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Supervised exercise training as an adjunct therapy for venous leg ulcers: a randomized controlled feasibility trial*

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Summary

Background Venous leg ulcers (VLUs) are typically painful and heal slowly. Compression therapy offers high healing rates; however, improvements are not usually sustained. Exercise is a low-cost, low-risk and effective strategy for improving physical and mental health. Little is known about the feasibility and efficacy of supervised exercise training used in combination with compression therapy patients with VLUs.

Objectives To assess the feasibility of a 12-week supervised exercise programme as an adjunct therapy to compression in patients with VLUs.

Methods This was a two-centre, two-arm, parallel-group, randomized feasibility trial. Thirty-nine patients with venous ulcers were recruited and randomized 1 : 1 either to exercise (three sessions weekly) plus compression therapy or compression only. Progress/success criteria included exercise attendance rate, loss to follow-up and patient preference. Baseline assessments were repeated at 12 weeks, 6 months and 1 year, with healing rate and time, ulcer recurrence and infection incidents documented. Intervention and healthcare utilization costs were calculated. Qualitative data were collected to assess participants’ experiences.

Results Seventy-two per cent of the exercise group participants attended all scheduled exercise sessions. No serious adverse events and only two exercise-related adverse events (both increased ulcer discharge) were reported. Loss to follow-up was 5%. At 12 months, median ulcer healing time was lower in the exercise group (13 vs. 34.7 weeks). Mean National Health Service costs were £813.27 for the exercise and £2298.57 for the control group.

Conclusions The feasibility and acceptability of both the supervised exercise programme in conjunction with compression therapy and the study procedures is supported.

What’s already known about this topic?

- Almost 70% of all leg ulcers have a venous component.
- Up to 30% of venous leg ulcers (VLUs) do not respond to compression alone, remain open after 1 year of treatment and need an average of 51 treatment visits to heal.
- Adjunct therapies to compression are needed.
- Exercise can form part of the therapeutic pathway, but evidence to determine whether exercise training has an effect on ulcer healing and quality of life is limited.
Almost 70% of all leg ulcers have a venous component. Occurrence of venous leg ulcers (VLUs) increases with age, with the U.K. prevalence in those >65 years of age being estimated at about 3%. VLUs arise from venous valve incompetence and calf muscle pump insufficiency, which leads to venous stasis and hypertension. This results in microcirculatory changes and localized tissue ischaemia. The natural history of VLUs is of a continuous cycle of healing and breakdown over decades. VLUs are typically painful and heal slowly, resulting in an impaired quality of life (QoL), social isolation and reduced work productivity. Treatment of this major health problem results in a considerable cost to the National Health Service (NHS): each ulcer costs up to £1981 per year; estimated total healthcare costs are between £198 million and £400 million per year, with 65% of these costs occurring in the community.

Lower-limb compression therapy is an established first-line therapy for VLUs, with approximately 50% of VLUs closing within 24 weeks. Nevertheless, recurrence rates remain high (up to 56% within 4 years). Furthermore, up to 30% of VLUs do not respond to compression alone, remain open after 1 year of treatment and need an average of 51 treatment visits to heal. Therefore, it is important to develop adjunct therapies to compression, which would improve healing outcomes.

Lifestyle factors, including nutrition, exercise and smoking, are mentioned in guidelines on the management of VLUs but receive relatively little emphasis. Exercise training might enhance ulcer healing and other aspects of health, and is routinely prescribed for other cardiovascular diseases (e.g. peripheral arterial disease and coronary artery disease). In patients with VLUs, supervised calf muscle exercise has been shown to increase calf muscle pump function and improve lower-limb haemodynamics, as well as mobility and QoL. A recent systematic review suggested further research to determine whether exercise training has an effect on ulcer healing and QoL.

Our team recently completed ‘FISCU’ (Feasibility of Implementing Supervised exercise training alongside Compression therapy in people with venous Ulceration; a National Institute for Health Research-funded study (PB-PG-0213-30029)) to assess the feasibility of a 12-week supervised exercise programme combining aerobic, resistance and flexibility exercises as an adjunct therapy to compression in patients with VLUs. We report on rates of screening, eligibility, recruitment, retention, outcome completion, exercise adherence and adverse events (AEs). We also report on reasons for exclusion and nonconsent, sample characteristics, the distribution and completeness of potential primary outcomes, and provide information on preliminary data on effectiveness and healthcare resource use.

Patients and methods
A full description of methods is available in our previously published protocol paper. The study was a two-arm, parallel-group, randomized controlled feasibility trial conducted in two U.K. sites (Lincoln and Sheffield). Ethics approval was granted by the NHS National Research Ethics Service, Yorkshire and the Humber (Sheffield) Committee (14/YH/0091), and all participants provided written informed consent prior to enrolment. The trial was prospectively registered (Current Controlled Trials ISRCTN10205425).

Participants
Participants were recruited from community nursing and tissue viability teams or services, community and outpatient leg ulcer clinics, and newspaper advertisement. Inclusion and exclusion criteria are given in Table 1.

Randomization, allocation concealment and blinding
Following baseline assessments, participants were randomly assigned 1:1 to an intervention group or a control group. Participants were stratified by ulcer size (maximum ulcer diameter 1–3 cm or >3 cm in any direction). Outcome assessors were blinded to group allocation.

Interventions
All participants received standard compression therapy directed by experienced tissue-viability nurses, following standard local practice. Patients were reviewed in clinics as considered clinically necessary, with no interference by the study team.

Participants randomized to the exercise group were invited to attend three sessions of supervised exercise each week for 12 weeks (total of 36 sessions) at one of the two study centers.
exercise training facilities (Sheffield Hallam University and University of Lincoln). For details on the exercise components see Table S1 (Supporting Information).

Study schedule and assessments

During visit 1, after written informed consent had been obtained and eligibility confirmed (which included a medical examination), the following baseline measurements were recorded at one of the two research centres (Sheffield Hallam University, University of Lincoln): (i) demographic data, including age, sex and socioeconomic status; (ii) clinical history, current medications, stature, body mass, ankle and calf circumference; (iii) ulcer size; (iv) ankle brachial pressure index (ABPI; a Doppler-determined measurement of ABPI was performed according to the procedures of Aboyans et al.,21 unless a reading < 3 months old could be obtained from clinical records, following the patient’s consent); (v) baseline exercise history; (vi) health-related QoL (HRQoL) questionnaires (EQ-5D-5L and VEINES-QOL);24–26 (vii) lower-limb cutaneous microvascular function (methods and results reported elsewhere);27 (viii) physical fitness, using three items from the Senior Fitness Test (6-min walking test, chair sit and reach, chair sit and stand)28 and ankle range of motion assessed using a bi-plane ankle goniometer.

All participants were given a resource use diary to complete at home for the duration of the study (to conduct health economics analysis).

Participants were then randomized to one of the two groups, as described above.

At 12 weeks and 12 months, participants had the following measures and tests repeated: physical fitness, microvascular function, ulcer-related clinical data (size, status and recurrence) and medications, body mass and HRQoL questionnaires. A copy of the resource use diary was also taken. A postal assessment involving the completion of HRQoL questionnaires was also undertaken at 6 months.

Feasibility and acceptability outcomes

Recruitment rates were measured as rate of invited participants who were eligible and consenting. Acceptability of allocation was assessed by examining reasons for dropout in discontinuing participants and comparing attrition rates between the two study groups. Suitability of measurement procedures was evaluated by outcome completion rates and reasons for missing data. Attrition rate was established as discontinuation of intervention and loss to follow-up measurement for all conditions. The acceptability of the exercise programmes was assessed by using session attendance and compliance data and participant feedback via one-to-one semi-structured interviews conducted with a subgroup of participants after the 3-month follow-up visit (detailed analysis will be presented elsewhere). The safety of exercise training was also assessed by exploring reasons for dropout from the exercise programme and the number and type of AEs that occurred in each group.

Sample size

Sample size calculation was based on willingness for randomization and aimed to recruit 80 participants within an 18-month recruitment period (Table S1; see Supporting Information).

Data analysis

All analyses were conducted on an intention-to-treat basis, conducted in SPSS version 24 (IBM, Armonk, NY, U.S.A.). Missing data were reported by trial arm with description of underlying reasons.

Baseline

Summary tables report all baseline variables, and clinical, fitness and patient-reported outcome variables. Continuous variables were summarized with descriptive statistics. Frequency counts and percentages were provided for categorical data.

Feasibility and acceptability

For success criteria, see Table 2. Outcomes used to assess the feasibility and acceptability of key trial parameters were rates of eligibility, recruitment, retention, outcome completion, exercise adherence and AEs. Group preference, reasons for

| Table 1 Study inclusion and exclusion criteria |
| Inclusion criteria | Exclusion criteria |
|--------------------|-------------------|
| At least 18 years old | Unsuitable for or unable to exercise (determined by clinician) |
| Have at least one VLU of primarily venous aetiology (determined by clinician) with maximum diameter of at least 1 cm | Insulin-controlled diabetes mellitus |
| ABPI of at least 0.8 (recorded within the previous 3 months) | N/A |
| Able and willing to tolerate lower-limb compression | Pregnancy |
| Coexisting skin conditions, vasculitis, deep venous occlusion or malignant/atypical ulceration | N/A |
| Require major surgery | N/A |
| Leg ulcer with maximum diameter < 1 cm | N/A |
| Have had an ulcer at the same site within the previous 3 months | N/A |
| Unable or do not wish to consent to participation in the trial | N/A |

VLU, venous leg ulcer; ABPI, ankle brachial pressure index.
exclusion and nonconsent, sample characteristics and the distribution of potential primary outcomes are presented.

Clinical, fitness and patient-reported outcomes
Descriptive statistics are presented for clinical, fitness and patient-reported outcomes at each time point.

Economic evaluation
A prospective economic evaluation was rehearsed to develop and refine the methods for a subsequent definitive trial (Appendix S1; see Supporting Information).

Results
Figure 1 shows the flow of participants through the trial. Recruitment took place between July 2014 and May 2016, with all follow-up data collection completed by May 2017. The trial was extended for 3 months to allow extra recruitment time.

Screening, eligibility and recruitment
A summary of feasibility and acceptability data is presented in Table 3. All success criteria were met (e.g. 72% of participants completed all exercise sessions, loss to follow-up was 5%, patient preference to the exercise group was 44%, whereas median ulcer healing time was chosen as the primary outcome for the definitive trial). Of 514 patients screened for participation, 109 met the eligibility criteria and 39 (24 men, 15 women) were recruited, giving eligibility and recruitment rates of 21% and 36%, respectively. Sites 1 and 2 recruited 38 and one participants, respectively. Reasons for nonconsent and exclusion are shown in Figure 1.

Group allocation, group preference and participant characteristics
Eighteen participants were allocated to exercise and 21 to usual care. Seventeen (63%) of 27 participants expressed a preference for exercise (12 expressed no preference). Participant characteristics at baseline are shown in Table 4; the groups were well balanced for most variables except QoL.

Retention
Retention rate was 95%. Two of 39 participants formally left the study; one from the exercise group for ulcer pain before the 3-month assessment and one from the control group for nonulcer-related health reasons before the 6-month assessment. All others completed all assessment sessions. Four participants withdrew from exercise training due to family commitments and nonulcer-related health reasons.

Exercise attendance and safety data
Of the 18 exercise participants, 13 (72%) completed all sessions; overall session completion rate was 79% (n = 512/648). No bandage slippage/misplacement was detected during exercise sessions. We observed two exercise-related AEs (both excessive discharge from the ulcer). Actions taken included the removal of resistance exercises and postponement of exercise sessions.

Physical function and body mass
Participants in the exercise group showed higher mean values at 3 months in all tests (Table 5). Results stabilized at 12 months for all tests except plantar flexion. Weight reduction was modest for the exercise group in relation to the baseline (mean ± SD 103.9 ± 24 kg at baseline vs. 99.8 ± 28.4 kg at 12 months). In contrast there was an increase in weight in the control group (mean ± SD 102.6 ± 25.6 kg vs. 105.7 ± 25.2 kg at 12 months).

Ulcer-related data
Median ulcer size was similar between groups at 12 months (Table 6), but healing rate was higher in the intervention group (83% vs. 60%), with shorter median (range) ulcer healing time [13 (3–9–52) vs. 34–7 (4–3–52) weeks]. Recurrence rates were low in both groups (two in the intervention group, one in the control group).

Health-related quality of life
Participants in the intervention group started the study with a higher EQ-5D utility score than the control group (Table 7; mean ± SD 0.8022 ± 0.17 vs. 0.6010 ± 0.35). This difference was maintained throughout the study. A similar difference was observed with EQ visual analogue scale, VEINES-QOL (overall score and symptom score) and pain score, although for VEINES-QOL and pain score, the difference between groups was increased from 3 months onwards.

Health economic data
There were no missing data for procedure costs. Mean exercise intervention costs per participant was £610–22, including staff time, room hire and patient reimbursement. Mean total NHS
Enrolment

Screened for eligibility \( (n = 514) \)
- Other types of wounds/nonvenous ulcer \( (n = 206) \)
- Venous ulcer not meeting the study criteria \( (n = 54) \)
- Patient not suitable for exercise \( (n = 85) \)
- Other reason (e.g. dementia, other mental health problems \( (n = 60) \)

Invited \( (n = 109) \)
- Work commitments/inability to travel \( (n = 52) \)
- Other reasons \( (n = 18) \)

Randomized \( (n = 39) \)

Exercise and standard care \( (n = 18) \)
- Received exercise \( \geq 1 \) sessions, \( n = 18 \)

Standard care only \( (n = 21) \)
- Received standard care \( (n = 21) \)

Invited \( (n = 109) \)
- Work commitments/inability to travel \( (n = 52) \)
- Other reasons \( (n = 18) \)

Randomized \( (n = 39) \)

Exercise and standard care \( (n = 18) \)
- Received exercise \( \geq 1 \) sessions, \( n = 18 \)

Standard care only \( (n = 21) \)
- Received standard care \( (n = 21) \)

Lost to follow-up \( (n = 1) \)
- Unwillingness to continue the study due to ulcer pain before 3-month follow-up
  - Discontinued exercise but remained in the study \( (n = 4) \)
  - One due to ulcer-related problems,
  - Three due to nonulcer-related health problems.

Lost to follow-up \( (n = 1) \)
- Unwillingness to continue the study due to non-ulcer-related health problems at after 3 months of follow-up

Analysis

1. HRQoL \( (n = 17 \text{ at 3, 6 and 12 months}) \)
2. Senior fitness test and physical functioning/fitness test \( (n = 17 \text{ at 3, 6 and 12 months}) \)
3. Health economics \( (n = 17 \text{ at 3, 6 and 12 months}) \)
4. Clinical data (e.g. ulcer size/healing, ulcer recurrence) \( (n = 17 \text{ at 3, 6 and 12 months}) \)

1. HRQoL \( (n = 21 \text{ at 3 months and } n = 20 \text{ at 6 and 12 months}) \)
2. Senior fitness test and physical functioning/fitness test \( (n = 21 \text{ at 3 months and } n = 20 \text{ at 6 and 12 months}) \)
3. Health economics \( (n = 21 \text{ at 3 months and } n = 20 \text{ at 6 and 12 months}) \)
4. Clinical data (e.g. ulcer size/healing, ulcer recurrence) \( (n = 21 \text{ at 3 months and } n = 20 \text{ at 6 and 12 months}) \)

Fig 1. Flow of participants through the trial. HRQoL, health-related quality of life.
Table 3 Summary of trial feasibility and acceptability data

| Methodological issues | Findings | Evidence |
|-----------------------|----------|----------|
| What factors influenced eligibility and what proportion of those screened were eligible? | Tissue viability clinics see a variety of patient wounds, the majority of which are not ulcers or of venous origin | 109/514 screened were eligible; the most common reasons for noneligibility were ulcer not of venous origin or other type of wound present (n = 206); the main reasons for nonconsent were mainly of social origin (e.g. work commitments or difficulty travelling; n = 52) |
| Was recruitment successful? | Recruitment was slower than anticipated | 39 participants were recruited within a 21-month period |
| Were eligible patients recruited? | Conversion rate to recruitment was within our primary targets | 39/109 (36%) eligible participants were recruited in the study |
| Were participants successfully randomized and did randomization yield equality in groups? | Randomization process worked well | Similar sized groups, well-balanced on stratification and most other variables; however, QoL scores were higher at baseline in the exercise group |
| Were blinding procedures adequate? | Blinding of outcome assessors and ulcer healing assessments worked well | Two different assessors were used at follow-up sessions. No discussions were reported between participants and assessors on their study experience during follow-up sessions. Assessment of digital ulcer photographs was completed by a team member unaware of the association between study ID numbers and group allocation |
| Did participants adhere to the intervention? | We experienced a very high attendance rate | 13/18 (72%) of the exercise group participants attended 100% of the scheduled exercise sessions; 512/648 (79%) of the scheduled sessions were completed |
| Was the intervention acceptable to the participants? | Qualitative and quantitative data from exercise participants suggest that the intervention was acceptable | Of the 27 participants who expressed a preference for a specific group before allocation (12 of the study participants did not express a preference), 17 (69% among those expressing preference; 44% among all) preferred exercise. Patient interviews (reported elsewhere) have also suggested a high degree of satisfaction |
| Was the intervention safe? | Our preliminary safety data appear favourable | Two nonserious AEs (excess fluid discharge from ulcer) were noted during the study; no bandaging was affected during the exercise sessions |
| Were outcome assessments completed? | Outcome completion rates were very high | See 'Results' section |
| Was it possible to calculate intervention and healthcare utilization costs? | Yes | Cost of exercise programme: £610.22 per participant. Total costs per participant were £2412.2 (including out-of-pocket expenses) and £1537.10 for control and exercise group patients, respectively |
| Was retention to the study good? | Retention was very high | Retention rate 95% |
| Did all components of the protocol work together? | From the point that the recruitment procedures were modified, components had strong synergy | There were no major difficulties identified in the various processes and the researchers’ ability to implement them. For example, if participants were recruited, there was excellent collaboration between the care and the research team in regards to data capture (e.g. tracing, ulcer photography) |
| Was an appropriate outcome defined for the definitive trial? | Yes | Based on our study and previous research experience, a reduction in ulcer healing time appears to be the most appropriate outcome for the definitive trial |

QoL, quality of life; AE, adverse event.
### Table 4 Summary of baseline demographics

| Baseline characteristics                  | Intervention (n = 18) | Control (n = 21) | Combined (n = 39) |
|-------------------------------------------|----------------------|-----------------|------------------|
| Male                                      | 9 (50)               | 14 (67)         | 23 (59)          |
| Mean ± SD age (y)                         | 65.4 ± 14.9          | 61.9 ± 10.9     | 63.5 ± 12.8      |
| Working                                   | 8 (44)               | 6 (29)          | 14 (16)          |
| White ethnicity                           | 17 (94)              | 21 (100)        | 38 (98)          |
| Mean ± SD body mass (kg)                  | 102.1 ± 29.4         | 104.9 ± 24.3    | 103.6 ± 26.5     |
| Mean ± SD SBP (mmHg)                      | 143 ± 20             | 140 ± 18        | 141 ± 19         |
| Mean ± SD DBP (mmHg)                      | 79 ± 10              | 84 ± 13         | 81 ± 12          |
| Mean ± SD HR (bpm)                        | 72 ± 13              | 69 ± 11         | 70 ± 12          |
| Smoking status                            | 4 (22)               | 5 (24)          | 9 (23)           |
| Mean ± SD alcohol consumption (units weekly) | 8 ± 13               | 9 ± 14          | 8 ± 13           |
| Key medications                           |                      |                 |                  |
| Antiplatelet/anticoagulant                | 7 (39)               | 5 (24)          | 12 (31)          |
| Statin                                    | 3 (17)               | 5 (24)          | 8 (21)           |
| ACE inhibitor                             | 1 (6)                | 1 (5)           | 2 (5)            |
| Beta blocker                              | 3 (17)               | 6 (29)          | 9 (23)           |
| Calcium channel blocker                   | 1 (6)                | 2 (10)          | 3 (8)            |
| Diuretic                                  | 4 (22)               | 3 (14)          | 7 (18)           |
| Comorbidities                             |                      |                 |                  |
| Hypertension                              | 7 (39)               | 4 (19)          | 11 (28)          |
| History of other CVD                      | 1 (6)                | 8 (38)          | 9 (23)           |
| Noninsulin-dependent diabetes             | 4 (22)               | 4 (19)          | 8 (21)           |
| History of cancer                         | 2 (11)               | 1 (5)           | 3 (8)            |
| Hypercholesterolaemia                     | 1 (6)                | 2 (10)          | 3 (8)            |
| Ulcer-related                             |                      |                 |                  |
| Had ulcer before                          | 11 (61)              | 14 (67)         | 25 (64)          |
| Mean ± SD duration of reference ulcer (months) | 12.7 ± 19.9         | 7.1 ± 8.1       | 7.9 ± 14.8       |
| Mean ± SD time since diagnosis of reference ulcer (months) | 8.9 ± 13.7          | 6.1 ± 8.0       | 7.4 ± 10.9       |
| Had ulcer at same site (> 3 months previously) | 3 (17)               | 3 (14)          | 6 (15)           |
| Median (range) ulcer length (cm)          | 2.6 (1.2 to 13.5)    | 2.8 (1.2 to 11.8) | 2.7 (1.2 to 13.5) |
| Median (range) ulcer width (cm)           | 1.9 (0.9–10.1)       | 1.9 (1.1–6.5)   | 1.9 (0.9–10.1)   |
| Median (range) ulcer area (cm²)           | 4.9 (1.9–136.4)      | 5.7 (1.3–56.6)  | 5.0 (1.3–136.4)  |
| Mean ± SD ABPI                            | 1.0 ± 0.1            | 1.1 ± 0.2       | 1.1 ± 0.2        |
| Physical activity and fitness             |                      |                 |                  |
| Walking with difficulty                   | 8 (44)               | 10 (48)         | 18 (46)          |
| No walking                                | 5 (28)               | 7 (33)          | 12 (31)          |
| Walking < 1 h                             | 3 (17)               | 5 (24)          | 8 (21)           |
| Walking 1–3 h                             | 6 (33)               | 5 (24)          | 11 (28)          |
| Walking ≥ 3 h                             | 4 (22)               | 4 (19)          | 8 (21)           |
| Exercise/physical activity other than walking | 14 (78)             | 16 (76)         | 30 (77)          |

Data are n (%) unless otherwise indicated. SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; bpm, beats per min; ABPI, ankle brachial pressure index.

### Table 5 Physical fitness/function indices

| Test                           | Exercise group          | Control group           |
|--------------------------------|-------------------------|-------------------------|
|                               | Baseline | 3 months | 12 months | Baseline | 3 months | 12 months |
| 6-min walk distance (m)        | 276 ± 100 | 290 ± 123 | 291 ± 122 | 280 ± 141 | 284 ± 138 | 273 ± 146 |
| Chair sit-to-stand (repetitions) | 8 ± 4   | 10 ± 4   | 9 ± 4     | 9 ± 4     | 9 ± 4     | 8 ± 4     |
| Chair sit-and-reach (score)    | -6.4 ± 11.4 | 2.6 ± 16.0 | 2.2 ± 11.8 | -2.8 ± 13.6 | -0.8 ± 11.3 | -1.7 ± 11.9 |
| Plantar flexion (°)            | 18.7 ± 21.0 | 22 ± 15.9  | 17.6 ± 12.8 | 15.1 ± 9.1 | 19.0 ± 22.3 | 14.7 ± 9.4 |
| Dorsiflexion (°)               | 20.5 ± 14   | 22.9 ± 14.8 | 18.9 ± 15.8 | 20.3 ± 16.5 | 18.7 ± 24.2 | 17.4 ± 15.3 |
| Ankle range of movement (°)    | 39.2 ± 19.9 | 44.9 ± 21.3 | 36.6 ± 20.8 | 35.4 ± 19.7 | 37.7 ± 43.2 | 32.1 ± 18.9 |

Data are mean ± SD.
### Table 6 Ulcer-related data

|                      | Exercise Control |          |          |          |          | Control |          |          |          |          |          |
|----------------------|------------------|----------|----------|----------|----------|---------|----------|----------|----------|----------|----------|
|                      | Baseline         | 3 months | 6 months | 12 months | Baseline | 3 months | 6 months | 12 months | Baseline | 3 months | 6 months |
| Median (range) ulcer size |                  |          |          |          |          |         |          |          |          |          |          |
| Length (cm)          | 2.6 (1.2–13.5)   | 0 (0–5)  | NA       | 0 (0–5)  | 2.8 (1.2–11.8) | 1.3 (0–10.2) | NA       | 0 (0–14)  |          |          |          |
| Width (cm)           | 1.9 (0.9–10.1)   | 0 (0–6.5) | NA       | 0 (0–3.4) | 1.9 (1.1–6.5) | 1.0 (0–7.7) | NA       | 0 (0–10.5) |          |          |          |
| Area (cm²)           | 4.9 (1.9–136.4)  | 0 (0–26) | NA       | 0 (0–18.7)| 5.7 (1.3–56.6)| 1.5 (0–78.5) | NA       | 0 (0–147) |          |          |          |
| Whether healed, n (%)|                  |          |          |          |          |         |          |          |          |          |          |
|                      | 9/17 (53)        | 11/17 (65)| 14/17 (83)| 3/21 (14)| 8/20 (40) | 12/20 (60) |          |          |          |          |          |
| Median (range) time of ulcer healing (weeks) |                  |          |          |          |          |         |          |          |          |          |          |
|                      | 13 (3–9–52)      |          |          |          |          |         |          |          |          |          |          |
| Reoccurrence of ulcer, n (%) |              |          |          |          |          |         |          |          |          |          |          |
|                      | 0/17 (0)         | 1/17 (6) | 2/17 (12)| 0/20 (0) | 2/17 (12) | 1/19 (5)  |          |          |          |          |          |

NA, not available.

### Table 7 Summary of health status, disease-specific quality of life and pain data

|                      | Exercise Control |          |          |          |          | Control |          |          |          |          |          |
|----------------------|------------------|----------|----------|----------|----------|---------|----------|----------|----------|----------|----------|
|                      | Baseline         | 3 months | 6 months | 12 months | Baseline | 3 months | 6 months | 12 months | Baseline | 3 months | 6 months |
| EQ-5D-5L utility score | 0.8022 ± 0.17 | 0.8567 ± 0.15 | 0.8147 ± 0.21 | 0.7874 ± 0.28 | 0.6010 ± 0.35 | 0.5698 ± 0.42 | 0.5740 ± 0.40 | 0.5825 ± 0.41 |
| EQ-VAS score          | 69.03 ± 15.13    | 75.35 ± 15.38 | 71.47 ± 21.24 | 75.53 ± 20.37 | 57.43 ± 19.84 | 64.33 ± 22.34 | 58.70 ± 26.21 | 56.20 ± 27.58 |
| VEINES-QoL: main      | 53.68 ± 24.62    | 69.53 ± 26.13 | 67.49 ± 27.75 | 67.23 ± 29.86 | 42.65 ± 24.70 | 47.24 ± 29.57 | 51.79 ± 33.62 | 52.46 ± 34.81 |
| VEINES symptom subdomain | 62.03 ± 26.52 | 75.18 ± 24.76 | 73.24 ± 26.26 | 73.41 ± 31.73 | 53.17 ± 28.82 | 54.60 ± 32.11 | 58.13 ± 30.05 | 58.53 ± 33.58 |
| Pain score            | 24.44 ± 27.3     | 15.9 ± 27.7 | 16.5 ± 28.4 | 7.9 ± 22.8 | 30.95 ± 31.6 | 22.1 ± 32.8 | 28.0 ± 36.1 | 30.5 ± 36.6 |

Data are mean ± SD.
as well as the feasibility and preliminary effectiveness of a supervised exercise programme for people with VLUs. Our main finding was that the study procedures were feasible and acceptable.

The feasibility and acceptability of using a supervised exercise regime as an adjunct therapy to compression therapy had been an area of uncertainty prior to this study. Indeed, during the preliminary study stages, such a notion was met with scepticism by some clinicians and patients, who believed that exercise may be either inappropriate or harmful, and may delay rather than promote healing – an attitude that has also been documented in the literature. Nevertheless, the majority of the eligible patients had a positive attitude towards undertaking exercise in addition to following a therapeutic pathway based on compression therapy. This was irrespective of whether they consented to take part and reasons for non-participation will help make the programme more accessible (i.e. by choosing appropriate venues). Our feasibility data show few AEs, with no bandage misplacement or slippage incidents, one of the biggest concerns of collaborating clinicians.

Exercise attendance was 79%, with 72% of participants completing all sessions. This is high considering that many participants were old, frail and had no previous exercise experience. This was achieved without employing any specific adherence-enhancing components or provision of behavioural change support, which could have potentially improved attendance rates and the effect of the intervention even further. This suggests great interest and self-motivation from our participants, which will be a decisive factor for the success of a definitive trial and any wider roll-out of the intervention. However, despite our success, it is our plan to incorporate cognitive–behavioural strategies as part of any future trial to optimize exercise adherence and increase any potential, positive effect.

With regard to practicality our intervention was primarily delivered within a university setting, at some distance from the clinics in which our participants were treated. The high attendance rate suggests that this did not have a negative impact on the outcome, although it may have affected recruitment rate. Recruitment rate may be improved in the definitive trial, where 12-week exercise referral schemes will be utilized for the intervention delivery. Delivery with an option of times in community-based venues increases accessibility but comes with a number of challenges (as adherence and success varies); recent research suggests that these schemes can offer QoL and physical activity gains.

Our findings support the feasibility of using diaries to collect economic data on patients’ usage of NHS resources, healthcare visits, prescriptions and out-of-pocket expenses. The findings suggest potential savings to both the NHS (£875.08 per patient) and patients (£60.95 reduction in out-of-pocket expenses). Nevertheless, as our analysis was purely descriptive, an appropriate health economics analysis in the definitive trial will provide greater certainty regarding cost-effectiveness.

Overall, no major difficulties were identified in the design or implementation of trial procedures. For example, the blinding procedures ran as intended, the rates of retention and outcome completion (including the 6-month postal assessment) was very good, and from a point onwards there was an excellent communication between clinical and research teams, which allowed smooth recruitment. There was an imbalance between groups in the EQ-5D-5L data; this did not affect the outcome, although it may have affected recruitment rate. The EQ-5D-5L data; this did not affect the outcome, although it may have affected recruitment rate.

Designing, setting up and managing a definitive, multicentre study has other challenges besides recruitment rate, data collection and exercise delivery. One important issue is the recruitment of a sufficient number of sites which will: (i) deliver the required number of participants; (ii) have experienced

### Table 8 Summary of annual costs to the National Health Service (NHS), out-of-pocket (OOP) expenses of treatment and intervention study cost by group

| Cost type                        | Total (£)    | Mean Per patient (£) |
|----------------------------------|--------------|----------------------|
|                                  | Exercise     | Control              | Combined          | Exercise     | Control              | Combined          |
| NHS healthcare professional      | 12 724.00    | 34 573.00            | 47 297.00         | 748.47       | 1464.33             | 1244.66           |
| A&E                              | 0            | 0                    | 0                 | 0            | 100.48              | 55.53             |
| Inpatient care                   | 0            | 9 365.00             | 9 365.00          | 0            | 445.95              | 246.45            |
| Diagnostic tests                 | 257.00       | 746.00               | 1 003.00          | 15.12        | 35.52               | 26.39             |
| Medicine (free prescriptions)    | 844.60       | 1 476.00             | 2 320.60          | 49.68        | 70.29               | 61.07             |
| Total cost to NHS                | 13 825.60    | 48 270.00            | 62 095.60         | 813.27       | 2298.57             | 1634.09           |
| Cost to patients                 |              |                      |                   |              |                     |                   |
| Travel                           | 1 081.66     | 2 341.68             | 3 423.34          | 63.63        | 111.51              | 90.09             |
| Medicine                         | 229.10       | 413.44               | 642.54            | 13.48        | 19.69               | 16.91             |
| Equipment                        | 621.00       | 911.00               | 1 532.00          | 36.53        | 43.38               | 40.32             |
| Total OOP expenses               | 1 931.76     | 3 666.12             | 5 597.88          | 113.63       | 174.58              | 147.31            |
| Intervention study cost          | 10 984.00    | NA                   | 10 984.00         | 610.22       | 610.22              |                  |
| Including study outcome measures | 14 051.17    | 32 555.17            | 17 306.33         | 780.62       | 155.01              | 455.43            |

A&E, Accident and Emergency; NA, not applicable.

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29,30 QoL and physical activity gains.

32 Delivery with an option of times in community-based venues increases accessibility but comes with a number of challenges (as adherence and success varies).

33 recent research suggests that these schemes can offer QoL and physical activity gains.

34 Our findings support the feasibility of using diaries to collect economic data on patients’ usage of NHS resources, healthcare visits, prescriptions and out-of-pocket expenses.
clinicians to act as local Principal Investigators; (iii) have dedicated tissue viability services, which will support and promote the study; and (iv) have a good communication level between exercise deliverers, tissue viability clinics, local stakeholders (e.g. NHS Trusts) and the main research team. It is therefore advisable that a clinical trials unit is utilised to safeguard data quality and guarantee database management, in addition to costing dedicated personnel (e.g. a trial coordinator and a trial manager) for day-to-day study management and involving experienced research sites in previous, similar studies (which would safeguard a consistent delivery of the trial protocol).

Our findings support the feasibility and acceptability of both the supervised exercise programme in conjunction with compression therapy and the study procedures and all our success criteria were met. In addition, our results suggest that there may be significant potential benefit in healing rates and that, if this were confirmed in a full trial, the introduction of supervised exercise for VLU may well also save costs for the NHS. The next step will be the design and implementation of an appropriately powered, multicentre trial, which is required to provide answers to the questions of the clinical and cost-effectiveness of the intervention.

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**Supporting Information**

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

**Table S1** Further particulars of the supervised exercise programme.

**Appendix S1** Health economics and quality of life analysis.

**Video S1** Author video.

**Powerpoint S1** Journal Club Slide Set.