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Comparison of 'Lite' reduced compression two-layer bandages for treatment of leg ulcers: Results of the pragmatic, single-centre randomized controlled PEACH trial

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Background: In a subset of patients with leg ulcer, reduced compression is indicated to aid wound healing whilst not compromising circulation. It is not clear if there are differences in efficacy between different two-layer compression bandages.
Methods: A single-centre, prospective, non-blinded, randomised, controlled trial was conducted in a Hospital's vascular department in England to determine 'wound healed' status at week 12 of treatment. Two 'Lite' compression bandaged were compared, each providing ~25 mmHg of pressure. Eligible patients could have leg ulcer of venous or mixed venous-arterial nature, with or without contributing comorbidities.
Results: In total, 78 patients were randomised. With Andoflex TLC Calamine Lite (also marketed under brand name Coflex, OVIK Health) 18 out of 34 (53%) wounds healed and for Coban2 Lite (3 M) this figure was 15 out of 33 (45%; p-value 0.63, Fisher exact test). A secondary outcome semi-quantitative measure of wound size, PUSH score, did not show a statistical difference between the two bandages either: median score of 0 (inter-quartile range 7) for Andoflex TLC Calamine Lite and 1.5 (inter-quartile range 8) for Coban2 Lite respectively (p-value 0.60, Mann-Whitney *U* test). Associated leg ulcer symptoms did not differ significantly either.
Conclusions: Andoflex TLC Calamine Lite and Coban2 Lite are non-inferior to each other to up to 20% difference in 'wound healed' status at twelve weeks of compression bandage treatment. Any preference in utilisation of one over the other can therefore be dictated by clinician and patient preference. Future research may focus on a comparison of two-layer compression in patients who can tolerate full compression, and/or of two-layer versus hosiery or four-layer devices.

Introduction

The treatment of leg ulcers poses a challenge for healthcare professionals; they affect patients' quality of life and are associated with further complications.[1,2] Often, patients enter a chronic cycle of ulcer healing and subsequent breakdown due to underlying venous insufficiency and additional chronic disease affecting the vasculature such as diabetes.[3] Though venous leg ulcers (VLUs) are the most common type of leg ulcers, there are many patients who have ulcers due to a mixed venous-arterial or other underlying condition.[4,5] Despite extensive research, the exact manner in which particularly venous leg ulcers develop is not yet fully understood; however, it is agreed that prolonged venous hypertension caused by chronic venous insufficiency (CVI) is a common aetiological factor.[6,7] The mainstay of treatment of venous leg ulcers, proven through clinical trials, is compression bandaging.[8] Yet, up to 15–30 % do not respond to this current first-line treatment and remain unhealed even after six months of treatment.[9,10] Depending on the degree of venous insufficiency, any arterial impairment and other clinical and patient-specific factors, the applied compression can be as high as 40–50 mmHg. Since many patients' leg ulcer pathologies are not suitable for the application of full compression, reduced compression bandaging (20–30 mmHg) may be applied.[11]

Though the application of bandaging and other products for ulceration goes back thousands of years, one of the earlier standard bandages for CVI was Unna's boot.[12] This involves a gauze dressing impregnated with Zinc oxide and calamine lotion. Unna's

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boot helps control pruritus in different conditions, including burns-related long-term itch.[13] The bandaging underwent subsequent development to include elasticity and improved compression, for a time using four layers around the leg. Modern compression bandaging products (including 3M's Coban2 and OVIK Health's Andoflex products) are two-layer short stretch compression bandaging systems.[14] OVIK Health has combined one of the elements of Unna's boot, namely the skin soothing ingredient Calamine, in the two-layer compression bandage design – the product being Andoflex TLC Calamine. A recent study showed that patients deem the Andoflex TLC Calamine compression bandaging more comfortable than Coban2 compression bandaging.[15] There is paucity in evidence regarding the efficacy of reduced compression concerning the key outcome of leg ulcer healing. The aim of this pragmatic randomised, controlled, prospective trial is to determine the efficacy of two types of two-layer compression bandaging with Andoflex TLC Calamine Lite and Coban 2 Lite respectively.

Methods

Study design and patients

Prospective, single centre, randomised controlled trial of two different 'Lite' compression bandages, with patients recruited between February 2023 and July 2024. The study title was Prospective Evaluation of Applied 'Lite' Compression for leg ulcer Healing, or PEACH, and setting was vascular surgery departments in two sister hospitals in England. A total of 78 patients were recruited into the trial, of which one patient wished to withdraw before randomisation. The study stopped when sufficient number of participants had been enrolled. The study visit schedule was week 0 (baseline), week 6 and week 12. Inclusion criteria were patients aged 18 years or older, with the mental capacity to provide informed consent and adhere to the trial intervention, and a clinical diagnosis of one or more leg ulcers(defined as any break in the skin on the lower leg that has been present for 2 weeks).[16] The underlying pathology of the leg ulcer could be either venous or mixed venous-arterial; recognised co-morbidities that may contribute to the development of leg ulcers (e.g. diabetes, rheumatoid arthritis, peripheral vascular disease) were not an exclusion criterion. The inclusion criterion in terms of ankle–brachial pressure index (ABPI) was a value of $\geq$ 0.5 – 0.8 taken within the previous three months. Where an ABPI measure was not feasible, use of locally-approved alternative diagnostic assessments to rule out significant peripheral artery disease and/or ischaemia (i.e. by pulse palpation and ultrasound diagnostics, toe pressure assessment or arterial imaging) was acceptable. Utilisation of reduced compression in patients with an ABPI value of $\geq$0.8 was only permitted subject to a recorded clinical assessment by qualified clinical staff, indicating rationale for reduced compression. Reasons could include the detection of abnormal Doppler waveform as well as other indications.[17,18] Patients were allowed to be receiving compression therapy prior to study enrolment. Exclusion criteria were treatment with oral antibiotics for the index ulcer within the last week, a foot ulcer located below the malleolar region, a wound size too small ($<$ 1 cm^2) or too large (larger than 50 cm^2).

Ethical considerations

Research study approval was received from English ethics (ref 22/SW/0158), health research authority (reference 280,418), and NHS study sponsor prior to study commencement. The trial registry number is ISRCTN37496076 (https://www.isrctn.com/ISRCTN37496076). Patients had more than 24 hours to consider the study, and written informed consent was obtained from all participants. All patients enrolled in the study were managed by specialist vascular nurses.

Compression systems

Two different two-layer compression bandages were appraised: Andoflex TLC Calamine Lite (OVIK Health) and Coban 2 Lite (3 M). The latter is a first-line product listed in the current formulary for the recruiting hospital site, and therefore Coban2 Lite was considered the usual care arm. Andoflex TLC Calamine Lite provides 20-30 mmHg compression (it is also marketed in some countries as Coflex TLC Calamine Lite). The skin-contact layer 1 is a soft foam roll impregnated with calamine, whereas the outer layer 2 is a non-latex short stretch compression bandage that sticks to itself and features 'Easy Hand Tear Technology', eliminating the need for scissors. 3M's Coban 2 Lite is also a two-layer compression system and just like the Andoflex product is designed to provide up to seven days of sustained therapeutic compression. A 'Lite' compression of 25-30 mmHg compression is achieved with Coban 2 Lite. The compression bandages were applied and intended to be worn continuously by the patient (ie re-application after, for example, a dressing change or wash). All bandages were stored away from direct sunlight at the temperature recommended by the respective manufacturers.

Treatment arms and outcomes dataset

Following written consent patients were allocated at random 1:1 to the one of two treatment arms, using a non-restricted randomised sequence generated for the whole sample using a freeware randomisation programme (https://www.sealedenvelope.com/). This was done by the person consenting the patient. The randomisation was stratified by ulcer size. For this stratification the PUSH (Pressure Ulcer Scale for Healing) score was applied.[19] The PUSH score tool – validated for leg ulcers as well as pressure ulcers - is a semi-quantitative measure of ulcer size. Eleven increasing ulcer size categories (starting with 0 cm^2 and up to $>$24cm^2) can give a sub-score of 0 to 10. It then also takes into account other characteristics, namely exudate levels (none, light, moderate, heavy, scored from 0 to 3 respectively) and tissue type (closed, epithelial tissue, granulation tissue, slough, necrotic tissue, scored from 0 to 4 respectively) to give a final score. The stratification cut-off values were a PUSH score of up to and including 10, or a PUSH score of 11 or higher. Upfront, a total of 60 randomisations were generated for each stratification, in blocks of 10 randomisations within said stratification.

Study data set

At each clinic visit, the leg ulcer size was determined using the PUSH score. If a patient had multiple ulcers, the largest was used as the index ulcer. At week 6 and week 12 follow-up visits the vascular specialist nurse determined the primary outcome measure, i.e. if the ulcer had healed, meaning complete epithelial cover in the absence of a scab (eschar) with no dressing required. Apart from a difference in type of compression bandage, each patient was managed as per standard clinical practice and this could involve debridement and application of a primary wound dressing. Patient overall quality of life was assessed using the validated EQ-5D-5 L survey and leg ulcer (and vascular lower limb disease) associated symptoms were captured using the VEINES Sym(ptoms) questionnaire.[20,21] For the former a compound score was calculated and for the latter the ten different symptoms were scored independently to allow insight in what specific symptoms could

Table 1
Patient and wound characteristics at baseline (week 0).

Variable	Outcome measure	Andoflex ($n = 40$)	Coban2 ($n = 37$)	p-value
Sex	male / female, n [%]	20 / 16 [60 % / 40 %]	18 / 19 [49 % / 51 %]	0.32#
Patient age	Years, mean (95 % CI)	77 (74 to 81)	79 (77 to 82)	0.40∼
BMI	kg/m^2, mean (95 % CI)*	31 (28 to 33)	27 (25 to 30)	0.08∼
Smoking status	never / ex-smoker / current, n [%]	18 / 17 / 5 [45 % / 43 % / 13 %]	25 / 11 / 1 [68 % / 30 % / 3 %]	0.08#
Patient mobility	unaided / some assistance / immobile, n [%]	20 / 17 / 3 [50 % / 43 % / 8 %]	10 / 24 / 3 [27 % / 65 % / 8 %]	0.11#
Wound chronicity	< 3months / 3–6 months / > 6 months, n [%]	22 / 8 / 10 [55 % / 20 % / 25 %]	19 / 9 / 9 [51 % / 24 % / 24 %]	0.90#
Prior use of compression bandaging	no / yes, n [%]	21 / 19 [53 % / 47 %]	21 / 16 [57 % / 43 %]	0.71#

95 % CI = 95 % confidence interval; * Andoflex $n = 37$, Coban2 $n = 36$, # Chi^2 test; ∼ unpaired t-test.

be associated with leg ulcers and treatment. For VEINES Sym, a lower score indicates worse symptoms. Patient characteristics such as age, sex, body mass index, smoking status and patient mobility status (unable to walk, walks with assistance [stick/frame], walks without assistance) were also recorded, and wound chronicity (<3 months, 3–6 months, or ≥6 months) was recorded.

Statistical analyses

Study data was processed using Microsoft Excel and analysed with IBM's SPSS statistics software (v24); for inferential statistical tests a p-value < 0.05 was considered significant. Even if a patient missed a research clinic appointment, the 'wound healed' status and wound size PUSH score were obtained from the medical records where possible, provided the result was obtained within the specific time-point visit window. For healed wounds, the corresponding PUSH score was considered to be a score of '0'. If there were pressures on clinic times, secondary outcome measures such as EQ5D5L and/or VEINES Sym did not have to be recorded (though every effort should have been made to record them). For analysis, all available outcomes were included in the analyses per time-point. Due to the missing data points, a direct comparison between week 0, week 6 and week 12 outcomes was not conducted; only outcomes between the two treatment arms were compared. Inferential tests were a comparison of two independent groups; Fisher exact test was applied instead of t-test if one outcome contained <10 patient data points. An a priori power analysis was conducted on the basis of a 'wound healed' rate of 40 % versus 50 % in each treatment arm respectively. A minimum total of 68 patients, minimum of 34 in each treatment arm, were needed to be certain that the treatment arms do not differ more than 20 % in terms of 'wound healed' rate after twelve weeks of treatment (assuming a two-sided significance level [alpha] of 0.05 and a power [1-beta] of 80 %).[22]

Results

Fig. 1 outlines the patient flow through the trial and gives numbers for patients that 'wound healed' status could be determined for, and how many patients were lost to follow-up and withdrawn. One single adverse event (AE) was observed during the trial. This concerned mild skin blistering on the leg of a patient where Andoflex TLC Calamine Lite had been applied; the chief investigator deemed the AE likely related to the intervention and a minor medical event. Two patients in the Coban2 Lite arm died whilst participating in the trial, but due to unrelated causes (not lower limb related); these are recorded as withdrawn in Fig. 1. On average, the patients in both treatment arms were comparable as summarised in Table 1. No significant difference was observed for any of the baseline patient or wound characteristics.

Table 2 summarises the results for the primary outcome, 'wound healed'. At both week 6 and week 12 of trial treatment, no statistical difference was observed between the percentage of wounds healed in the Andoflex TLC Calamine Lite and Coban2 Lite treatment arms. Healing across the whole cohort was progressive and improved over time with a ∼50 % healing rate achieved overall. Wound size was measured with the PUSH score. Fig. 2 shows that, as with 'wound healed' rates, wounds got smaller over time. At week 0, the median PUSH score was 10 (inter-quartile range [IQR] 3.8; $n = 40$) for Andoflex TLC Calamine Lite and 10 (IQR 4; $n = 37$) for Coban2 Lite respectively (p-value 0.76, Mann-Whitney *U test*). This reduced to 6 (IQR 10.5; $n = 29$) and 7 (IQR 11; $n = 27$) by week 6 (p-value 0.88), and then to a median of 0 (IQR 7; $n = 32$) for Andoflex TLC Calamine Lite and 1.5 (IQR 8; $n = 30$) for Coban2 Lite at end of the trial period at week12 (p-value 0.60).

The VEINES Sym questions highlight that leg ulcer patients experience certain symptoms more than others (see Table 3). At baseline, participants reported issues particularly with aching legs, leg swelling, throbbing sensation, and leg pain and these symptoms were comparable between treatment arms. However, these symptoms improved as they proceeded through the trial period and no significant difference was observed between Andoflex TLC Calamine Lite and Coban2 Lite treatment arms. No significant deterioration in leg ulcer related symptoms was observed between baseline and follow-up visits.

Overall quality of life, measured with the EQ5D5L questionnaire which covers the domains 1) mobility, 2) self-care, 3) usual activities, 4) pain/discomfort, and 5) anxiety/depression, was also very similar between the two treatment groups at baseline. The median score was 0.70 (IQR 0.24; $n = 40$) for Andoflex TLC Calamine Lite and 0.71 (IQR 0.20; $n = 36$) for Coban2 Lite, p-value 0.84 with Mann-Whitney *U test*. Approximately half of the participants completed EQ5D5L at the 12-week follow-up appointments There was however no indication that the median index score differed between treatment arms. At week 0, for Andoflex TLC Calamine Lite the score was 0.65 (IQR 0.24; $n = 40$) and for Coban2 Lite the median score was 0.67 (IQR 0.20; $n = 37$), p-value 0.84 (Mann-Whitney *U test* comparing the two treatment arms). At week 12, for Andoflex TLC Calamine Lite the score was 0.72 (IQR 0.37; $n = 20$) and for Coban2 Lite the median score was 0.74 (IQR 0.32; $n = 17$) with a p-value of 0.99.

Discussion

Complete healing of leg ulcers can be challenging but is essential to minimise healthcare costs and reduce the risk of fur-

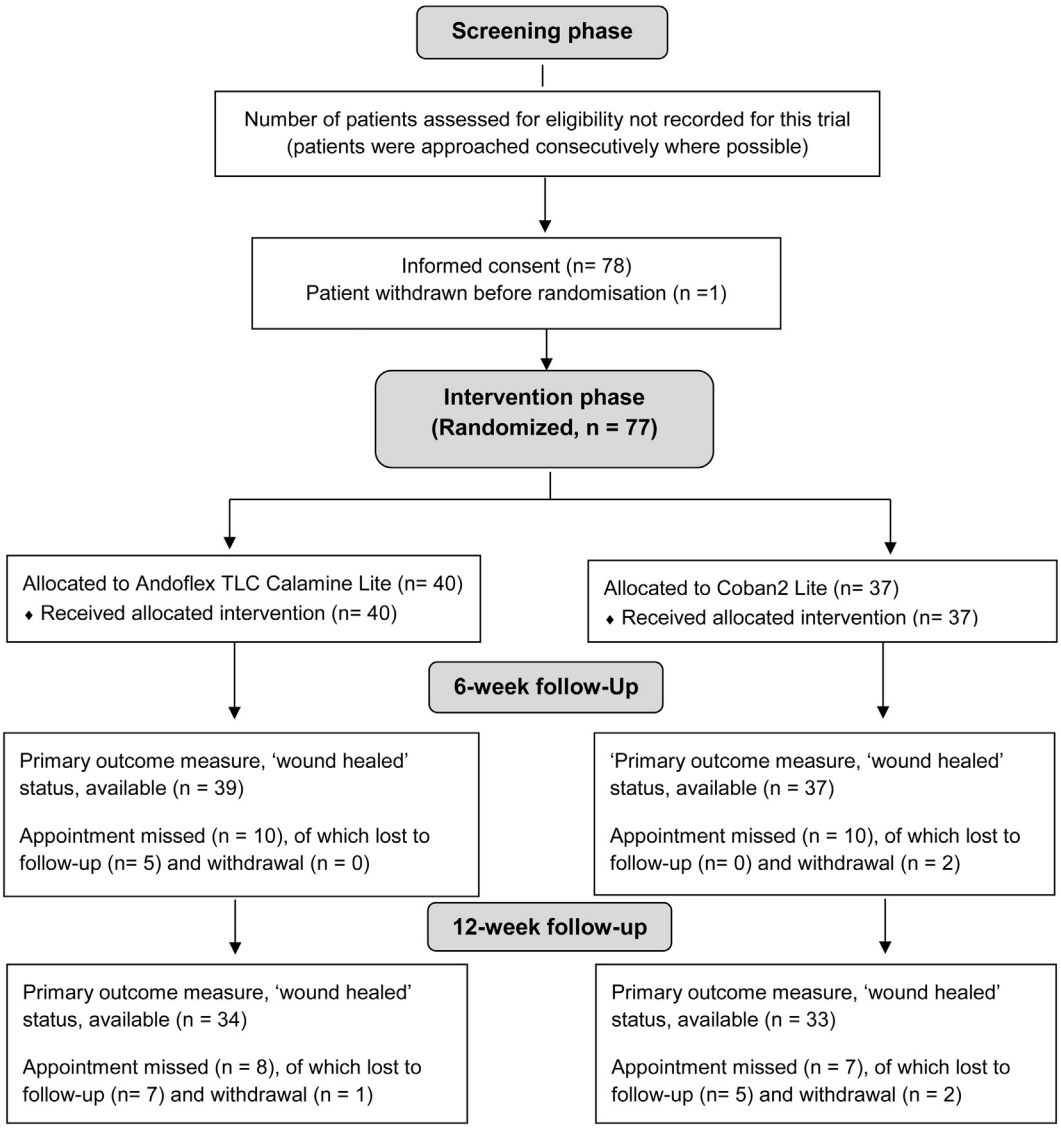

Fig. 1. Recruitment flowchart for PEACH trial.

Table 2
Comparison of 'wound healed' status at different time points.

Time point	Wound status	Andoflex	Coban2	p-value~
Week 6	healed / not healed, n [%]	10 / 29 [26 % / 74 %]	8 / 29 [22 % / 78 %]	0.79
Week 12	healed / not healed, n [%]	18 / 16 [53 % / 47 %]	15 / 18 [45 % / 55 %]	0.63

~ Fisher exact test.

ther complications. There is a considerable body of published work available showing the effectiveness of compression to accelerate wound healing of leg ulcers.[10,23] Coban2 is an established short-stretch adhesive two-layer compression bandage product and is listed on formularies of National Health Service organisations across the United Kingdom.[24] Two-layer products have gained popularity at the expense of four-layer compression bandage products, despite limited evidence of their (relative) clinical effectiveness.[25] Therefore, for any newly developed two-layer product, a direct comparison with Coban2 is indicated.

This PEACH trial is a follow-up study to the APRICOT study (A Patient and clinician Reported Impression of COmpression Therapy study).[15] There, a cross-over design was applied to determine if there was any variation in pruritus and pain symptoms between Andoflex TLC Calamine and Coban2 products (both normal and reduced compression versions of the products). Based on results from the APRICOT and PEACH studies, there is substantial evidence that symptomology related to the leg ulcer and wearing of compression bandage is equivalent between Andoflex TLC Calamine Lite and Coban2 Lite. For the benefit of correct application of compression bandaging, the Andoflex line of products have visual indicators on the outer layer, where the shape should change from oval to circular, which may be useful for (inexperienced) clinical staff. Although no significant differences in clinical effectiveness

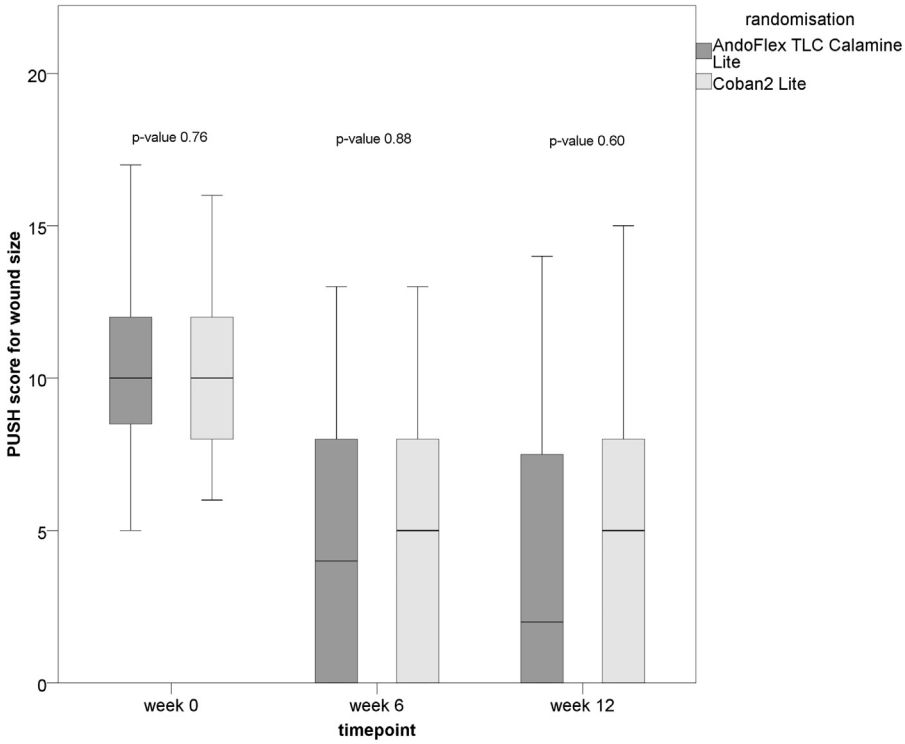

Fig. 2. Wound size comparison as measured with PUSH score tool.

Table 3
Patients' VEINES Symptoms outcomes at different time points.

VEINES Question (experienced in last four weeks)	Week 0, median (IQR)			Week 6, median (IQR)			Week 12, median (IQR)		
	Andoflex (n = 40)	Coban2 (n = 37)	p-value#	Andoflex (n = 22)	Coban2 (n = 26)	p-value#	Andoflex (n = 21)	Coban2 (n = 16)	p-value#
1a - heavy legs~	5 (3.0)	5 (2.5)	0.66	5 (0.5)	5 (1.5)	0.60	5 (3)	5 (0.8)	0.56
1b - aching legs~	4.5 (3)	4 (3)	0.63	5 (2)	5 (1)	0.75	5 (3)	5 (2.3)	0.32
1c - swelling~	2 (3.8)	2 (3)	0.86	3.5 (4)	5 (3.3)	0.28	5 (4)	5 (4)	0.91
1d - night cramps~	5 (1)	5 (0)	0.26	5 (0.3)	5 (0)	0.56	5 (0)	5 (0)	0.66
1e - heat/burning~	5 (1.8)	5 (1)	0.66	5 (0)	5 (0)	0.79	5 (1)	5 (0)	0.24
1f - restless legs	5 (3)	5 (0.5)	0.15	5 (0.3)	5 (2.3)	0.35	5 (3)	5 (2.3)	0.38
1 g - throbbing	3 (4)	4 (3)	0.35	5 (1)	5 (0)	0.33	5 (1.5)	5 (0)	0.49
1 h - itching	5 (3)	5 (2.5)	0.54	5 (3)	4.5 (3)	0.31	5 (0)	5 (2.8)	0.16
1i - tingling	5 (0)	5 (0)	1.00	5 (0)	5 (0)	0.32	5 (0)	5 (0)	0.95
7 - leg pain@	3.5 (3)	4 (2.5)	0.11	5 (3)	6 (3)	0.74	6 (2.5)	5.5 (2.8)	0.84

IQR = inter-quartile range; #Mann-Whitney *U test*; @Answer options are every day (1), several times a week (2), about once a week (3), less than once a week (4), never (5); Answer options are very severe (1), severe (2), moderate (3), mild (4), very mild (5), none (6).

– i.e. ulcer healing rates - could be detected, patients did prefer the Andoflex TLC Calamine product over the Coban2 product. In turn, earlier research found that two-layer compression bandaging (Coban2) was preferred over four-layer compression bandaging.[26] It appears that the inclusion of Calamine in the inner skin-contact layer of Andoflex TLC Calamine may not have additional benefits over a standard inner layer used for e.g. Coban2.

A shortcoming of this trial is the lack of wound size quantification through wound tracing or digital measurement. The intention was to conduct this, but due to a changeover from wound tracing to digital measurement during the course of the trial both non-compliance and non-consistent measurement technique were an issue and results could not be analysed. Nonetheless, this did not affect the primary outcome measure of 'wound healed' status, and the semi-quantitative PUSH score was recorded to determine wound size. The trial was pragmatic in that leg ulcers of differing underlying aetiologies could be included; this does reflect clinical practice in that a large proportion of patients are complex and do not simply present with pure venous leg ulcers. It is recognised that a larger ulcer is an independent risk factor for delayed healing.[27] By applying this stratification at randomisation and applying ulcer size limits (>1 to <50 cm^2), the risk of confounding was controlled for. Ideally, both clinical staff and patients would be blinded to the intervention but due to the different designs of the two compression systems this was not possible.

It is challenging to make a comparison of results achieved in this study with those obtained by other studies. One study looked at leg ulcer healing achieved with Coban2 Lite over a 16-week period; complete healing was observed in 20 % of patients rather than the 50 % observed in this PEACH trial.[28] Studies differ in terms of the compression bandage applied (full or reduced compression, or either compression options) and other methodological approaches such as time of outcome endpoint. For example, a retrospective study compared Coban2 with another two-layer compression system (K-Two) and a four-layer compression system (Profore) and concluded that healing rates and cost effectiveness were

superior for Coban2.[29] One therefore cannot conclude that Andoflex TLC Calamine Lite or indeed Coban2 Lite are therefore – by extrapolation – are also superior to K-Two and Profore bandages. The VenUS6 trial that is currently ongoing addresses this to some extend by comparing a) Compression wraps, b) 'evidence-based compression' treatment (choice of four-layer bandage or two-layer compression hosiery), and c) two-layer bandage. Only full compression therapy is assessed. Despite being a very large trial, even VENUS6 is taking a pragmatic approach and the two-layer compression bandage treatment arm does not use one single brand; instead, brands that delivers 40 mmHg pressure can be applied, and in the protocol they have listed Coban2, K-Two and Proguide.[25]

Conclusions

In a patient population where reduced (or 'Lite') compression is indicated for treatment of leg ulcers, a 50 % healing rate can be achieved after twelve weeks of therapy. No discernible difference in healing rate can be observed between Andoflex TLC Calamine Lite and Coban2 Lite compression bandage products. Furthermore, the safety profile and degree of improvements in leg ulcer related symptoms such as leg swelling and leg throbbing does not differ markedly either. In cases of leg ulcers where two-layer (reduced) compression bandaging is indicated, both Andoflex TLC Calamine Lite and Coban2 Lite are suitable compression systems. Since the clinical efficacy of these products is similar, the choice of use can be determined by clinician (e.g. ease of use) and/or patient preference (e.g. comfort level).

Conflict of interest

Jane Todhunter and Helen Greenhow have no conflict of interest to declare. Leon Jonker has previously received grant funding and a presentation honorarium from Milliken Healthcare (now trading as OVIK Health)

CRediT authorship contribution statement

Jane Todhunter: Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization. **Helen Greenhow:** Project administration, Methodology, Investigation. **Leon Jonker:** Writing – original draft, Formal analysis, Data curation, Conceptualization.

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References

1. Graves N, Phillips CJ, Harding K. A narrative review of the epidemiology and economics of chronic wounds. *British J Dermatol*. 2022;187(2):141–148.
2. Guest JF, Fuller GW, Vowden P. Cohort study evaluating the burden of wounds to the UK's National Health Service in 2017/2018: update from 2012/2013. *BMJ Open*. 2020;10(12):e045253.
3. Raffetto JD, Ligi D, Maniscalco R, Khalil RA, Mannello F. Why venous leg ulcers have difficulty healing: overview on pathophysiology, clinical consequences, and treatment. *J Clin Med*. 2020 Dec 24;10(1):29.
4. SIGN. *Management of Chronic Venous Leg Ulcers*. Edinburgh: SIGN; 2010.
5. Graham ID, Harrison MB, Nelson EA, Lorimer K, Fisher A. Prevalence of lower limb ulceration: a systematic review of prevalence studies. *Advanc Skin Wound Care*. 2003;16(6):305–316.
6. Eberhardt RT, Rafetto JD. Chronic venous insufficiency. *Circulation*. 2005;111(18):2398–2409.
7. White JV, Ryjewski C. Chronic venous insufficiency. *Perspect Vasc Surg Endovasc Ther*. 2005;17(4):319–327.
8. Ashby RL, et al. Clinical and cost-effectiveness of compression hosiery versus compression bandages in treatment of venous leg ulcers (Venous leg Ulcer Study IV, VenUS IV): a randomised controlled trial. *Lancet*. 2014 Mar 8;383(9920):871–879.
9. Moffatt CJ, Franks PJ, Doherty DC, Smithdale R, Martin R. Sociodemographic factors in chronic leg ulceration. *British J Dermatol*. 2006;155(2):307–312.
10. O'Meara S, Cullum N, Nelson EA, Dumville JC. Compression for venous leg ulcers. *Cochrane Datab Syst Rev*. 2012(11). doi:10.1002/14651858.CD000265.pub3.
11. Lim SL, Chung RE, Holloway S, Harding KG. Modified compression therapy in mixed arterial–venous leg ulcers: an integrative review. *Int Wound J*. 2021 Dec;18(6):822–842.
12. Rubin JR, Alexander J, Plecha EJ, Marman C. Unna's boot vs polyurethane foam dressings for the treatment of venous ulceration: a randomized prospective study. *Archiv Surgery*. 1990 Apr 1;125(4):489–490.
13. Shohrati M, Davoudi M, Almasi M, Sadr B, Peyman M. Comparative study of Unna's boot and betamethasone cream in the treatment of sulfur mustard–Related pruritus. *Cutan Ocul Toxicol*. 2007 Jan 1;26(4):303–309.
14. Hanna R, Bohbot S, Connolly N. A comparison of inferface pressures of three compression bandage systems. *British J Nurs*. 2008 Nov 13;17(Sup9):S16–S24.
15. Jonker L, Todhunter J, Robinson L, Fisher S. Open-label, randomised, multicentre crossover trial assessing two-layer compression bandaging for chronic venous insufficiency: results of the APRICOT trial. *Br J Commun Nurs*. 2020 Jun 2;25(Sup6):S6–13.
16. National Institute for Health and Care Excellence, Clinical Knowledge Summary, Leg Ulcer – Venous. https://cks.nice.org.uk/topics/leg-ulcer-venous/. Last revised in August 2024 [last accessed 17 October 2024]
17. Kim ES, Sharma AM, Scissons R, Dawson D, Eberhardt RT, Gerhard-Herman M, Hughes JP, Knight S, Marie Kupinski A, Mahe G, Neumyer M. Interpretation of peripheral arterial and venous doppler waveforms: a consensus statement from the Society for Vascular Medicine and Society for Vascular Ultrasound. *Vascul Med*. 2020 Oct;25(5):484–506.
18. Lim SL, Chung RE, Holloway S, Harding KG. Modified compression therapy in mixed arterial–venous leg ulcers: an integrative review. *Int Wound J*. 2021 Dec;18(6):822–842.
19. Ratliff CR, Rodeheaver GT. Use of the PUSH tool to measure venous ulcer healing. *Ostomy Wound Manag*. 2005;51(5):58.
20. Lamping DL, Schroter S, Kurz X, Kahn SR, Abenhaim L. Evaluation of outcomes in chronic venous disorders of the leg: development of a scientifically rigorous, patient-reported measure of symptoms and quality of life. *J Vasc Surg*. 2003 Feb 1;37(2):410–419.
21. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, Bonsel G, Badia X. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality Life Res*. 2011 Dec;20:1727–1736.
22. Dunn DT, Copas AJ, Brocklehurst P. Superiority and non-inferiority: two sides of the same coin? *Trials*. 2018 Dec;19(1):1–5.
23. Patton D, Avsar P, Sayeh A, Budri A, O'Connor T, Walsh S, Nugent L, Harkin D, O'Brien N, Cayce J, Corcoran M. A meta-review of the impact of compression therapy on venous leg ulcer healing. *Int Wound J*. 2023 Feb;20(2):430–447.
24. National Institute for Health and Care Excellence, Medtech Innovation Briefing [MIB140], Coban 2 for Venous Leg Ulcers, https://www.nice.org.uk/advice/mib140/chapter/summary, published 16 February 2018 [last accessed 17 October 2024]
25. Kletter M, Griffiths J, Arundel C, Dumville J. VenUS 6 collaborators. Compression therapies for the treatment of venous leg ulcers: study protocol for a process evaluation in a randomised controlled trial, VenUS 6. *Trials*. 2023 Nov 14;24(1):727.
26. Moffatt CJ, Edwards L, Collier M, Treadwell T, Miller M, Shafer L, Sibbald G, Brassard A, McIntosh A, Reyzelman A, Price P. A randomised controlled 8-week crossover clinical evaluation of the 3M™ Coban™ 2 layer Compression System versus Profore™ to evaluate the product performance in patients with venous leg ulcers. *Int Wound J*. 2008 May;5(2):267–279.
27. Parker CN, Finlayson KJ, Shuter P, Edwards HE. Risk factors for delayed healing in venous leg ulcers: a review of the literature. *Int J Clin Pract*. 2015 Sep;69(9):967–977.
28. Ivins N, Jones N. Two-layer reduced compression system for lower limb wounds: a non-comparative evaluation. *Br J Commun Nurs*. 2020 Apr 1;25(Sup4):S10–S16.
29. Guest JF, Fuller GW, Vowden P. Clinical outcomes and cost-effectiveness of three different compression systems in newly-diagnosed venous leg ulcers in the UK. *J Wound Care*. 2017 May 2;26(5):244–254.