nurse consultation was defined as the time at which the nurse and patient were together in the treatment area. The following time points were recorded on the proforma:

1. time at which consultation started
2. time when bandage removal was started
3. time when bandage and dressing removal ended
4. time when ulcer cleansing started and finished
5. time when application of ointment/creams to skin started and finished
6. time when application of new dressing and bandage started
7. time when application of new dressing and bandage finished
8. time of nurse leaving the treatment area.

Calculation of times

The total time for the consultation was calculated by subtracting time 1 from time 8. The time during which the nurse applied the compression bandage was calculated from times 6 and 7. Both the mean time for the complete consultation and the mean time to apply the compression bandage were calculated. Comparisons were made between the total consultation times for each bandage in each setting, and between the bandage application times for each bandage in each setting.

Results

Time for complete consultation and treatment

The average visit times for each bandage and setting are summarised in *Figure 17*.

Time for complete consultation – clinic setting

The 4LB consultation and application was timed on 11 occasions and the length of each SSB consultation/bandage application was recorded 10 times.

The SSB clinic consultation lasted an average of 18.2 minutes (range 10–30 minutes). The 4LB clinic consultation took an average of 19.2 minutes

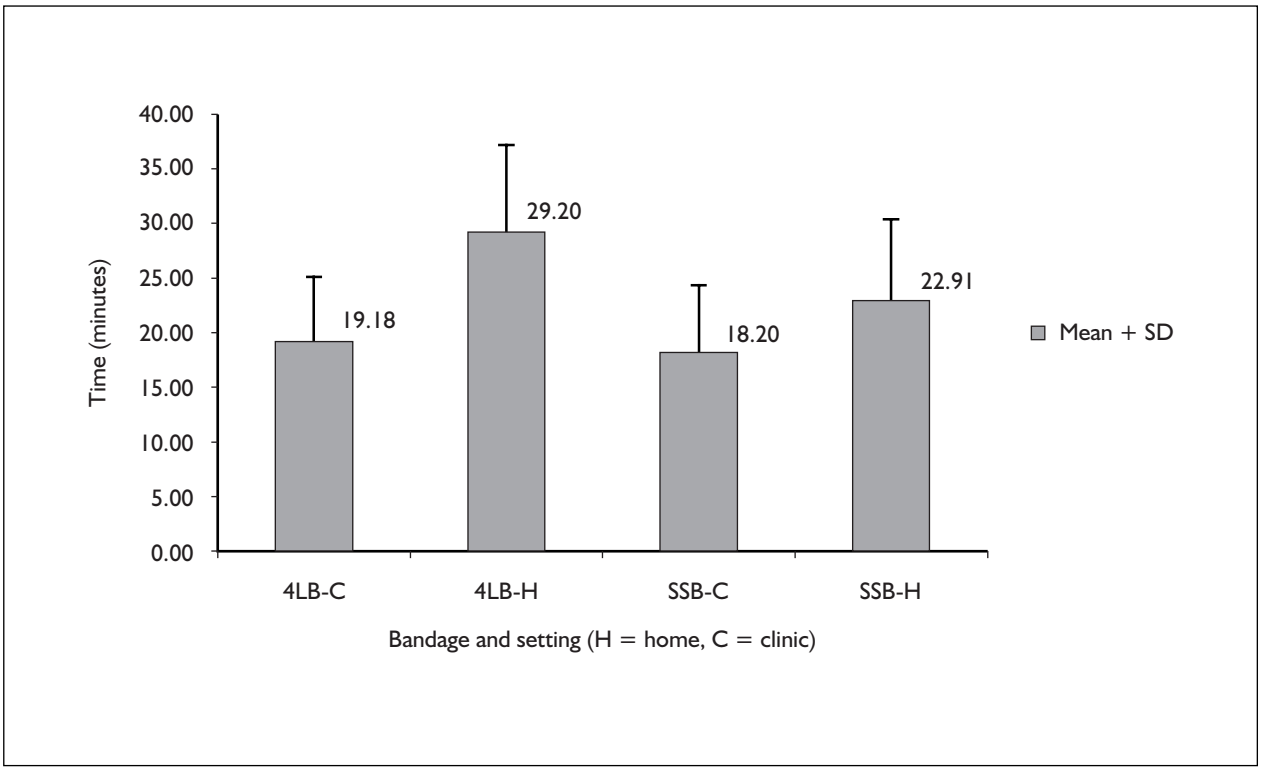

FIGURE 17 *Mean total consultation times for 4LB and SSB in clinics and home*

(range 8–28 minutes). There was no evidence of a statistically significant difference between the consultation times in the clinic for the two bandage systems, $t = 0.37$, $p = 0.71$ (two-tailed).

Time for complete consultation – home setting

Home visits were longer, with an SSB consultation lasting an average of 22 minutes (range 13–35 minutes). A home visit for the 4LB lasted an average of 29.2 minutes (range 20–42 minutes). There was no evidence of a statistically significant difference between the time taken for a home visit between the two bandages, $t = 1.86$, $p = 0.079$ (two-tailed).

Home consultations lasted 7 minutes longer for patients treated with 4LB than SSB, $t = 3.24$, $p = 0.0048$ (two-tailed). In order to determine whether this was due to the bandages taking more time to apply, the time to apply the bandage system was inspected.

Time to apply bandages

The bandage application times are summarised in *Figure 18*.

There was no evidence of a statistically significant difference between the times required to apply the 4LB and SSB in a clinic, at 5.8 and 4.3 minutes, respectively ($t = 1.8$, $p = 0.083$, two-tailed). Similarly, there was no evidence of a statistically significant difference in the time taken to apply the two bandage systems in the home, the 4LB taking an average of 5.7 and the SSB 4.8 minutes ($t = 1.04$, $p = 0.31$, two-tailed).

The average time for applying a 4LB, 5.75 minutes, accounts for 24% of the complete consultation period, an average of 24 minutes. The proportion of time spent on each aspect of treatment can be seen in *Figures 19* and *20*.

The initial part of the consultation, labelled as 'welcome', and the final part of the consultation, labelled as 'departure', took longer in the home than in the clinic. There was no difference in the bandage application time, or in the time to cleanse the leg or apply any creams.

The SSB mean bandage application time, 4.6 minutes, accounts for 22% of the average time for a complete consultation, 20.6 minutes. The proportion of various aspects of the total consultation to apply a SSB at home are shown

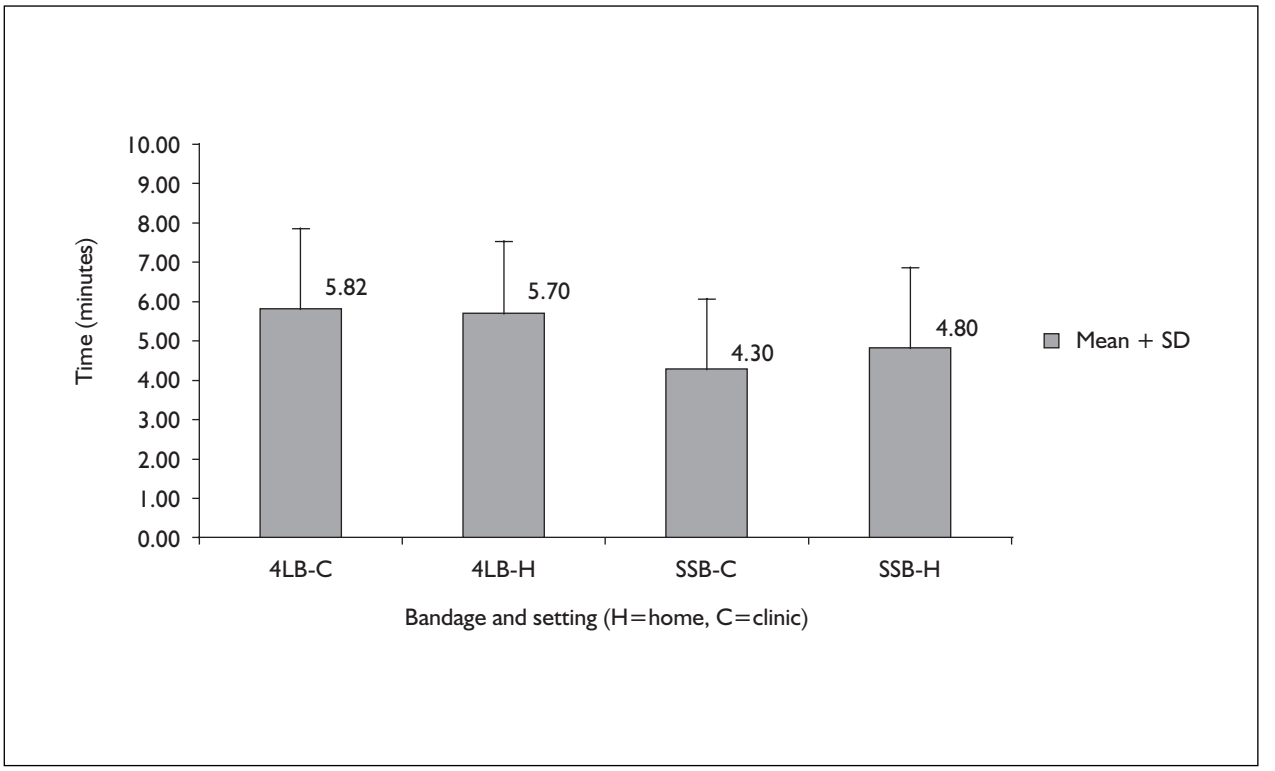

FIGURE 18 *Mean bandage application time for 4LB and SSB in clinics and home*

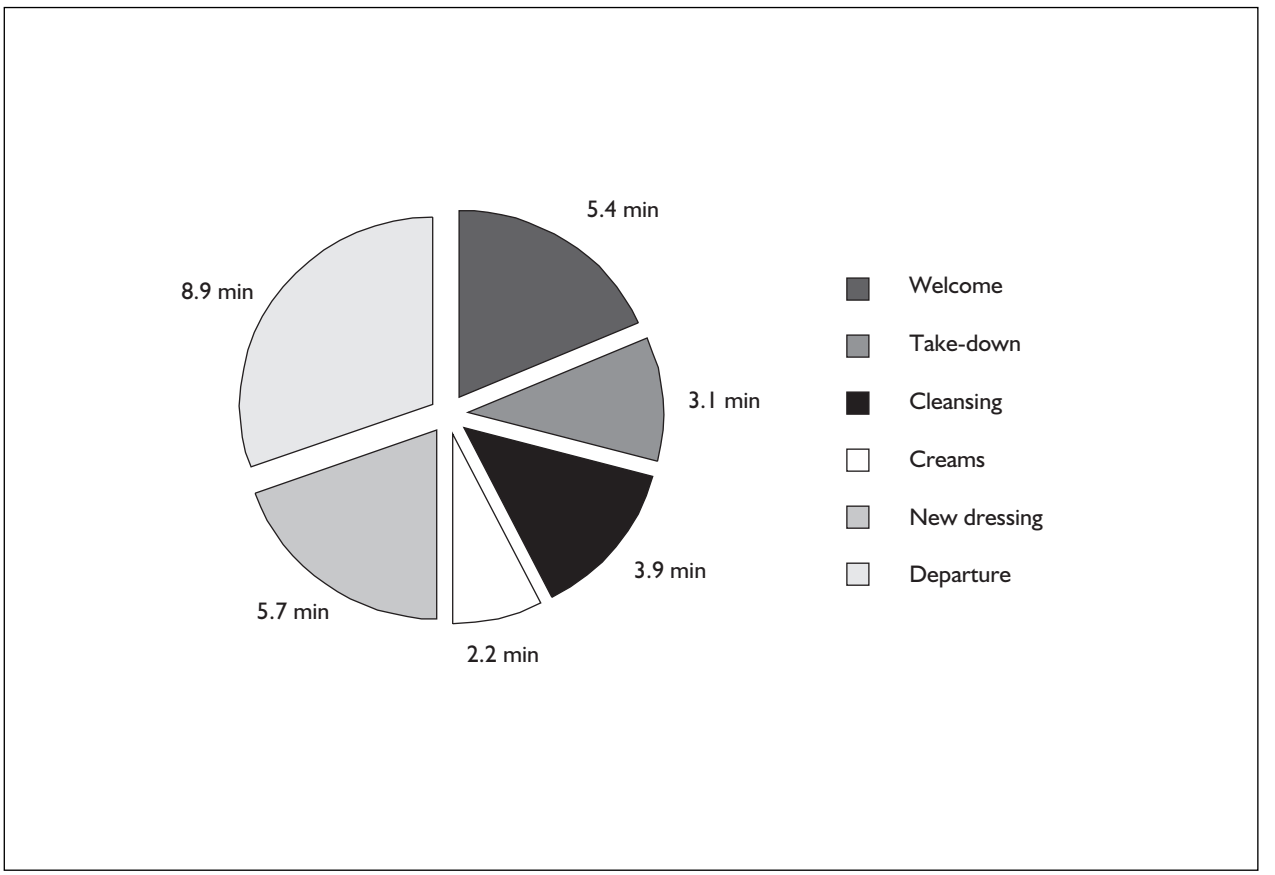

FIGURE 19 *Mean time of aspects of consultation while applying 4LB at home*

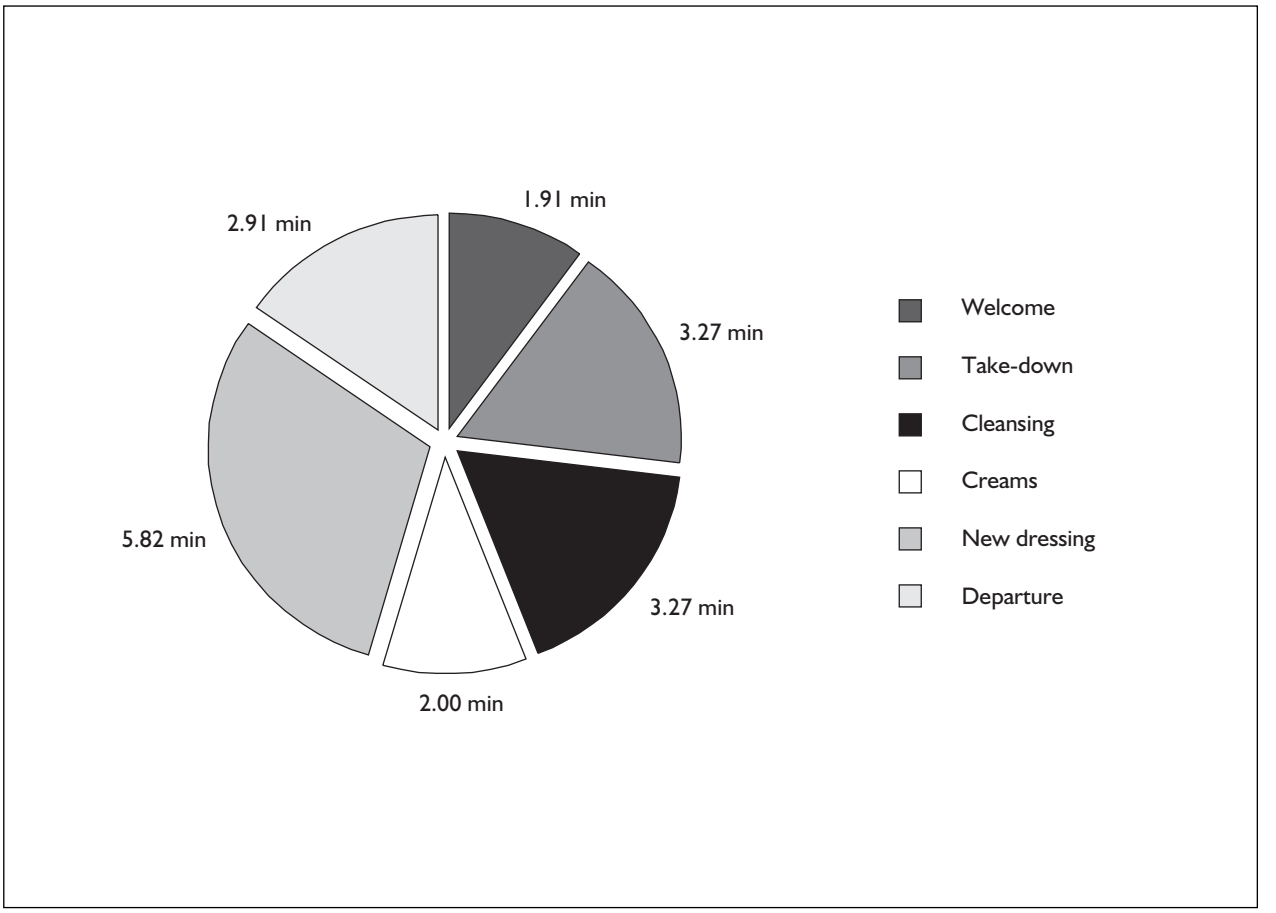

FIGURE 20 *Mean time of aspects of consultation while applying 4LB in clinic*

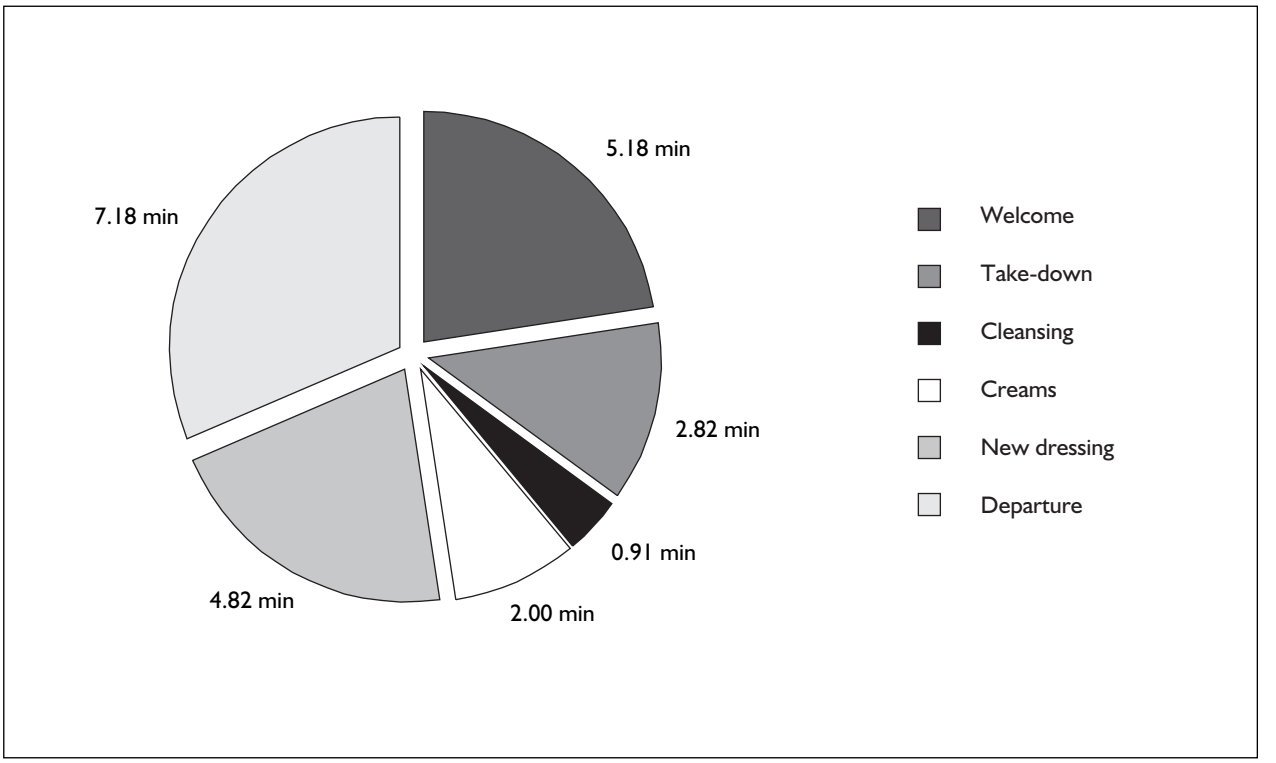

FIGURE 21 *Mean time of aspects of consultation while applying SSB at home*

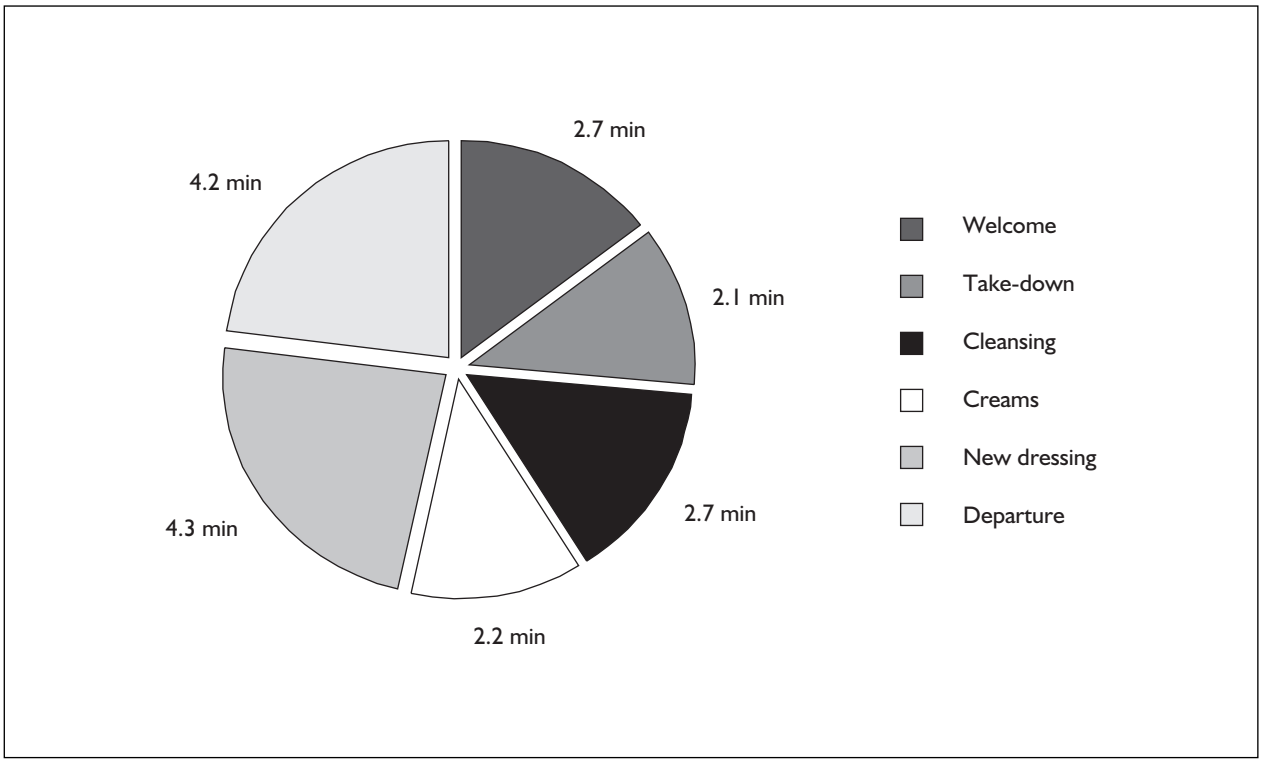

FIGURE 22 *Mean time of aspects of consultation while applying SSB in clinic*

in *Figure 21*. *Figure 22* shows the time for all aspects of the consultation for applying a SSB in the clinic.

The initial and final parts of the consultation took longer in the home than in the clinic. There was no apparent difference between the times for bandage removal, application of creams or application of the compression bandage system.

Discussion

This survey demonstrates that a bandage system with a shorter application time has the potential to make only a small difference to the overall duration of a consultation. Choosing a bandage system which takes a very short time to apply would have the greatest relative impact on consultation time when the total consultation time is short, such as in a clinic setting. The total nurse's time for setting up the clinic is likely to be small in comparison with the consultation time. For patients treated at home, however, the nurse's time for each patient includes not only the consultation time but also travelling time, and therefore any potential saving in nurses' time is likely to be much smaller than the total consultation cost.

Large reductions in the cost of treating a venous ulcer are likely to be achieved by reducing the total number of nurse visits, rather than by reducing the length of time required to apply a compression bandage system.

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We look forward to hearing from you.

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