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Clinical outcomes and cost-effectiveness of three different compression systems in newly-diagnosed venous leg ulcers in the UK

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Objective: To assess clinical outcomes and cost-effectiveness of using a two-layer cohesive compression bandage (TLCCB; Coban 2) compared with a two-layer compression system (TLCS; KTwo) and a four-layer compression system (FLCS; Profore) in treating newly-diagnosed venous leg ulcers (VLUs) in clinical practice in the UK, from the perspective of the NHS.
Method: This was a retrospective cohort analysis of the case records of patients with newly-diagnosed VLUs randomly extracted from The Health Improvement Network (THIN) database (a nationally representative database of clinical practice among patients registered with general practitioners in the UK) who were treated with either TLCCB (n=200), TLCS (n=200) or FLCS (n=200). The clinical outcomes and cost-effectiveness of the alternative compression systems were estimated over six months after starting treatment.
Results: Patients' mean age was 72 years and 58% were female. Time from wound onset to the start of compression was a mean of two months, and when starting compression the wound size was a mean of 45 cm^2. The distribution of healing was significantly different between the three groups; 76% of wounds in the TLCCB group healed by six months compared with 70% and 64% in the TLCS and FLCS groups, respectively (p=0.006). Time to healing was significantly less in the TLCCB group compared with the two other groups (p=0.003). Patients in the TLCCB group experienced better health-related quality of life over six months (0.413 quality-adjusted life years (QALYs) per patient), compared with the TLCS and FLCS groups (0.404 and 0.396 QALYs per patient, respectively). The mean six-month NHS management cost was £3045, £3842 and £4480 per patient in the TLCCB, TLCS and FLCS groups, respectively.
Conclusion: Real-world evidence demonstrates that treating newly-diagnosed VLUs with TLCCB, compared with the other two compression systems, affords a more cost-effective use of NHS-funded resources in clinical practice since it resulted in an increased healing rate, better health-related quality of life and a reduction in NHS management cost.
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venous leg ulcers • compression • health-related quality of life • cost-effectiveness • economic evaluation

The application of external compression[1,2] to venous leg ulcers (VLUs) has been advocated to minimise or reverse the vascular changes that occur in the presence of lower limb venous disease, by forcing fluid from the interstitial spaces back into the vascular and lymphatic compartments.[2] Pressures of about 40mmHg at the ankle are widely quoted in the literature for the prevention or treatment of VLUs, but more recently it has been suggested that rigidity of the applied compression product is also important.[2–4] In clinical practice in the UK, patients with lower limb ulceration are generally treated by nurses in the community.[5,6] Therefore, clinical outcomes from the effective application of compression (in terms of ulcer healing) are heavily dependent on nurses' skills in the application of compression systems and patient concordance with wearing compression therapy. Moreover, optimum care is determined by consideration of a number of factors, including the severity of the wound and the height and limb size of the patient.

Many different compression systems are available, which vary greatly in their ability to provide effective compression over a prolonged period owing to differences in their rigidity and content of elastomeric yarns.[2] In addition to a nurse's skill in assessment, compression system selection and bandage application, other factors such as limb shape and circumference affect the pressure produced beneath a compression system.[2] The relative efficacy of different compression systems on ulcer healing has been the subject of a systematic review of 4321 randomised controlled trial

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participants.[2] One of the conclusions from the review was that multicomponent systems were more efficacious than single-component systems, and those with elastic bandages were more efficacious than inelastic systems. However, there were no clear differences in the efficacy of different types of high compression.[2]

The UK's NHS managed 2.2 million wounds and associated comorbidities in 2012/2013 at a cost of £5.3 billion.[7] Of these, 278,000 were VLUs[7] of which 52% were new in the study year and 47% healed.[8] The resources required to manage these VLUs and associated comorbidities cost the NHS £941.1 million in 2012/2013.[8] The increasing use of more cost-effective interventions has the potential to improve outcomes and lessen workload and associated health-care resource use, leading to reductions in the cost of wound care.

We previously estimated the cost-effectiveness of using a two-layer cohesive compression bandage (TLCCB; Coban 2) compared with a two-layer compression system (TLCS; KTwo) and a four-layer compression system (FLCS; Profore) to treat VLUs with a mean duration of 6.9, 6.1, and 6.7 months respectively, in the UK.[9] The analysis found that despite these compression systems reporting similar compression levels when tested in controlled studies,[10–15] initiating treatment with TLCCB compared with the other two compression systems afforded a more cost-effective use of NHS-funded resources in clinical practice, since it resulted in an increased healing rate, better health-related quality of life (HRQoL) and a reduction in NHS management cost. This study analysed a heterogeneous group of wounds, since 38% (TLCCB), 42% (TLCS) and 38% (FLCS) of patients in the cohort were receiving their first application of compression even though the mean duration of their VLU ranged across 6–7 months for the three groups. Accordingly, the aim of the present study was to assess the clinical outcomes and cost-effectiveness of using TLCCB compared with TLCS and FLCS in the treatment of patients with a newly-diagnosed VLU in clinical practice in the UK, from the perspective of the NHS.

Method

The Health Improvement Network database

The Health Improvement Network (THIN) database (IMS, London, UK) contains computerised information on more than 11 million anonymised patients entered by GPs from 562 practices across the UK. General practices across the UK using Vision Practice Management Software are invited to participate in the database and are self-selecting. The patient data within THIN have been shown to be representative of the UK population in terms of demographics and disease distribution.[16] Read codes are a coded thesaurus of clinical terms that are used by clinicians in the UK to record patient findings and procedures in health and social care information technology systems,[17] and have been used to code specific diagnoses in the THIN database. A drug dictionary based on data from the Multilex classification has been used to code drugs in the database. Successive updates of patients' records to the database include any subsequent changes made by GPs. The computerised information in the THIN database includes patients' demographics, details from GP consultations, specialist referrals, nurse and other clinician visits, hospital admissions, diagnostic and therapeutic procedures, laboratory tests and prescriptions issued by GPs. Hence, the information contained in the THIN database reflects actual clinical practice. Moreover, GPs are the gatekeepers to health care in the UK and patients' entire medical history is theoretically stored in their primary care record.

Study design

This was a retrospective cohort analysis of the case records of patients with newly-diagnosed VLUs randomly extracted from the THIN database.

Study population

The study population comprised a sample of patients who were randomly selected from the THIN database according to the following criteria:

- Were 18 years of age or over
- Had a Read code for a VLU
- Received TLCCB, TLCS or FLCS as the first compression system for their VLU
- Had at least six months' continuous medical history in their case record from the first mention of their VLU unless they healed or died.

The TLCCB-treated patients were matched with two randomly selected cohorts of TLCS-treated and FLCS-treated patients according to:

- Age (±5 years). Patients were ≥18 years of age
- Gender (however, this criterion was relaxed in order to fulfil the other criteria)
- Date of diagnosis of their VLU (±5 years).

Ethics approval

Ethics approval to use patients' records from the THIN database for this study was obtained from the Research Ethics Committee that appraises studies using the THIN database.

Study variables and statistical analyses

Information was systematically extracted from the patients' records over a period of six months from the start of compression and included age, gender, wound size (estimated to be 80% of the size of the primary contact dressing), wound-related health-care resource use, prescribed medication and clinical outcomes. It was assumed that if a patient received a bandage or dressing on a specific date, but a clinician visit was not documented in their record, the patient had been seen outside of the general practice by a community nurse. Patients' outcomes and resource use were quantified for each group. Differences between the groups were tested for statistical significance using a Kruskal-Wallis test or chi-square test.

Analysis of covariance (ANCOVA) enabling differences in patients' outcomes and resource use between treatments to be adjusted for any heterogeneity in age, gender, year of diagnosis, time from diagnosis to the start of compression, wound size at baseline and comorbidities found no adjustments were necessary.

Kaplan-Meier analyses were undertaken to determine whether the healing distribution of each group was significantly different from one another.

Logistic regression was used to investigate relationships between baseline variables and clinical outcomes. Multiple linear regression was also used to assess the impact of patients' baseline variables on resource use and clinical outcomes.

All statistical analyses were performed using IBM SPSS Statistics (version 22.0; IBM Corporation).

Health economic modelling

A patient-level case-control model was constructed in MS Excel and populated with health-care resource use, and clinical outcomes extracted from the THIN data set. Non-wound-related resource use was excluded from the model. The model spanned a period of six months from the start of compression.

Utility scores express patient preferences for specific health states on a scale ranging from 0, representing death, to 1, representing perfect health. These scores provide the weights to estimate health-related quality of life (HRQoL) in terms of the number of quality-adjusted life years (QALYs) gained by an intervention or service. HRQoL was not collected in the THIN database. Hence, published utility scores for different VLU health states (i.e. unhealed, improving and healed)[18] were assigned in a blinded manner (to eliminate potential bias) to each individual patient in the data set according to the health state of their wound at the end of each month in the study period. This enabled an estimation of patients' expected health status in terms of the number of QALYs at six months from the start of treatment with one of the three compression systems.

Model outputs

The primary measure of clinical outcome was patients' health status in terms of the number of QALYs at six months. Secondary measures were a range of outcomes that included healing rate, wound size reduction and time to healing. Unit resource costs at 2014/2015 prices[19–21] were assigned to the resource use estimates to enable an estimation of the health-care cost of managing patients in each group over six months from the start of compression.

Cost-effectiveness analyses

The relative cost-effectiveness of the three compression systems was calculated as the difference between the expected costs of two treatment groups divided by the difference in the number of QALYs between the same two groups and expressed as the incremental cost per

Table 1. Patient characteristics in the dataset at study start

	TLCCB	TLCS	FLCS
Cohort size	200	200	200
Mean (±SD) age per patient (years)	70.9±15.8	71.6±15.1	72.7±21.5
Percentage female	60%	57%	58%
Percentage with the following comorbidities:			
Endocrinological	28%	18%	22%
Cardiovascular	22%	16%	18%
Musculoskeletal	17%	13%	14%
Respiratory	14%	9%	14%
Other	10%	6%	10%
Dermatological	8%	5%	11%
Neurological	8%	5%	8%
Oncological	8%	6%	4%
Renal	6%	3%	10%
Psychiatric	6%	10%	8%
Gastroenterological	4%	4%	6%
Mean (±SD) wound size per patient at diagnosis (cm^2)	50.2±24.8	52.4±25.2	48.7±25.4
Mean (±SD) time from wound onset to starting compression per patient (months)	2.1±1.8	2.0±1.4	2.1±1.7
Mean (±SD) wound size per patient at the start of compression (cm^2)	41.7±22.9	43.9±21.7	48.6±22.8
Percentage reduction in wound size from onset to the start of compression	10%	10%	0%

SD–standard deviation; TLCCB: two-layer cohesive compression bandage; TLCS: two-layer compression system; FLCS: four-layer compression system

Table 2. Patient outcomes at the end of the six month study

	TLCCB	TLCS	FLCS
Percentage of patients in each group whose VLU healed*	76%	70%	64%
Mean (±SD) time from starting compression to healing per patient (months)**	1.6±1.8	2.0±1.7	2.1±1.9
Mean (±SD) wound size per patient at six months after the start of compression (cm^2)	14.6±28.4	14.1±26.1	18.7±29.5
Percentage who switched from the study compression system	8%	3%	23%
Mean (±SD) time on the study compression system before switching per patient (months)	3.2±1.4	2.0±0.9	3.1±1.8
Percentage reduction in wound size from the start of compression	65%	68%	62%
Mean number of QALYs per patient ***	0.413±0.059	0.404±0.057	0.396±0.056

TLCCB: two-layer cohesive compression bandage; TLCS: two-layer compression system; FLCS: four-layer compression system; SD–standard deviation; QALYs– quality-adjusted life years; *TLCCB versus TLCS versus FLCS, $p<0.05$; ** TLCCB versus TLCS and FLCS, $p<0.003$; *** TLCCB versus TLCS and FLCS, $p=0.006$

Table 3. Health-care resource use

	Mean amount of health-care resource use per patient in each group over the six-month study period		
	TLCCB	**TLCS**	**FLCS**
Health-care resource use			
Community nurse visits*	34.0±36.6	37.2±33.5	53.2±39.5
Practice nurse visits**	4.4±10.2	7.6±10.6	3.6±8.5
GP consultations	0.2±0.5	0.3±0.5	0.2±0.7
Hospital outpatient visits	<0.1	<0.1	<0.1
Diagnostic tests	<0.1	<0.1	<0.1
Dressings and bandages			
Dressings***	44.0±54.3	41.9±50.0	69.3±62.6
Compression bandages***	24.4±28.2	24.1±24.5	37.9±33.9
Other bandages	8.5±15.6	3.7±12.8	18.8±38.4
Prescribed drugs			
Prescriptions for analgesics	2.4±5.0	2.8±5.8	4.0±7.1
Prescriptions for anti-infectives	1.1±1.8	1.3±2.0	1.8±2.6

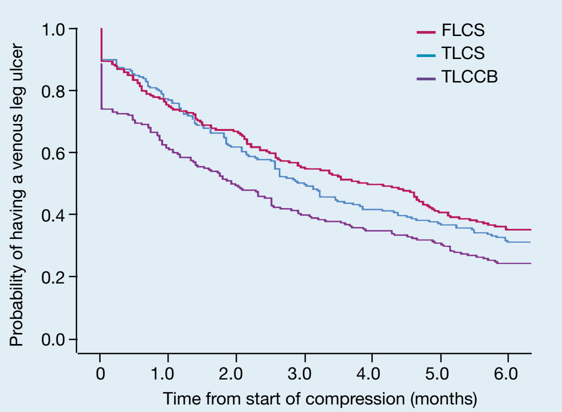
TLCCB–two-layer cohesive compression bandage; TLCS–two-layer compression system; FLCS–four-layer compression system; * TLCCB and TLCS versus FLCS, p<0.001; ** TLCCB and FLCS versus TLCS, p=0.003; *** TLCCB and TLCS versus FLCS, p<0.001

QALY gained. If one of the compression systems generated more QALYs for less cost it was considered to be the dominant (cost-effective) intervention.

Sensitivity analyses

To assess uncertainty, bootstrapping was undertaken to estimate the distribution of expected costs, QALYs and incremental cost-effectiveness ratios. This involved generating 10,000 subsets of the data from each group on the basis of random sampling and replacing the data once sampled. Use of these subsets enabled the construction of cost-effectiveness acceptability curves showing the probability of the alternative compression systems being cost-effective at different cost per QALY thresholds. Additionally, deterministic sensitivity analyses were performed on all of the model's inputs to identify how the relative cost-effectiveness of the alternative treatments would change by varying the different parameters in the model.

Fig 1. Kaplan-Meier time to healing analysis. The healing distribution between the three groups was significantly different (Log Rank (Mantel-Cox): p=0.006)



Results

Patient characteristics

The study population comprised 200 patients in each group in accordance with the inclusion/exclusion criteria and matching criteria. There were no significant differences in patients' age, gender, comorbidities, initial wound size and time from wound onset to starting compression between the three groups (Table 1). The mean time from wound onset to starting compression was 2 months (median of 1.9 months), which is consistent with current guidelines.

Patient management and outcomes

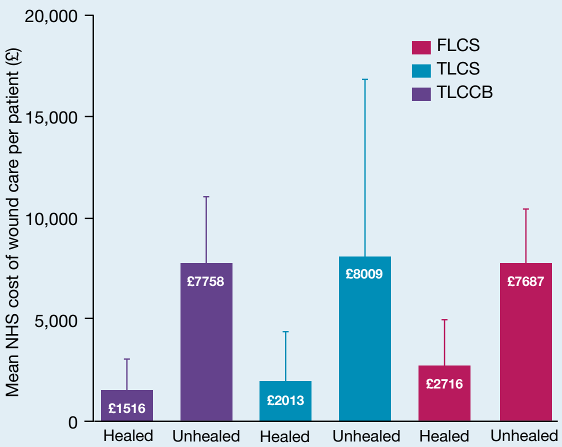
Overall, 76% of wounds in the TLCCB group healed by 6 months compared to 70% and 64% in the TLCS and FLCS groups, respectively (Table 2). A Kaplan-Meier analysis (Fig 1) showed the healing distributions were significantly different between the three groups (Log Rank (Mantel-Cox): p=0.006). Also, the mean time to healing was significantly shorter in the TLCCB group than the other two groups (Table 2). These findings are reflected in the QALY analysis, which estimated that patients in the TLCCB group experienced significantly better HRQoL than those in the other two groups (Table 2).

Logistic regression showed length of time to the start of compression (odds ratio 0.991; p<0.001) and wound size at the start of treatment (odds ratio 0.982; p<0.001) were independent risk factors for non-healing. Additionally, a patient's wound size at the start of treatment was an independent risk factor for switching compression system (odds ratio 1.016; p<0.001). Linear regression showed that the time to healing was reduced by 0.25 months for each additional cm^2 of wound area at the start of treatment (p<0.001).

Health-care resource use

There were some significant differences in health-care resource use between the three groups (Table 3). Patients were predominantly managed by community nurses and to a lesser extent by practice nurses, but patients rarely saw the same nurse on consecutive visits. There were negligible tissue viability nurse visits. One patient in the TLCCB and FLCS group each had one such visit, whereas none of the patients in the TLCS group had a visit. Some 11% of patients in the TLCCB and TLCS groups and 15% of patients in the FLCS group were seen by a GP because of their VLU and fewer than 5%

Fig 2. Mean NHS cost of wound care over the 6 months from the start of compression



in each group were referred to a hospital physician in an outpatient clinic. Some 11%, 18% and 9% of patients in the TLCCB, TLCS and FLCS groups, respectively, had a Doppler ankle brachial pressure index (ABPI) recorded in their records and fewer than 1% of patients in each group had undergone debridement. The amount of dressings that patients received in six months is shown in Table 4. Patients' dressings were changed, on average, every two days in the first month, decreasing to every three to five days by the sixth month of the study period for those wounds that remained unhealed. However, patients invariably received a different dressing at successive nurse visits. Patients in the FLCS group received more prescriptions for analgesics and anti-infectives than those in the other two groups. Despite this, there were no significant differences in the number of prescriptions between the three groups and no inference can be drawn on whether patients in the FLCS group were in more pain or more susceptible to infections than those in the other two groups.

Healthcare cost of patient management

The NHS cost of managing patients in each group over the six-month study period is summarised in Table 5. The six-month NHS cost of managing a VLU with TLCCB was £3,045 per patient, which was 21% and 32% lower than the cost of managing patients in the TLCS group (£3,842 per patient) and FLCS group (£4,480 per patient) respectively. Furthermore, an unhealed ulcer cost up to five times more to manage than a healed ulcer (Fig 2).

Community nurse visits were the primary cost drivers in all groups, accounting for 65–80% of the six-month NHS cost. Practice nurse appointments accounted for up to a further 6% of the costs, while GP consultations and hospital outpatient visits collectively accounted for less than 1% of costs. Dressings and compression bandages accounted for up to a further 5% and 15%, respectively, of the costs (Table 5).

Table 4. Dressing use

	Mean number of dressings per patient in each group over the six-month study period		
	TLCCB	**TLCS**	**FLCS**
Absorbent	9.6	9.4	15.8
Low-adherence	9.0	7.0	9.6
Soft polymer	8.2	9.8	11.5
Antimicrobial	5.5	5.8	12.1
Hydrocolloid	5.3	3.6	9.9
Foam	3.9	2.6	5.3
Hydrogel	1.2	1.1	1.5
Alginate	0.7	1.5	2.3
Permeable	0.4	0.8	1.0
Odour-absorbent	0.1	0.3	0.1
Capillary-action	0.1	0.0	0.0
Protease-modulating matrix	0.0	0.0	0.2
TOTAL	**44.0**	**41.9**	**69.3**

TLCCB–two-layer cohesive compression bandage; TLCS–two-layer compression system; FLCS–four-layer compression system

Table 5. Cost of health-care resource use

	Mean cost of resources used per patient in each group over the six-month study period (2014/2015)					
	TLCCB		**TLCS**		**FLCS**	
Community nurse visits	£2,279.80	(75%)	£2,494.24	(65%)	£3,564.90	(80%)
Compression bandages	£293.54	(10%)	£571.44	(15%)	£227.11	(5%)
Dressings	£126.35	(4%)	£125.63	(3%)	£207.52	(5%)
Compression hosiery	£134.33	(4%)	£373.66	(10%)	£137.81	(3%)
Practice nurse visits	£121.94	(4%)	£212.52	(6%)	£101.50	(2%)
Topical treatments	£32.24	(1%)	£7.67	(<1%)	£155.23	(3%)
Analgesics	£23.86	(1%)	£26.95	(1%)	£34.45	(1%)
Other bandages	£12.66	(<1%)	£5.42	(<1%)	£27.84	(1%)
GP consultations	£9.43	(<1%)	£8.78	(<1%)	£14.95	(<1%)
Anti-infectives	£4.12	(<1%)	£7.03	(<1%)	£8.53	(<1%)
Laboratory tests	£0.53	(<1%)	£0.25	(<1%)	£0.56	(<1%)
Outpatient visits	£6.54	(<1%)	£7.99	(<1%)	£0.00	(<1%)
TOTAL	**£3,045.34 (100%)**		**£3,841.58 (100%)**		**£4,480.40 (100%)**	

TLCCB–two-layer cohesive compression bandage; TLCS–two-layer compression system; FLCS–four-layer compression system

Table 6. Cost-effectiveness analysis

Treatment group	Mean NHS cost per patient over six months from the start of compression	Mean number of QALYs per patient at six months from the start of compression	NHS cost difference	QALY difference	Incremental cost per QALY gained
TLCCB	£3045	0.413			
TLCS	£3842	0.404	–£797	0.009	Dominant
FLCS	£4480	0.396	–£638	0.008	Dominant

TLCCB: two-layer cohesive compression bandage; TLCS: two-layer compression system; FLCS: four-layer compression system; QALY– quality-adjusted life year

Cost-effectiveness analyses

Use of TLCCB resulted in a lower six-month NHS cost and more QALYs than the other two compression systems. Hence, starting treatment with TLCCB was found to be the dominant strategy. Similarly, starting treatment with TLCS was a dominant strategy compared with FLCS since it also improved outcome for less cost (Table 6).

Fig 3. Scatterplot of the incremental cost-effectiveness of TLCCB versus TLCS, TLCS versus FLCS and TLCCB versus FLCS (10,000 bootstrapped samples per comparison)

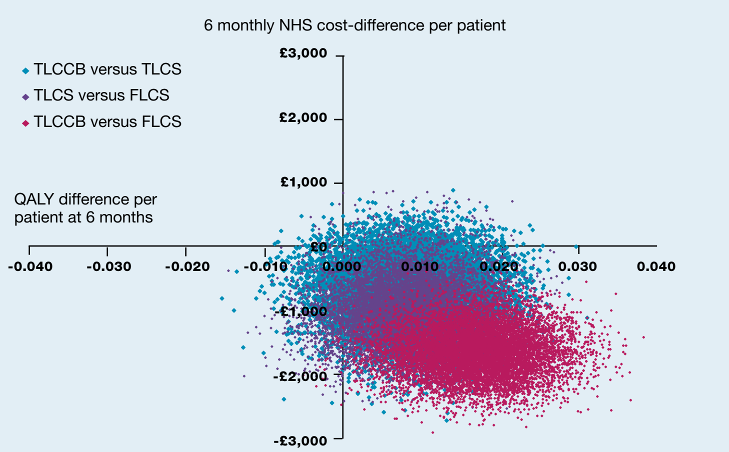
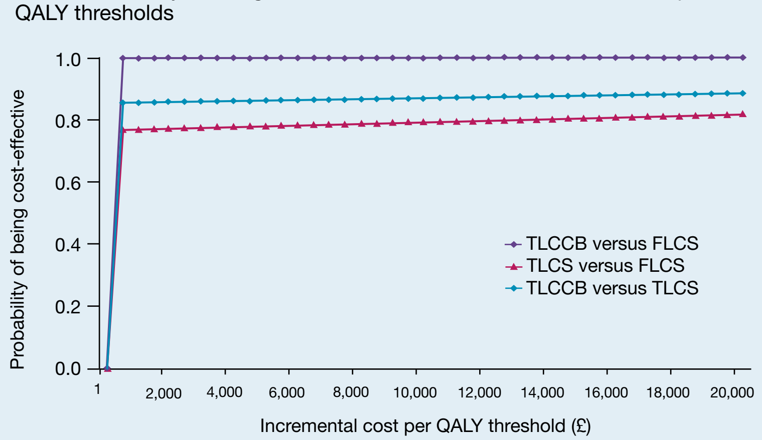


Fig 4. Probability of being cost-effective at different incremental cost per QALY thresholds



Sensitivity analyses

Bootstrapping was performed to identify the distribution in the incremental costs and QALYs at six months for each compression system (Fig 3), with samples from the more cost-effective bandage (TLCCB) being located in the bottom right-hand (dominant) quadrant. Cost-effectiveness acceptability curves were generated from the bootstrapped subsets (Fig 4), showing the probability of the different compression systems being cost-effective for different incremental cost per QALY thresholds. Fig 4 demonstrated that, at a cost-effectiveness threshold of £20,000 per QALY, up to 89% and 99% of a cohort is expected to be treated cost-effectively with TLCCB compared with TLCS and FLCS respectively, and up to 82% of a cohort is expected to be treated cost-effectively with TLCS compared with FLCS.

Deterministic sensitivity analyses were performed on all the model's inputs, but only the main findings have been presented (Table 7). These analyses found the relative cost-effectiveness of the three compression systems remained unchanged for plausible changes in the model's inputs (i.e. initiating treatment with TLCCB remains the most cost-effective of the three strategies).

Minimal changes in outcomes and costs were observed when patients' age, gender, year of diagnosis, time from diagnosis to the start of compression, wound size at the start of compression and comorbidities were adjusted for any heterogeneity between the groups (Table 8). The ANCOVA reiterated the findings from the base case analysis that starting treatment with TLCCB is the most cost-effective strategy, since it leads to better outcomes for less cost.

Discussion

This study demonstrated the costs and outcomes experienced by the patients in our THIN data set following the initial decision to treat a VLU with one of three compression systems in clinical practice in the UK. TLCCB was found to exhibit superior clinical effectiveness and was more cost-effective than TLCS and FLCS in treating newly-diagnosed VLUs. Over a six-month period from the start of compression, 9% and 19% more wounds healed in the TLCCB group compared with the TLCS and FLCS groups respectively (p=0.006), and the time to healing was significantly shorter in the TLCCB group (p=0.003). Additionally, patients in the TLCCB group experienced a better HRQoL and cost the NHS 21% and 32% less to manage than patients in the TLCS and FLCS groups respectively.

Healing is not achievable in all wounds. However, it is the primary desirable outcome for all wound types. The healing rates in this study were higher than those seen in our previous study comparing these three compression systems.[9] This is probably due to the wounds in our earlier study being hard-to-heal wounds with a mean duration of more than six months.[9] The healing rates in this study were also higher than those seen in several phase three trials.[10,12–14] This may be due to the VLUs in this study being newly-diagnosed, whereas these trials compared wounds of varying duration,[10, 12–14] and wound duration has been reported to be a risk factor for delayed healing.[9,22] However, the healing rate in the FLCS group was lower than that seen in another controlled trial.[11] The inevitable variation between healing rates reported in clinical trials and those observed in clinical practice and the differences observed between the three groups in our study may reflect the practical difficulties experienced by non-specialist nurses in the community in achieving the correct levels of compression, as well as the lack of specialist involvement, compared to trained investigators in a randomised controlled trial. Notwithstanding this, the narrow admission criteria of clinical trials compared with the cohort of patients who receive treatment in clinical practice may also contribute to this variance. These differences may also highlight some of the practical problems associated with wound care in the community and the lack of skills required to both select and apply appropriate compression therapy. Patients in our data set rarely saw the same nurse at successive visits and invariably received different dressings at each visit. Hence, there was a lack of continuity of care. Patients' adherence with their compression bandaging may also be a contributory factor to these differences. We have previously highlighted inconsistencies in wound care in clinical practice, staff involvement and dressing choice, with an apparent lack of a patient-specific treatment plan in many instances.[7,8] Furthermore, fewer than 20% of all patients appeared to have undergone a Doppler ABPI measurement, contrary to national guidance.[23,24] Although this may be indicative of the difficulties experienced by non-specialist health-care professionals in the community in acquiring necessary skills or accessing Doppler equipment, it also raises the question of how accurate the VLU diagnosis was. Notwithstanding this, the patients had a VLU diagnosis documented in their records and they were managed with compression as if they had a VLU. Hence, the findings from this study reinforce the importance of training non-specialist nurses in the diagnosis and the correct management of VLUs and the application of compression systems in order to overcome some of the problems encountered in clinical practice and to achieve better health outcomes than those currently being observed.

Table 7. Sensitivity analyses

Scenario	Range in the cost per QALY gained with TLCCB versus TLCS	Range in the cost per QALY gained with TLCS versus FLCS
Probability of healing in all three groups ranges from 0.5 below to 1.25 above the base case value	£299,000 to £73,000	£160,000 to £59,000
Number of community nurse visits ranges from 50% below and above the base case value	£84,000 to £110,000	£121,000 to £137,000
Number of practice nurse visits ranges from 50% below and above the base case value	£92,000 to £103,000	£81,000 to £68,000
Number of compression bandages ranges from 50% below and above the base case value	£80,000 to £114,000	£95,000 to £55,000
Number of compression hoseries ranges from 50% below and above the base case value	£83,000 to £112,000	£89,000 to £61,000
Number of dressings ranges from 50% below and above the base case value	£97,000 to £97,000	£70,000 to £80,000

TLCCB: two-layer cohesive compression bandage; TLCS: two-layer compression system; FLCS: four-layer compression system; QALY– quality-adjusted life year

Table 8. Outputs from ANCOVA

Treatment group	Mean NHS cost per patient over six months from the start of compression	Probability of being healed at six months after starting compression	Mean number of QALYs per patient at six months from the start of compression
TLCCB	£3183	0.74	0.411
TLCS	£3980	0.68	0.402
FLCS	£4203	0.67	0.401

TLCCB: two-layer cohesive compression bandage; TLCS: two-layer compression system; FLCS: four-layer compression system; QALY– quality-adjusted life year

Some 8%, 3% and 23% of patients in the TLCCB, TLCS and FLCS group, respectively, switched from their initial compression system. Consequently, a minority of patients would not have been receiving their initial compression system at the end of the study period and thus may not have been healed by that compression system. Nevertheless, decision analysis considers the costs and consequences of the initial decision. Hence, this outcome is a consequence of the initial decision to treat with TLCCB, TLCS or FLCS and is reflected in the costs, healing rates and QALYs for each group.

The advantages and disadvantages of using patients' records in the THIN database for economic evaluations in wound care have been discussed elsewhere.[9] In summary, the advantage of using the THIN database is that the patient pathways and associated resource use were based on real-world evidence derived from clinical practice. However, patients were not randomised to their received treatment. Hence, there may have been differences between the groups resulting in the clinician's decision to treat with one of the three compression systems and the patient's willingness to accept the clinician's preferred treatment. The wounds were of a comparable size both at the time of diagnosis and at the start of compression. Consequently, there may have been some differences that have not been accounted for. For example, there was greater use of absorbent and antimicrobial dressings in the FLCS group, perhaps indicative of wounds with higher levels of exudate and possibly more infection. Alternatively, this difference in dressing use with FLCS may be due to less effective compression having been obtained with this system. Furthermore, some would argue that selection of an FLCS is often based on the need for exudate control and prolonged wear time. Dressing selection may indicate that this was the case in a small number of patients. However, this did not appear to drive compression system selection and this study showed that the wear time with FLCS was no longer than that with the two alternative systems that have been assessed. Notwithstanding this, ANCOVA showed differences in patients' outcomes and resource use between treatments did not need to be adjusted for any heterogeneity in patients' baseline characteristics, and when they were adjusted the relative cost-effectiveness of the three compression systems remained unchanged.

Other limitations, in particular, should be considered when interpreting this study's findings. The analyses were based on clinicians' entries into their patients' records and inevitably subject to a certain amount of imprecision and lack of detail. Consequently, wound severity and exudate levels were not included in the matching criteria, since they were not fully documented in the patients' records. Moreover, the information in the THIN database is collected by GPs for clinical care purposes and not for research. Prescriptions issued by GPs and practice nurses were recorded in the database, but it does not specify whether the prescriptions were dispensed or detail patient adherence. Despite these limitations, it is the authors' opinion that the THIN database affords one of the best sources of real-world evidence for clinical practice in the UK. This view is supported by the publication of more than 500 research articles in peer-reviewed journals that have used the database as the source of their underpinning evidence.[25]

The study results were truncated at six months and excluded the costs and consequences of managing patients with an unhealed ulcer beyond this period. The THIN database may have under-recorded use of some health-care resources outside the GP's surgery if they had not been documented in the GP records. The analysis only considered NHS resource use and associated costs for the 'average patient' and was not stratified according to gender, comorbidities, suitability of patients for different treatments, other disease-related factors and level of clinician's skills. Patients' costs and indirect societal costs as a result of patients being absent from work were also excluded from the analysis. However, patients' mean age was over 65 years, so it is unlikely that many were in employment.

Despite these limitations, all the patients in this data set had a VLU diagnosis and they were predominantly managed locally by community and practice nurses. This is consistent with the findings from previous studies in the management of VLUs.[7–9,26,27] Furthermore, the six-month cost of patient management is concordant with our previous studies on the cost of managing VLUs in clinical practice.[8,9,26,27] VLU management remains challenging and the number of new VLUs in the UK has been estimated to rise to 170,000 in 2017.[28] The majority of expenditure for managing these wounds is expected to comprise community and practice nurse visits. However, the cost of managing an unhealed wound was three-to-five times more than that of managing a healed wound (Fig 2). This study indicates that up to 35% of patients who receive compression therapy have a hard-to-heal wound and there is an accumulating pool of such patients. Clearly, interventions that improve outcomes for less cost have the potential to reduce the ever-increasing burden that VLUs impose on the UK's NHS.

In conclusion, this real-world evidence study shows that starting treatment of newly-diagnosed VLUs with TLCCB instead of the other two compression systems affords a more cost-effective use of NHS-funded resources, since it resulted in an increased healing rate, better HRQoL and a reduction in NHS management cost. The evidence also highlighted the lack of continuity between clinicians managing a wound, the inconsistent nature of the administered treatments and the lack of specialist involvement, all of which may impact on healing and the patient's experience. Clinicians managing VLUs may wish to consider the findings from this study when making treatment decisions. **JWC**

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