Testing the feasibility of a co-designed intervention comprising self-managed, home-based exercise training with embedded behavioral support and compression therapy for people with venous leg ulcers, receiving treatment at home (FISCU-II)

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Clin Exp Dermatol 2023; **00**:1–8
https://doi.org/10.1093/ced/lad342
Advance access publication date: 11 October 2023

CED
Clinical and Experimental Dermatology
Original Article

Testing the feasibility of a co-designed intervention, comprising self-managed, home-based, exercise training with embedded behavioural support and compression therapy for people with venous leg ulcers receiving treatment at home (FISCU-II)

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Abstract

Background Venous leg ulcers (VLUs) heal slowly, are painful for patients and are costly for healthcare systems; they also affect patients' quality of life. Previous work suggests that supervised exercise training used in combination with compression therapy may offer clinical benefits. However, a large population of people with VLUs are unable to access such an intervention due to frailty and age.

Objectives To assess the feasibility of 'FISCU Home' (a co-designed, 12-week home-based self-managed lifestyle programme based on exercise and behaviour support) as an adjunct therapy to compression in people with VLUs.

Methods Forty people with VLUs, receiving treatment at home, were recruited from community nursing and tissue viability teams, and via a newspaper advertisement. Participants were randomized 1 : 1 either to exercise with behaviour support (three times per week) plus compression therapy or compression only. The feasibility of the programme was assessed using progression criteria that included exercise attendance rate, loss to follow-up, patient preference(s) and adverse events (AEs). Baseline assessments were repeated at 12 weeks and 6 months. Secondary outcomes (i.e. ulcer recurrence, healing rate and healing time) were also documented at these intervals. Intervention and healthcare utilization costs were calculated.

Results The study recruitment rate was 65%, while 75% of the exercise group participants attended all scheduled exercise sessions. All participants completed compression therapy. No serious AEs or exercise-related AEs were reported. Median (interquartile range) ulcer healing time was shorter in the exercise group [29 (7–108) vs. 42 (6–116) weeks].

Conclusions The feasibility and acceptability of both a home- and exercise-based lifestyle intervention in conjunction with compression therapy and the study procedures are supported.

What is already known about this topic?

- Supervised exercise is a feasible adjunct therapy to compression for people with venous leg ulcers (VLUs), with potential clinical benefits.
- These benefits remain to be explored in a full-scale study.
- Nevertheless, supervised exercise cannot be undertaken by people with VLUs receiving treatment at home, for whom special provisions need to be made.

What does this study add?

- This is the first study to co-design, together with people with VLUs, a home- and exercise-based lifestyle intervention as an adjunct to compression therapy.
- Our results suggest that the developed intervention is a feasible adjunct therapy (e.g. high completion and retention rates) that can offer potential clinical benefits (e.g. reduced ulcer healing time).

Accepted: 1 October 2023

Venous leg ulcers (VLUs) are a growing health problem, accounting for almost 70% of all leg ulcers.[1] Their occurrence is strongly linked to advanced age, with the annual UK prevalence in those aged > 65 years estimated to be about 3% (approximately 400 000 patients).[2] Current treatments are not fully effective. The natural history of VLUs is of a continuous cycle of healing and breakdown over decades.[3] The underlying aetiology of VLUs is venous valve failure and calf muscle pump insufficiency, leading to venous stasis and hypertension. This results in microcirculatory changes and tissue ischaemia. Typically, VLUs are painful and heal slowly, resulting in an impaired quality of life (QoL), social isolation and reduced work productivity in patients.[4] Compression (e.g. stockings or bandages) is the current gold-standard treatment.[5] Nevertheless, recurrence rates reach up to 69% within 12 months,[6] while up to 30% of VLUs are non-responsive to compression,[5] remaining open after 1 year of treatment.[7] Therefore, it is important to explore acceptable adjunct therapies to compression that would improve healing outcomes.

Exercise is encouraged in clinical guidelines for the treatment for VLUs.[8] However, it receives little emphasis in everyday clinical management. FISCU, our National Institute for Health Research (NIHR)-funded study that explored the feasibility of using a 12-week community- and group-based (primarily aerobic) exercise programme as an adjunct therapy to compression, suggested that multiple benefits from supervised exercise may be gained by people with VLUs.[9,10] Our research suggests that the observed health benefits are due to the reversal of the underlying microangiopathy,[11] which appears at early disease stages.[12] Therefore, exercise holds considerable potential as an adjunct therapy for enhancing healing, as well as improving the physical and mental health of patients.

Nevertheless, FISCU statistics suggest that about 40% of patients (most of whom receive treatment at home) cannot attend group sessions,[9] owing to mobility issues and frailty. Therefore, we do not know if results can be replicated in the frailer, older population who receive treatment at home; however, these patients appear to be willing to try an adjunct therapy, which could potentially improve their wellbeing. We completed a pilot survey (data not published) in those who declined to take part in FISCU, the results of which suggested that about 74% would be willing to take part in an intervention at their residence. Thus, a study targeting this group is warranted.

The current study aimed to close this knowledge gap. We co-designed and tested the feasibility of a home-based exercise intervention ('FISCU Home').

Materials and methods

Design and setting

The FISCU II trial was a three-phase study (comprising intervention design and pilot testing) informed by the Medical Research Council's complex interventions framework, using both qualitative (phase I: a participatory approach based on focus groups/interviews) and mixed methods (phase II: feasibility testing of the intervention via a randomized controlled trial; phase III: qualitative study and intervention refinement), conducted in Sheffield, UK.

Phase I co-designed processes (involving interviews and focus groups with 18 participants conforming to the FISCU inclusion criteria) and phase III findings have been or will be reported separately.[13]

The trial was prospectively registered in the ISRCTN registry (16899826).

Participants

Participants were recruited from community nursing and via a newspaper advertisement. The inclusion and exclusion criteria are provided in Table 1. A diagnosis of VLU was completed clinically, with venous aetiology confirmed by an ankle brachial pressure index (ABPI) > 0.8.

Randomization, allocation concealment and blinding

Following baseline assessments, participants were randomly assigned 1 : 1 to our intervention ('FISCU Home' + compression therapy) or a control (compression therapy only) group. Participants were stratified by ulcer size (maximum ulcer diameter 1–3 cm or > 3 cm). Randomization was performed by a blinded statistician using nQuery Advisor 6.0 (Statistical Solutions, Cork, Ireland). Outcome assessors were blinded to group allocation.

Interventions

All participants received standard compression therapy (based on the application of four- or two-layer compression bandages at a pressure of approximately 40 mmHg), directed by experienced community nurses. There was no interference by the researchers. Participants randomized to the intervention group followed the 'FISCU Home' intervention, developed in phase I.[13] This meant undertaking a self-managed exercise programme (three times per week, for approximately 1 h on each occasion) with an embedded behavioural support element (focusing on the provision of lifestyle advice), supported via face-to-face visits ($n = 5$) and telephone calls ($n = 6$) by an experienced exercise physiologist. The programme was tailored against the participants' baseline assessments (Appendix S1; see Supporting Information).

Study schedule and assessments

During visit 1, following consent and confirmation of eligibility, the following baseline measurements were recorded by a blinded assessor: (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) ABPI (a Doppler-determined measurement of ABPI was performed according to the procedures of Aboyans *et al.*,[14] unless a reading < 3 months old could be obtained from clinical records, following the participant's consent); (v) baseline exercise history; (vi) health-related QoL (HRQoL) questionnaires [EuroQol-5D-5L (EQ-5D-5L)

and VEINES-QOL];[15,16] and (vii) physical fitness, using two items from the Senior Fitness Test (2 Minute Walk Test, chair sit and stand)[17] and ankle range of motion assessed using a biplane ankle goniometer.

All participants were given a resource use diary to complete at home during the study (to support a health economics exercise).

Participants were then randomized to one of the two groups, as described above. At 12 weeks and 6 months, participants had the following measurements and tests repeated: physical fitness, ulcer-related clinical data (size, status and recurrence) and medications, body mass and HRQoL questionnaires. A copy of the resource use diary was also made. Measurement of ulcer size involved taking a leg ulcer tracing by using a fine-nibbed indelible pen onto a conformable acetate film with a pre-printed grid. When a participant had multiple venous ulcers, all ulcers were traced and the eligible ulcer with the largest surface area was deemed the reference ulcer for the trial. The reference ulcer and any other ulcers were drawn onto a leg diagram. A digital image of the reference ulcer was also taken.

Feasibility and acceptability outcomes

Recruitment rates were measured as the rate of invited participants who were eligible and consented to take part. Acceptability of allocation was assessed by examining reasons for dropout in discontinuing participants and comparing attrition rates between the two study groups. The suitability of measurement procedures was evaluated by outcome completion rates and reasons for missing data. The attrition rate was established as discontinuation of intervention and loss to follow-up measurement for all conditions. The acceptability of the lifestyle programme was assessed 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 adverse events (AEs) that occurred in each group. For success/progression criteria see Table 1.

Sample size

The sample size needed to be adequate to estimate critical metrics, to assess the feasibility of conducting a definitive trial with sufficient precision. The critical metrics in this trial were recruitment rate (i.e. the number of eligible individuals randomized), compliance with treatment and attrition, as well as standard deviation precision. Twenty participants per group (in total, $n=40$) provided sufficient precision (within 11 percentage points for a 95% confidence interval) to estimate the proportion willing to be randomized, assuming an intention to be randomized rate of 40%. Based on previous experience on working with this population, we used elements from our 'six pillars of adherence' framework (based, on this occasion, on 'social support', 'education', 'reachability', 'reminders' and 'simplicity'), to maintain high levels of retention and completion.

Data analysis

All analyses were conducted on an intention-to-treat basis, conducted in SPSS version 26 (IBM, Armonk, NY, USA). QoL data were missing for one participant. 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. Descriptive statistics are presented for clinical, fitness and patient-reported outcomes at each timepoint.

As this was a feasibility study, no statistical comparison was undertaken as per standard statistical practice (e.g. 'no hypothesis' – 'no statistical test')[18] and no primary outcome existed; its primary aim was to assess the feasibility of 'FISCU Home'. However, 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 nonconsent, sample characteristics and the distribution of potential primary outcomes in a definitive trial are also presented. Secondary outcomes included health economics, physical function and body mass, ulcer-related data and HRQoL.

Table 1 Study inclusion and progression criteria

Inclusion criteria	Exclusion criteria
People with at least one VLU with a maximum diameter $\geq$ 1 cm. The VLU must have been wholly or partially within the gaiter region; VLUs that were partially within the gaiter region and also extended onto the foot were permitted; however, VLUs confined to the foot only were not permitted for inclusion	People who were unsuitable or unable to exercise (according to treating nurse/doctor judgement)
People with an ABPI $\geq$ 0.8	Pregnancy or scheduled major surgery
People > 18 years old, able and willing to tolerate compression, receiving it in an at-home setting	People intolerant of lower-limb compression delivered by compressions stockings or multilevel bandaging
People who were primarily housebound or unable to travel	People with vasculitis and infections (when fully treated, people were to be reassessed for inclusion if willing and otherwise eligible)
Success and progression criteria	
At least 67% of randomly assigned patients in the exercise group were compliant with the intervention (defined as at least 75% of the scheduled sessions completed as planned)	
Loss to follow-up rate at 6 months was < 20%	
Participant preferences being < 60% in favour for either group	

ABPI, ankle brachial pressure index; VLU, venous leg ulcer.

Economic evaluation

A prospective economic evaluation was rehearsed to develop and refine the methods for a subsequent definitive trial (Appendix S2; see Supporting Information). The mean exercise intervention cost (based on the total number of sessions that participants attended) was calculated separately to the NHS cost.

Results

Figure 1 shows the flow of participants through the trial. Phase II recruitment started at the beginning of the second wave of the COVID-19 pandemic in the UK (autumn 2020). Recruitment was paused twice as per National Health Service (NHS) research guidelines, to allow treating clinicians to concentrate on their core activities. In total, 40 participants were recruited over 11 months.

Feasibility and acceptability

Screening, eligibility and recruitment

All success criteria were met. A summary of the feasibility and acceptability data are presented in Table 2. Reasons for nonconsent and exclusion are provided in Figure 1.

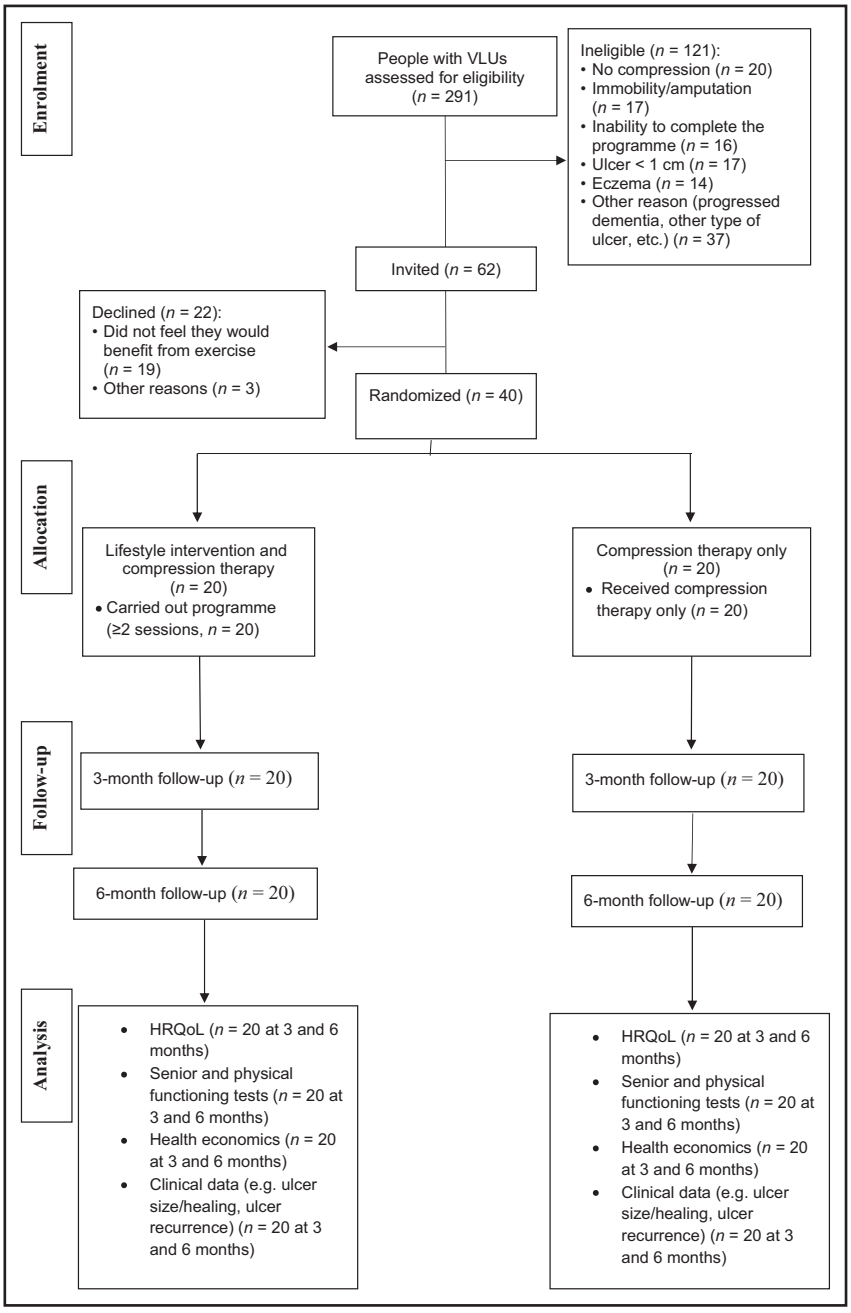

Figure 1 CONSORT flowchart of the study population. HRQoL, health-related quality of life; VLU, venous leg ulcer.

Table 2 Summary of trial feasibility and acceptability data

Methodological issues	Findings	Evidence
What factors influenced eligibility and what proportion of those screened were eligible?	Community nurses see a variety of patient wounds; many of which are not ulcers or of venous origin	170/291 screened were eligible; the most common reasons for noneligibility were ulcer < 1 cm ($n=17$) or inability to take part in the programme ($n=16$)
Was recruitment successful?	Recruitment was successful, although it was paused during COVID-19 pandemic restrictions	40 participants were recruited within an 11-month period
Were eligible patients recruited?	Conversion rate to recruitment was within our primary targets	40/62 (65%) of invited participants were recruited to the study
Were participants successfully randomized and did randomization yield equality in groups?	Randomization process worked well	Same sized groups, well balanced on stratification and most other variables
Were the blinding procedures adequate?	Blinding of outcome assessors and ulcer healing assessments worked well	A single assessor was 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 identification numbers and group allocation
Did participants adhere to the intervention?	We experienced a very high attendance rate	15/20 (75%) of the exercise group participants attended 100% of the scheduled exercise sessions; 636/720 (88%) 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 19 participants who expressed a preference for a specific group before allocation (21 of the study participants did not express a preference), 12 (30% among all) preferred exercise. Patient interviews (reported elsewhere) also suggested a high degree of satisfaction
Was the intervention safe?	Our preliminary safety data appear favourable	No AEs 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: £170 per participant. Total costs per participant were £1256.72 (including NHS expenses) and £1215.33. for control and exercise group patients, respectively
Was retention to the study good?	Retention was very high	Retention rate was 100%
Did all components of the protocol work together?	From the point of view 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

AE, adverse events; NHS, National Health Service.

Group allocation, group preference and participant characteristics

Twenty participants were allocated to exercise and 20 to usual care. Twelve of 40 (30%) participants expressed a preference for exercise (21 expressed no preference). Participant characteristics at baseline are provided in Table 3; the groups were well balanced for most variables.

Retention

The study retention rate was 100%. Three participants did not complete their exercise training owing to nonulcer-related health reasons (e.g. back pain and hospitalization).

Exercise and safety data

Of the 20 exercise participants, 15 (75%) completed all sessions; the overall session completion rate was 88.3% ($n=636/720$). No bandage slippage/misplacement was detected during the exercise sessions. No exercise-related AEs were reported by the participants.

Secondary outcomes

Physical function and body mass

Participants in the exercise group showed greater improvement in all tests at 3 months, with no great variation at 6 months (Table 4).

Ulcer-related data

Median ulcer size among active ulcers was lower in the intervention group at 6 months (Table 4). A shorter median [interquartile range (IQR)] ulcer healing time [29 (7–108) vs. 42 (6–116)] was also observed. Faster healing in the intervention group was reflected by the highest healing rate at 3 months (60% vs. 30%), with rates between groups equalizing at 6 months (65% vs. 70%). Among those whose ulcers healed, low recurrence rates were reported in both groups (5% in each group).

Health-related quality of life

Participants in the intervention group started the study with a higher EQ-5D utility score than those in the control group (Appendix S3; see Supporting Information). This difference was maintained throughout the study. EQ VAS and Pain scores showed greater improvement in the intervention group (Appendix S3).

Health economic data

There were no missing data for procedure costs. The mean exercise intervention cost 'per participant' was £170, including staff time and staff travelling expenses. Mean NHS 'per participant' costs (based on NHS National Tariff Schedules and calculated based on visits and use of NHS resources) were calculated as £1045.33 for those in the

Table 3 Summary of baseline demographics

Baseline characteristics	Control (*N*=20)	Intervention (*N*=20)
Male sex	8 (40)	6 (30)
Age, years	78 (13)	80 (10)
Working	0	1 (5)
White	20 (100)	20 (100)
Stature, cm	160.5 (7.8)	160.2 (12.3)
Body mass, kg	91.8 (33.0)	83.7 (30.3)
Smoking status		
Current	2 (10)	2 (20)
Never smoked	12 (60)	11 (55)
Alcohol consumption: none	17 (85)	14 (70)
No. of comorbidities reported	3 (1)	3 (2)
Main comorbidities		
Hypercholesterolaemia	5 (25)	5 (25)
Hypertension	6 (30)	4 (20)
Number of prescribed medications	8 (3)	8 (6)
Ulcer-related		
Had ulcer for how long (months)	45 (58)	109 (121)
Duration of reference ulcer (months)	14 (15)	20 (37)
Time since diagnosis of reference ulcer (months)	9 (11)	6 (6)
ABPI	1.1 (0.2)	1.1 (0.3)
Physical activity and fitness		
Walking pace: immobile/slow pace	20 (25)	17 (5)
Unable to do housework/childcare	11 (55)	8 (40)
Driving before: do not drive	13 (65)	10 (50)
Driving after ulcer: do not drive	18 (90)	16 (80)

Data are presented as *n* (%) or mean (SD). ABPI, ankle brachial pressure index.

exercise group and £1256.72 for those in the control group. 'Per participant' personal costs were calculated using a diary, with 'out-of-pocket' expenses being estimated at £23.95 and £17.50 for those in the exercise and control groups, respectively. The mean 'per participant' cost savings to the NHS as a result of the intervention and after its costs were accounted for were £41.39 (Appendix S2; see Supporting Information).

Discussion

To our knowledge, this is the first study to have successfully co-designed a self-managed, expertly supported, exercise programme for people with VLUs who receive treatment for their condition at home. We assessed several feasibility aspects, including recruitment, baseline and follow-up measurements, as well as the preliminary effectiveness of

Table 4 Ulcer- and fitness-related data

	Control			Exercise		
	Baseline	3 months	6 months	Baseline	3 months	6 months
Participants with active ulcers (*n*)	20	14	6	20	8	7
Size of active ulcer						
Length (cm)	2.0 (0.9–7.0)	1.4 (0.5–4.0)	3.0 (0.4–4.0)	2.0 (0.5–4.5)	2.5 (1.0–3.4)	1.1 (0.5–2.0)
Width (cm)	2.0 (0.5–6)	1.9 (0.5–8.1)	2.0 (0.4–8.0)	2.5 (0.9–8.0)	2.4 (1.0–6.5)	2 (0.5–6.4)
Area (cm^2)	4.7 (1.0–24.0)	2.1 (0.3–32.0)	8.0 (0.2–28.0)	4.9 (1.0–25.5)	6.0 (2.4–10.4)	1.0 (0.3–11.5)
Healed	0/20	6/20 (30)	14/20 (70)	0/20 (0)	12/20 (60)	13/20 (65)
Recurrence		0/20 (0)	1/20 (5)		0/20 (0)	1/20 (5)
Time taken to heal from original diagnosis (weeks)		42 (6–116)			29 (7–108)	
Test, mean (SD)						
Flexibility (°)	−15.3 (11.6)	−17.1 (9.9)	−16.3 (9.2)	−16.5 (13.7)	−13.8 (10.4)	−14.4 (13.4)
Angular plantar (°)	10.9 (8.0)	9.3 (7.4)	8.8 (5.8)	10.5 (7.1)	13.3 (7.3)	11.1 (7.6)
Angular dorsi (°)	11.9 (7.7)	13.9 (6.8)	14.4 (6.4)	13.8 (7.3)	15.6 (8.6)	16.1 (8.6)
Ankle range (°)	22.8 (12.9)	23.8 (11.5)	23.2 (8.3)	24.3 (11.1)	28.9 (13.1)	27.3(13.7)
Ankle circumference (cm)	27 (6)	27 (7)	27 (7)	24 (3)	23 (4)	24 (4)
Calf circumference (cm)	40 (11)	38 (11)	38.7 (12)	36 (8)	36.5 (9)	37 (8)
No. of steps taken in 2 min	27 (15)	26 (17)	26 (16)	34 (17)	41 (23)	37 (18)
Chair sit-to-stand (no. of repetitions)	5 (3)	4 (3)	4 (2)	6 (3)	7 (4)	7 (6)

Data are presented as median (range) unless otherwise stated.

'FISCU Home'. 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 previously proven by our group and others.[9,19] Despite the generally positive attitude of using exercise as an adjunct therapy to compression, at a regional level, there are still clinicians and patients who view the concept critically, if not negatively.[20,21] This can be considered as another side of NHS gatekeeping, which is known potentially to have a negative effect on patient clinical outcomes.[22] Nevertheless, most of the eligible patients we approached for the study had a positive attitude towards trying 'FISCU Home'. This becomes more apparent, when it is considered that recruitment took place during periods when case numbers of COVID-19 were high in the UK, and it was difficult for people (who potentially felt more vulnerable as a result) to participate in a research trial and allow visits from nonfamily members. Our 'six pillars of adherence' framework,[23] which was used to support the delivery of the programme and to run the trial, played a role in our patient retention success. Bearing in mind that the potentially positive impact that exercise has on the severity of COVID-19 symptoms was unknown at the time of the study,[24] participants' willingness to consider taking part in our programme should be considered as a vote of confidence in our intervention.

Our feasibility data did not reveal any AEs, and no incidents of bandage misplacement or slippage, which was one of the biggest concerns for treating clinicians, particularly as the programme was primarily self-managed.

The exercise adherence rate was 88%, with 75% of participants completing all sessions. These rates are higher than those found in FISCU I,[9] which was fully supervised. The high adherence and completion rates are positive signs for the wider future implementation of 'FISCU Home', considering that all participants were >70 years of age, most were frail and only one had previous exercise experience. This suggests great interest and self-motivation, which will be decisive factors in the success of a definitive trial.

The delivery of self-managed exercise programmes can be challenging, even in less frail/younger populations (e.g. people with patellofemoral pain).[25] Yet the interest in implementing self-managed exercise interventions for people with VLUs remains high, with at least one study ongoing for the general VLU population at the time of writing.[26] Considering the possibility of new COVID-19 waves or new pandemics, and the challenges faced by community-based interventions,[27] self-managed delivery can be considered as an option – if delivered appropriately, as our feasibility study shows.

Our findings support the feasibility of using diaries to collect economic data on patients' use of NHS resources, healthcare visits, prescriptions and out-of-pocket expenses. Indications for small NHS cost savings also exist (e.g. approximately £42 per participant after exercise costs were considered). Nevertheless, as our analysis was purely descriptive, an appropriate health economics analysis in a definitive trial will provide greater certainty on cost-effectiveness.

As with the FISCU I study, no major difficulties were identified in the design or implementation of trial procedures. This included blinding procedures, carrying out assessments, and rates of retention and outcome completion. The good communication that our team had with clinical teams suggests that recruitment for larger trials will not be an issue, provided that the treating nurses are in support of the study and willing to aid recruitment, as was the combined FISCU I and FISCU II experience.

Designing, setting up and managing a definitive multicentre study has additional challenges besides recruitment rate, data collection and exercise delivery.[28] Our findings support the feasibility and acceptability of both the co-designed, exercise-based lifestyle intervention in conjunction with compression therapy and the study procedures, as all our success criteria were met. To move to a definitive trial, we require preparatory work to be done, to ensure that NHS support is in place. To gain this we need to show clear evidence that clinical benefits may exist. Our results suggest that there may be significant benefit in healing rates (as well as small NHS cost benefits), even in the more (medically) complex group of people with VLUs who receive treatment at home.

In an equally positive outcome, our results suggest that positive fitness changes were experienced, and exercise progression was achieved. These findings build on observations from our FISCU I trial, which was based on a similar intervention of aerobic exercises. The latter are needed to gain the microcirculatory benefits to facilitate healing.[29]

Thus, the next step will be the design and implementation of an appropriately powered, multicentre trial that will provide answers to the questions of both the clinical effectiveness and cost-effectiveness of the intervention. Considering that the clinical benefits seen in both FISCU studies appear to be similar, it can safely be suggested that these two delivery options (at home vs. in the community) can be offered simultaneously and explored in a full trial.

Our study was designed as a feasibility study, and as such, no statistical comparisons could be made between groups. Nevertheless, the positive clinical findings in the intervention group should substantiate investment in a definitive trial. Also, the full effect of 'FISCU Home' on VLU recurrence has not been explored due to funding limitations. This will need to be assessed in a future study.

Acknowledgements

We would like to acknowledge the study participants for their invaluable support in these challenging times. We would also like to acknowledge the following people: the tissue viability nurses who supported recruitment and data collection; Mrs Paula McDonald (Sheffield STH NHS FT) for acting as a clinical liaison, Dr Helen Crank (Sheffield Hallam University) for her contribution to the development of our grant application; and Mr Tom Parkington (Sheffield Hallam University) for supporting various aspects of the study. We also thank our patient and public involvement steering group members – they supported this series of studies from the beginning, and we are in debt to them for their help. Finally, we thank Dr Geoff Middleton (University of Lincoln; Steering Group Chair) and Professor Lee Ingle (University of Hull) for being the academic external members of our steering group and for stepping in when this group was severely affected by COVID-19.

Funding sources

This article presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit programme (grant reference number PB-PG-0418-20021). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Conflicts of interest

The authors declare no conflicts of interest.

Data availability

The data that support the findings of this study are not publicly available due to ethical constraints but are available from the corresponding author upon reasonable request.

Ethics statement

Ethics approval was granted by the NHS National Research Ethics Service, London – Surrey Research Ethics Committee (18/LO/1983), and all participants provided written informed consent prior to enrolment.

Supporting Information

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

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SOTYKTU™
(deucravacitinib) 6 mg tablets

INTENDED FOR UK & IRELAND HEALTHCARE PROFESSIONALS WITH AN INTEREST IN THE MANAGEMENT OF PLAQUE PSORIASIS ONLY

CHANGING THE LANDSCAPE OF ORAL PSORIASIS TREATMENT[1-4]

SOTYKTU is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy[1]

SOTYKTU is a novel, efficacious oral treatment that is generally well-tolerated[1–4]*

DURABLE EFFICACY

Demonstrated superior PASI 75 response rates, and rates of clear or almost clear skin (sPGA 0/1), vs. placebo at Week 16 (co-primary endpoints)[2,3]*

PASI 75 response rates were observed at Week 24 and maintained at Week 52[1]*

GENERALLY WELL-TOLERATED

The most commonly reported adverse reaction is upper respiratory infections (18.9%)[1]

Less than 3% of patients discontinued treatment due to AEs between Weeks 0–16[1-4]

ONCE DAILY, ORAL DOSING

Once-daily, oral treatment that can be taken with or without food, with no routine blood monitoring requirements after initiation and no identified DDIs[1†]

Learn more at sotyktu.co.uk

Adverse events should be reported. Reporting forms and information can be found at: UK – via the yellow card scheme at: www.mhra.gov.uk/yellowcard, or search for MHRA Yellow Card in the Google Play or Apple App Store. Ireland – via HPRA Pharmacovigilance at www.hpra.ie. Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (UK); 1 800 749 749 (Ireland)

*SOTYKTU was studied in two global, Phase 3, randomised, multi-arm clinical studies: POETYK PSO-1 and PSO-2. **PASI 75 and sPGA 0/1 vs. placebo at Week 16 were co-primary endpoints**. PASI 75 was defined as ≥75% reduction from baseline in the Psoriasis Area and Severity Index. sPGA was defined as sPGA score of 0 or 1 with ≥2-point improvement from baseline. N numbers: PSO-1: SOTYKTU (n=332); apremilast (n=168), placebo (n=166); PSO-2: SOTYKTU (n=511); apremilast (n=254), placebo (n=255). SOTYKTU delivered superior PASI 75 response rates vs placebo (PSO-1: 58.4% vs. 12.7%, p<0.0001; PSO-2: 53.0% vs. 9.4%, p<0.0001) at Week 16, and superior results achieving clear or almost clear skin (sPGA 0/1) vs. placebo (PSO-1: 53.6% vs. 7.2%, p<0.0001; PSO-2: 49.5% vs. 8.6%, p<0.0001) at Week 16 (co-primary endpoints).[2,3]

†Via enzyme inhibition, enzyme induction, or transporter inhibition.[1]

Abbreviations: AE, adverse event; DDI, drug–drug interaction; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment; TYK2, tyrosine kinase 2.

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Bristol Myers Squibb™

Job code: 1787-GB-2300026 Date of preparation: September 2023

SOTYKTU® (deucravacitinib) PRESCRIBING INFORMATION

Great Britain

Consult Summary of Product Characteristics (SmPC) before prescribing. **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.**

PRESENTATION: Film-coated tablet containing 6 mg of deucravacitinib.

INDICATION: Treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

DOSAGE AND ADMINISTRATION: Treatment should be initiated under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis. Posology: 6 mg orally once daily. If a patient shows no evidence of therapeutic benefit after 24 weeks, treatment discontinuation should be considered. The patient's response to treatment should be evaluated on a regular basis. Special populations: *Elderly:* No dose adjustment is required in elderly patients aged 65 years and older. Clinical experience in patients ≥ 75 years is very limited and deucravacitinib should be used with caution in this group of patients. *Renal Impairment:* No dose adjustment is required in patients with renal impairment, including end stage renal disease (ESRD) patients on dialysis. *Hepatic impairment:* No dose adjustment is required in patients with mild or moderate hepatic impairment. Deucravacitinib is not recommended to be used in patients with severe hepatic impairment. *Paediatric population:* The safety and efficacy of deucravacitinib in children and adolescents below the age of 18 years have not yet been established. No data are available. Method of administration: For oral use. Tablets can be taken with or without food. Tablets should be swallowed whole and should not be crushed, cut, or chewed.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients (see SmPC). Clinically important active infections (e.g. active tuberculosis).

WARNINGS AND PRECAUTIONS: Infections: Treatment should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Caution should be exercised when considering the use in patients with a chronic infection or a history of recurrent infection. Patients treated with deucravacitinib should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a clinically important infection or is not responding to standard therapy, monitor carefully and deucravacitinib should not be given until the infection resolves. Pre-treatment evaluation for tuberculosis (TB): Prior to initiating treatment with deucravacitinib, patients should be evaluated for TB infection. Deucravacitinib should not be given to patients with active TB. Treatment of latent TB should be initiated prior to administering deucravacitinib. Anti-TB therapy should be considered prior to initiation of deucravacitinib in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving deucravacitinib should be monitored for signs and symptoms of active TB. Malignancies*: Malignancies, including lymphomas and non-melanoma skin cancer (NMSC), were observed in clinical studies with deucravacitinib. Limited clinical data are available to assess the potential relationship of exposure to deucravacitinib and the development of malignancies. Long-term safety evaluations are ongoing. The risks and benefits of deucravacitinib treatment should be considered prior to initiating patients**. Major adverse cardiovascular events (MACE), deep venous thrombosis (DVT) and pulmonary embolism (PE)*: An increased risk was not observed in clinical trials with deucravacitinib. Long-term safety evaluations are ongoing. The risks and benefits of deucravacitinib treatment should be considered prior to initiating patients**. Immunisations: Consider completion of all age-appropriate immunisations according to current immunisation guidelines prior to initiating therapy. Use of live vaccines in patients being treated with deucravacitinib should be avoided. Excipients: Contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicinal product. Contains less than 1 mmol of sodium (23 mg) per tablet, essentially 'sodium-free'. *serious. **It is not known whether tyrosine kinase 2 (TYK2) inhibition may be associated with the adverse reactions of Janus Kinase (JAK) inhibition. In a large randomised active-controlled study of a JAK inhibitor in rheumatoid arthritis (RA) patients 50 years and older with at least one additional cardiovascular risk factor, a higher rate of malignancies (particularly lung cancer, lymphoma and NMSC), a higher rate of MACE (defined as cardiovascular death, non-fatal myocardial infarction and non-fatal stroke), and a dose dependent higher rate of venous thromboembolism (including DVT and PE) were observed with a JAK inhibitor compared to TNF inhibitors.

INTERACTIONS: Deucravacitinib does not have any known clinically relevant drug interactions. Refer to SmPC for full details.

PREGNANCY AND LACTATION: Pregnancy: There is a limited amount of data on the use of deucravacitinib in pregnant women. As a precautionary measure, it is preferable to avoid the use of deucravacitinib during pregnancy. Breast-feeding: It is unknown whether deucravacitinib/metabolites are excreted in human milk. A risk to the newborns/infants by breast-feeding cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from deucravacitinib therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. Fertility: The effect of deucravacitinib on human fertility has not been evaluated.

UNDESIRABLE EFFECTS: The most commonly reported adverse reaction is upper respiratory infections (18.9%), most frequently nasopharyngitis. The longer-term safety profile of deucravacitinib was similar and consistent with previous experience. Very common (≥ 1/10): Upper respiratory infections*** (including nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, pharyngitis, sinusitis, acute sinusitis, rhinitis, tonsillitis, peritonsillar abscess, laryngitis, tracheitis, and rhinotracheitis). Common (≥ 1/100 to < 1/10): Herpes simplex infections*** (including oral herpes, herpes simplex, genital herpes, and herpes viral infection), Oral ulcers (including aphthous ulcer, mouth ulceration, tongue ulceration, and stomatitis), Acneiform rash (including acne, dermatitis acneiform, rash, rosacea, pustule, rash pustular, and papule), Folliculitis and Blood creatine phosphokinase increased. Uncommon (≥ 1/1,000 to < 1/100): Herpes zoster***. Refer to SmPC for full details on adverse reactions.

***serious adverse drug reaction

LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE: PLGB 15105/0179: Carton of 28 film-coated tablets 6 mg NHS price: £690.00; Carton of 84 film-coated tablets 6 mg NHS price: £2070.00.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland.

FOR FURTHER INFORMATION CONTACT:

medical.information@bms.com or 0800 731 1736 (Great Britain).

DATE OF PREPARATION: May 2023

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 1787-GB-2300080

Adverse events should be reported. Reporting forms and information can be found at: Great Britain – www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store; Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (Great Britain).

SOTYKTU® (deucravacitinib) PRESCRIBING INFORMATION

Northern Ireland / Ireland

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***serious adverse drug reaction

LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE: EU/1/23/1718/006: Carton of 28 film-coated tablets 6 mg NHS price: £690.00.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland.

FOR FURTHER INFORMATION CONTACT:

medical.information@bms.com or 0800 731 1736 (Northern Ireland) / 1 800 749 749 (Ireland).

DATE OF PREPARATION: June 2023

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 1787-IE-2300001

Adverse events should be reported. Reporting forms and information can be found at: Northern Ireland – www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store; Ireland – via HPRA Pharmacovigilance at www.hpra.ie Adverse events should also be reported to Bristol-Myers Squibb via medical.information@bms.com or 0800 731 1736 (Northern Ireland); 1 800 749 749 (Ireland).