NICE National Institute for Health and Care Excellence

Health Tech Programme

Medical Technologies Advisory Committee (MTAC

Compression products for treating venous leg ulcers: late stage assessment – 1st meeting

13 March 2025

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Link to SCM/Experts register for topic:	https://www.nice.org.uk/guidance/indevelopment/gid-hte10048/documents

The following documents were made available to the Committee:

1. Cover sheet
2. Patient organisation submission – Lindsay Leg Club
3. External assessment report overview (ARO)
4. External assessment report (EAR)
5. Confidential appendix to the External Assessment Report (EAR)
6. Stakeholder comments and EAG responses on the External Assessment Report (EAR)
7. User preference report (includes patient survey results)
8. Comments and NICE responses on the user preference report

HealthTech Programme

Patient organisation submission

Compression products for wound care: Late Stage Assessment

Thank you for agreeing to give us your organisation's views on this technology and its possible use in the NHS.

You can provide a unique perspective on patient experience of using the technology in the context of current clinical practice that is not typically available from the published literature.

To help you give your views, please use this questionnaire. You do not have to answer every question – they are prompts to guide you. The text boxes will expand as you type.

Information on completing this submission

- Please do not embed documents (such as a PDF) in a submission because this may lead to the information being mislaid or make the submission unreadable

- We are committed to meeting the requirements of copyright legislation. If you intend to include **journal articles** in your submission you must have copyright clearance for these articles. We can accept journal articles in NICE Docs.

Your response should not be longer than 10 pages

Information about your organisation	
Organisation name	The Lindsay Leg Club Foundation
Contact person's name	Ellie Lindsay
Role or job title	Life President
Email	[redacted]
Telephone	[redacted]
Brief description of the organisation, such as: • who funds it We are a registered charity and are funded by public donations / Wound Care Companies • How many members does it have c 23,000? • What region your organisation represents: England & Wales	

Declarations	
Do you have any conflicts of interest? Please let us know if you have a question on the NICE policy on declaring and managing interests. No conflict of interest	
How did you gather information about the experiences of patients and carers to include in your submission? Our Leg Club member survey's and by talking to our Leg Club members	
Are you willing for this submission to be shared on our website?	Yes x☐ No ☐
We may invite you to a scoping meeting and/or committee meeting where this technology is to be discussed. Would a member of your organisation be willing to join such a meeting (this may be in person or virtually)?	Yes ☐ No ☐ n/a

Does the organisation have any direct or indirect links with, or funding from, the tobacco industry?	Yes ☐ No x☐

Impact of the symptoms, condition or disease on patients and / or family and carers

1. What is it like to live with the condition? What do carers experience when caring for someone with the condition?

Living with problems of the lower limb can be physically and emotionally challenging for the individual already confronted with quality of life issues. This impacts on carers / loved ones who are looking after someone with conditions in the lower limb often face a range of emotional, physical, and practical challenges.

Experiences and availability of current health technologies

2. How do the existing health technology/ies play a role in managing the condition, and what are their advantages and disadvantages?

Existing health technologies play a significant role in managing long term and conditions of the lower limbs, hence apps, smart watch, wearable sensors and telemedicine and can act as a preventive etc.

Equality issues

3. Are there any groups of people who might benefit more or less from the technology than others?

Young age groups, individuals with long term conditions, carers and loved one. However, the degree to which individuals benefit depends on factors like the challenges in utilisation of today's technology within the older group is lack of familiarity with digital or those with limited access to technology. Hence, methods of public education to provide additional support, such as training, assistance, or alternative methods of monitoring and treatment, is vital to ensure that technology doesn't become a barrier to good quality care are.

4. Are there any groups of people that might need further consideration in using the technologies (for example, because they have higher levels of ill health, poorer outcomes, problems accessing or using treatments or procedures)?

Consider groups such as the senior population, individuals with long term conditions, cognitive impaired individuals who may require support to ensure the benefits of using health technologies are seen as positive as opposed to negative experiences. There are potential equality and health inequality factors to consider when using e.g low income, limited connectivity, financial cost re smartphones, lack of literary skills, complex health related issues all play an important factor. Addressing these disparities is crucial to ensuring that all individuals, regardless of socioeconomic status or technical ability, have equitable access to effective treatment and care.

5. Are there any potential equality or health inequality issues that should be taken into account when considering this condition and the technology?

There are potential equality and health inequality factors to consider when using e.g low income, limited connectivity, financial cost re smartphones, lack of literary skills, complex health related issues all play an important factor. Addressing these disparities is crucial to ensuring that all individuals, regardless of socioeconomic status or technical ability, have equitable access to effective treatment and care.

Additional information

6. Please include any additional information you believe would be helpful in assessing the value of the technologies.

The assess the value of technologies it is important to consider the following: cost-effectiveness, ease of use, an individual's dexterity and adherence and reassurance to provide ongoing support to both the individual and cares / loved ones that integration of technology in today's NHS healthcare systems is to complement traditional care and improve long-term outcomes. Finally, most importantly to obtain the individuals feedback on comfort, barriers they may have encountered.

Key messages

In up to 5 bullet points, please summarise the key messages of your submission. bullet points.

- **Compression therapy as the gold standard**: Compression stockings are highly effective in treating chronic venous insufficiency, venous ulcers, and preventing their recurrence. They improve calf pump function and reduce oedema.
- **Important assessment before application**: Prior to using compression therapy, the individual's arterial status must be assessed with tools like Doppler ultrasound to ensure safety, especially when mixed venous and arterial diseases are present.
- **Barriers to compliance**: Some individuals, especially the elderly or those with mobility issues, struggle with wearing compression hosiery due to difficulties in application, discomfort, aesthetics, and the need for lifelong use, leading to poor compliance.
- **Personalised fitting and aids**: Proper measuring and fitting by a trained practitioner are essential for comfort. Providing aids, like stocking frames or toe liners, can help individuals with limited dexterity apply hosiery more easily and improve adherence.
- **Maintenance of hosiery**: Regular prescription renewal is crucial to maintain the proper pressure and prevent complications like skin breakdown and leg ulcers. Compression hosiery should be worn daily as prescribed, and damaged hosiery should be replaced immediately to ensure effectiveness.

Late-stage assessment

Compression products for treating venous leg ulcers

Assessment report overview

This overview summarises key information from the assessment and sets out points for discussion in the committee meeting. It should be read together with the final scope, the external assessment report and the user preference report. List of abbreviations used in this overview is in appendix A.

1. The technology

Compression products are products that work by squeezing the lower limb, thereby reducing oedema and helping venous return to the heart. Compression products can vary in the level of pressure applied. For venous leg ulcers (VLUs), strong compression is recommended, which is either elastic, inelastic or a combination compression system, applied in accordance with manufacturer's recommendations, and designed to give at least 40mmHg of pressure at the ankle.

The 4-layer compression bandage system was developed in 1988 and has been regarded as the gold standard compression system for treating venous leg ulcers (Moffatt et al. 1988). After this, 2-layer compression hosiery became available as a treatment option following the results from the VenUS 4 trial (Ashby et al. 2014). In addition, two alternative types of compression treatments are available in the NHS and are being assessed in the VenUS 6 trial: the 2-layer bandage compression system and compression wraps. Currently, the most commonly used compression products in the NHS are 4- and 2-layer compression bandage systems.

Short stretch bandaging (SSB) was identified as a particular sub-type of compression bandaging that featured frequently in the identified studies. Clinical experts advised that SSB is most frequently used as 2-layer compression bandages (2LCB) and have therefore been placed alongside 2LCB. This fits with this features-based approach to LSAs even if some studies used SSB with for example an additional top layer for particularly oedematous limbs or in case of slippage. However, noting that SSB are a sub-type of bandage, differing in its features from multi-component 2LCB systems, it has been emphasised where studies used SSB.

Supporting products for example a hosiery applicator, a ‘boot’ to protect bandages when showering, a ‘shoe’ or an oversized sandal to help walking with bandages, or a foot, ankle or toe piece for wraps to provide full leg compression are available to use with compression products. They are commonly used but the use may vary in different settings.

Late-stage assessments can focus on the innovative features that individual products may possess or the products in their entirety. In this assessment, the ‘features’ were agreed to be the 4 types of compression product as listed in the final scope. Any product of 1 of these 4 types used in the NHS was eligible for inclusion.

There are at least 20 companies providing over 200 compression products (including different sizes, products and colours) to the NHS across a range of procurement routes including NHS Drug Tariff, NHS Supply chain and alternative off medical prescription procurement platforms for compression products. There is price variation between and within the different types of compression products. For more detail on the included compression product types including their potential benefits and price range, see table 1.

Table 1. Description, potential benefits and price range of included compression products

	Description	Potential benefits	Price range*
4-layer compression bandage (4LCB)	Typically, the 4LCB system has the following layers: • First layer: single layer of orthopaedic wool which is applied in a spiral from toe to knee • Second layer: type 1 conforming or type 2 light support bandage (British standard classification) applied in a spiral • Third layer: elastic long stretch bandage applied by a figure of eight method or a spiral method • Fourth layer: cohesive bandage applied in a spiral	Allows self-care: No Own footwear: No Increased mobility: No Reusable: No	£5.73 to £11.04
2-layer compression bandage (2LCB)	There are 2 types of 2LCB systems: • A system where the first bandage layer typically uses a padding layer for comfort and gripping the skin and the second layer consists of a SSB • A multicomponent system where both layers are compression bandages	Allows self-care: No Own footwear: Yes Increased mobility: Yes Reusable: No	£7.26 to £10.93
2-layer compression hosiery (2LCH)	Consists of 2 stockings, typically an understocking and overstocking, that are designed to deliver strong compression (40mmHg) at the ankle	Allows self-care: Yes Own footwear: Yes Increased mobility: Yes Reusable: Yes	£15.67 to £35.32***
Compression wraps (CW)	A system which has either: • Velcro straps which fit together or • A hook and eye system	Allows self-care: Yes Own footwear: Yes Increased mobility: Yes Reusable: Yes	£13.80 to £168.55

*Of products listed on part IX of the NHS Drug Tariff (June 2024); **Comparative products in terms of size and compression level;

***Excludes made-to-measure hosiery which are priced up to £69.08

Further details, including descriptions of the interventions, comparator, care pathway and outcomes, are in the final scope.

2. Clinical effectiveness

The EAG did a systematic search to identify relevant published clinical evidence. The search and selection methods are in section 5.1 of the external assessment report [EAR]. The EAG made 2 minor deviations from the decision problem. It considered including evidence that reported strong compression delivering 30 to 40mmHg as opposed to 40mmHg or higher, where the evidence otherwise is eligible. Due to the volume of clinical evidence, including several randomised controlled trials (RCTs), it was also decided to only consider full-text articles for inclusion rather than conference abstracts. In total, 125 full text studies were assessed for eligibility. Further detail is provided in section 1 and section 5 of the EAR.

2.1 Overview of key studies

The EAG identified 34 studies that met the decision problem, of which 2 were excluded following clinical input as they included tubular bandages, which do not offer graduated compression. Due to the large volume of studies, the EAG prioritised 15 studies for inclusion in their clinical evidence review, which are summarised in table 2. The rationale for prioritisation is in Appendix D and a landscape map showing the evidence that was available for each feature of interest is in Table 3 of the EAR. Of the prioritised 15 studies, 14 were RCTs and the other study was a large UK retrospective cohort study comparing different forms of compression for VLUs in the context of routine NHS practice. Six studies were exclusively conducted in the UK, and 1 other study included some UK sites. There is 1 study conducted in the USA and 1 study in Australia which both may have limited generalisability because of differences in service organisation, and the remaining studies were conducted in Europe. Evidence covered all 4 compression product features listed in the scope and

head-to-head RCT evidence was available directly comparing features with each other. Studies reflected a typically older population and were generally well balanced for gender. Ethnicity was only reported in 1 study, in which all participants were Caucasian. Prioritised evidence did not present evidence specifically for any scoped subgroups: people with conditions that may limit self-care, people with low or high exudate wounds, people with very fragile skin, or people with irregular leg shapes.

2.1.1 Quality appraisal of studies

Of the 14 RCTs included in the EAG's evidence review, 7 studies were also included in the Venus IV network meta-analysis which were assessed using an adapted version of the original Cochrane risk of bias tool. For consistency, the EAG used the same version of the adapted tool to assess the quality of the additional 9 RCTs included in their evidence review. The evidence was generally considered to be fairly high quality. However, open label studies do pose an increased risk of bias. Blinding of participants and clinicians is not possible due to the visual appearance of the different types of compression products. But the EAG noted that blinding of outcome assessors should be possible, which did not occur often in the studies. In addition, the EAG highlighted that caution should be taken when interpreting the results of the 6 studies for which there may have been imbalances at baseline on unmeasured prognostic indicators. For more detail see section 5.3 and Appendix F of the EAR.

2.1.2 Results from the evidence base

The EAG did not conduct its own network meta-analysis, but used the VenUS 6 study's network meta-analysis, see section 5.4 and 5.5 of the EAR. It conducted a narrative synthesis to explore potential patterns across the evidence that could be used to draw conclusions about the clinical effectiveness of product features. Seven prioritised studies compared 4-layer

compression bandages (4LCB) with 2-layer compression bandages (2LCB). Studies showed that 2LCB was at least as good as 4LCB, with some evidence showing that 2LCB may be better. Two of these studies assessed tolerability, ease of use and/or acceptability and both favoured 2LCB over 4LCB. Resource use in terms of number of dressings per month was higher for 4LCB than 2LCB.

Both 2-layer compression hosiery (2LCH) and compression wraps (CW) were shown to be equivalent to 4LCB, noting that there was only 1 study on CWs for this comparison. There was some evidence that CWs may be better than 2LCB for wound healing rate, but this was based on only 2 studies and 1 used short stretch bandages (SSB). Discontinuation was higher for the 2LCB arm and this arm also needed more nursing time compared with CWs.

All three included studies comparing 2LCH with 2LCB in the form of 2-layer short stretch bandages (2LSSB) showed that 2LCH offered better wound healing rates than 2LSSB. However, these were not the same products that were typically assessed in the studies that compared them with 4LCB. Adherence, ease of application, staff satisfaction and intervals between visits were greater for the 2LCH.

There was 1 study that compared different types of 2LCB, which showed that the type of bandages may influence outcomes, i.e. this product type feature is not necessarily unitary. Time to healing and wound size were similar for both 2LCBs, however percentage of wounds healed, and treatment switching was higher for the cohesive 2-layer compression bandage than the 2-layer compression system.

Table 2. Summary of prioritised studies

Study name, design, location	Intervention, comparator	Population, setting, length of follow up	Results	Comments
4-layer compression bandaging compared with 2-layer compression bandaging (n=7)				
Guest et al. (2017), retrospective cohort study, UK	Cohesive 2LCB (Coban 2, 3M) 2LCB (KTwo, Urgo) 4LCB (Profore, Smith & Nephew)	600 people with VLUs GP setting 6 months	**More wounds were healed** in the cohesive 2LCB arm (76%) compared with the 2LCB (70%) or the 4LCB arm (64%), overall effect p<0.05. **Time to complete healing** was significantly shorter in the cohesive 2LCB than in the other 2 groups (p<0.003). **Wound size reduction** was similar in all 3 arms. **QALY gain** was 0.413 for cohesive 2LCB. 0.404 for 2LCB and 0.396 for 4LCB, overall effect p=0.006. **Percentage of who switched treatment** was highest for the 4LCB (23%) compared with 8% for the cohesive 2LCB and 3% for the 2LCB. **Mean number of dressing changes** was higher for the 4LCB arm (69.3) compared with the cohesive 2LCB (41.9), or the 2LCB (44).	Only non-randomised study included. It is a large retrospective analysis of clinical outcomes by compression type in routine NHS practice.
Lazareth et al. (2012), non, inferiority RCT, France, UK and Germany	2LCB (KTwo, Urgo) 4LCB (Profore, Smith & Nephew)	187 people with VLUs (ITT = 186) Outpatient and inpatient clinics 12 weeks	**Percentage of wounds healed** was higher in the 2LCB arm compared with the 4LCB arm (p=0.0165). **Median time to healing** was 91 days in both arms. **Relative wound area reduction, median number of compression systems used per week,** and **pain** were similar in both groups. The 2LCB arm had less **de novo ulcerations** (4.30% vs. 6.40%, p-value NR), less **% participants with any adverse events** (12% vs. 17%, p=0.99), and lower **discontinuation rates prior to week 12** rates (11.83% vs. 16.13%) compared with the 4LCB arm. There was a 6%-point increase in **healthy peri-lesional skin condition** from baseline to completion for the 2LCB arm and 3% points for the 4LCB arm. More participants found **application 'very easy'** for the 2LCB arm (62%) compared with the 4LCB arm (47%), p=0.038.	European RCT (including UK sites) comparing 2LCB and 4LCB. There was some variation between countries for some of the outcomes
Dolibog et al. (2014), RCT, Poland	Group B: CH (Ulcer X, Sigvaris; 30-40mmHg) Group C: 4LSSB (Sigvaris; 45-55mmHg)	147 people with VLUs Hospital setting 2 months	**Percentage of wounds healed** was similar in the CH arm (56.66%) and the 4LSSB arm (58.62%) but lower in the 2LSSB arm (16.66%), with a significant difference between the 2LSSB and CH and 4LSSB arms (p=0.03 for both comparisons). **Wound size reduction** was similar in the compression hosiery arm (-14.74) and the 4LSSB arm (-	EU RCT comparing 5 types of compression; not all arms were within scope.

	Group D: 2LSSB (Sigvaris; 20-30mmHg)		13.97), but smaller in the 2LSSB arm (-6.17). **Adherence to treatment** was reported as 100% in all groups.	Group D received reduced compression
Franks et al. (2004), RCT, UK	2LSSB (Flexiban and, Activa Healthcare) 4LCB (Flexiban, Activa Healthcare; Setocrepe and Elset, SSL, and Coban, 3M)	159 people with VLUs (156 were analysed) Clinical centres 24 weeks	**Percentage of wounds healed, discontinuation rates, pain** and **maceration** were similar in both arms. **Percentage of participants with an adverse event** were higher in the 4LCB arm (31.1%) compared with the SSB arm (26.8%), p-value NR. **Tissue damage or new ulcers** were more common in the SSB arm (3.7%) compared with the 4LCB arm (2.7%), p-value NR.	UK RCT comparing 4LB with 2-layer cohesive SSB (underlayer with Actico).
Gillet et al. (2019), non-inferiority RCT, France	2LCB (BIFLEX, Thuasne) 4LCB (Profore, Smith & Nephew)	92 people with VLUs (full analysis = 88) Medical centres 16 weeks	More **wounds healed** in the 2LCB arm compared with the 4LCB arm (p=0.02). There was no statistically significant difference for **mean change in SF-12** and **adjusted mean change in wound related pain** between arms. **Percentage of participants** experiencing any **adverse events or pain in extremities** were similar between arms. **Participant satisfaction** was significantly higher in the 2LCB arm for softness (p=0.024), breathability (p=0.010), thickness (p=0.011) and ease of putting shoes on (p=0.033) compared with the 4LCB arm. **Physician satisfaction** was significantly higher in the 2LCB arm for application simplicity (p=0.024), application time (p=0.003), practicality of the system (p=0.002) and comfort during handling (p=0.002) compared with 4LCB arm. No difference in slippage was reported between groups (p=NS).	European RCT comparing 2LCB and 4LCB. This is considered a relevant prioritised study, though the specific 2LCB does not appear on the NHS Drug Tariff or Supply Chain.
Iglesias et al. (2004), VenUS 1, RCT, UK	4LCB (multilayer elastic; Profore, Smith and Nephew; system 4, SSL; original 4LB) SSB (multilayer, inelastic; Comprilan, Beirsdorf; Rosidal K, L&R)	387 people with VLUs Community and hospital leg ulcer clinics, and district nurse led services 12 weeks	**Percentage of wounds healed** was higher and median **time to healing** was shorter in the 4LCB arm compared with the SSB arm (NS). **In terms of SF-12, the mental component** is similar between the 2 arms, but for the physical component there is a slight imbalance between the arms (36.1 for the 4LCB group and 35.6 for the SSB arm). Discontinuation **of intervention** was more common in the SSB arm. **Percentage of participants with any adverse events, occurrence of new ulcers, skin damage,** and **maceration** were similar in both arms. **Death rates** were 7.69% in the 4LCB arm and 10.42% in the SSB arm.	UK RCT comparing 4LCB with SSB. For the SSB arm, the first layer was orthopaedic wool padding, and the upper 2 layers were cotton SSBs. In the event of slipping, protocol allowed an additional

				cohesive bandage layer (Coban, 3M) over the SSB system
Moffatt et al. (2003), RCT, UK	4LCB (Profore, Smith and Nephew) 2LCB (Surepress, ConvaTec)	112 people with VLUs (ITT = 109) Community leg ulcer clinics 24 weeks (or until full closure)	**Percentage of wounds healed** at 24 weeks was higher in the 4LCB arm (88%) compared with the 2LCB arm (77%), p=0.55. **Mean time to closure** was similar for both groups. The 4LCB arm had lower **study withdrawal** (p<0.001), **mean frequency of compression change** (p=0.0002), and **device-related adverse events** (p=0.01), **tissue breakdown** and **pain or discomfort** compared with the 2LB arm.	UK RCT comparing 4LCB with 2LCB
4-layer compression bandaging compared with compression hosiery (n=2)				
Ashby et al. (2014), VenUS IV, RCT, UK	2LCH (35-40mmHg) (Carolon MLCS, H&R Healthcare; Clini Duo40, CliniSupplies; Mediven Ulcer kit, Medi UK; Activa leg ulcer hosiery kit, Activa Healthcare; Jobst UlcerCARE, BSN medical; VenoTrain ulcertec, Bauerfeind UK) 4LCB (various UK products; 40mmHg)	457 people with VLUs (analysed = 453) Community nursing teams, GP practices and leg ulcer clinics 12 months	**Percentage wounds healed** (76.1% vs. 79.3%), **median time to healing** (99 days vs 98 days)**, quality of life**, **ulcer-related pain**, **percentage of participants with a serious adverse event** (14.3% vs. 14.7%), **hospitalisation rates** (74.4% vs. 76.2%) and **infection rates** (5.7% vs. 6.9%) were similar in the compression hosiery and 4LCB arm, respectively. **Change to non-trial treatment** (38.3% vs. 27.8%), **non-serious adverse events** (67.0% vs. 58.0%) and **death** (20.9% vs. 7.1%) were more common in the 2LCH arm compared with the 4LCB arm, respectively. **Daytime adherence** (wearing every day) was high in both the 2LCH (90.7%) and 4LCB (96.9%) arms.	Large UK RCT that is likely to provide some of the most valuable results besides VenUS 6. However, it does not include 2LCB.
Finlayson et al. (2014), RCT, Australia	4LCB (Profore) Class 3 CH (NR; 30-35mmHg)	103 people with VLUs Outpatient clinics 24 months	**Percentage of wounds healed** was higher in the 4LCB arm (84%) compared with CH (72%), p=0.14. **Median time to healing** was significantly shorter (p=0.003) in the 4LCB arm (10 weeks) compared with CH (15 weeks). **Quality of life**, **adherence** (at least three quarters of the time), **adverse events** and **reduction in ulcer area** were similar in both groups. **MOS Pain Measures Pain Severity Scale:** mean (SD) for 4LCB at baseline was 51·8 (28·3), and 23·0 (22·1) at 24 weeks. Mean (SD) for CH was 50·0 (26·4) at baseline and 34·0 (23·3) at 24 weeks, p<0.001 for main effect.	RCT comparing CH with 4LCB. It is understood that the product range in Australia is generally comparable with the UK.

4-layer compression bandaging compared with compression wraps (n=1)				
Blecken et al. (2005), RCT, USA	CW (CircAid, Medi UK) 4LCB (various)	12 people with bilateral VLUs Hospital setting 12 weeks	**Percentage of wounds healed** and **adherence to treatment** was the same in both groups, 33% and 100% respectively, NS. **Wound size reduction (cm2 per week)** was similar in the CW arm (change -35.16) compared with the 4LCB arm (change -27.6), p=0.369. No significant differences were found in **patient satisfaction scores.**	Small scale RCT in the USA, potentially limiting generalisability. However, one of the few studies assessing CWs.
2-layer compression bandaging compared with compression hosiery (n=3)				
Junger et al. (2004, Curr Med Res Opin), RCT, Netherlands and Germany	2LCH (U-Stocking, Venotrain UlcerTec) 2LSSB (Roselastic S 530, KOB)	131 Caucasian people with VLUs (121 eligible for primary efficacy analysis) Phlebology outpatient clinics 12 weeks	**Percentage wounds healed** was higher in the 2LCH arm 47.5% compared with the SSB arm (31.7%, p=0.0129). **Mean time to healing** was similar in both groups. Early **discontinuation** was more common in the SSB arm (8.33%) compared with the 2LCH arm (3.27%). **Regression in the ulcer surface** was more common in the 2LCH arm (74.8%) compared with the SSB arm (51.4%, p=0.0679). Percentage of participants with any **adverse events** was numerically higher in the SSB arm (39%) than the 2LCH arm (31%). There was greater **staff satisfaction** with 2LCH compared with SSB (p=0.0123). There was a tendency (p=0.07) for those in the 2LCH arm to have **more pain.**	European RCT comparing 2LCH and 2-layer SSB. The specific hosiery does not appear on the NHS Drug Tariff or Supply Chain.
Mariani et al. (2008) RCT, Italy	2LCH (Ulcer X, SIGVARIS) SSB (details: NR)	60 people with VLUs (of which 4 were excluded) Centres specialised in leg ulcer care 4 months	**Percentage wounds healed** was higher in the 2LCH arm (96.2%) compared with the SSB arm (70.0%, p=0.011). **Mean time to healing** was comparable in both arms (p=0.52). **Pain** was significantly higher in the SSB arm compared with the 2LCH arm when applied, when removed, when walking, and with a trend (p=0.06) for when wearing shoes. **Inhibition of activities** was more common for the SSB arm than the 2LCH arm (p=0.025) and **mean interval between visits** was longer for the 2LCH arm (8.2 days) compared with the SSB arm (6.7 days, p=0.002).	European RCT comparing 2LCH and SSB (in 2 or more layers).
Polignano et al. (2004), RCT, Italy	2LCH (SurePress comfort, ConvaTec) 2LSSB system (Comprilan, BSN)	56 people with VLUs (of which 2 were excluded) Medical centres 12 weeks	**Percentage wounds healed** (44% vs. 17.2%, p=0.027) and **adherence** (92.3-100% vs. 80.8-92.9%) were higher in the 2LCH arm compared with the SSB arm, respectively. **Mean time to healing** was significantly shorter in the 2LCH arm (72 days) compared with the SSB arm (101 days, p=0.0265). **Mean VAS pain score** (p=0.017) and **% of any adverse event** (11.11% vs. 24.14%) were lower in the	European RCT comparing 2LCH with SSB (2 layers are normally used).

			2LCH arm compared with the SSB arm. 2LCH was significantly **easier to apply** than SSB (p=0.0439).	
2-layer compression bandaging compared with compression wraps (n=2)				
Mosti et al. (2020), RCT, Italy	CW (CircAid JuxtaCures, Medi) 2LCB inelastic (Coban 2 layer, 3M)	66 people with VLUs Wound care clinics 12 weeks	**Percentage wounds healed** (78.7% vs. 69.6%) and **wound size reduction in not healed participants** (80% vs. 71.2%) were numerically higher in the CW arm compared with the 2LCB arm, respectively. Although these differences were not statistically significant. There was no statistically significant difference in **pain VAS scores** between arms. Median (IQR) **itching scores** were 1 (0-2) for the CW arm and 2 (0-3) for the 2LCB arm, reported as p<.0.5 (unclear if this is a reporting error).	European RCT CW with short stretch bandaging consisting of a comfort and compression layer
Stather et al. (2021), RCT, UK	CW (JuxtaCures, Medi UK) SSB (Actico, L&R or K2, Urgo)	40 people with VLUs Primary care, vascular and leg ulcer clinics 26 weeks	**Percentage wounds healed** (60% vs. 55%), and **mean time to healing** (12.67 weeks vs. 13.64 weeks, NS) were comparable in both the CW and SSB arm, respectively. **Wound size reduction** was greater in the CW arm than the SSB arm, p=0.06. For **quality of life**, there was a statistically significant difference favouring CWs at 3 months (p=0.04). However, no statistically mean significant difference in EQ5D scores were found at 1 and 6 months. **Mean nursing time duration** (41.7 vs 53.9 minutes, p=0.003) and **discontinuation** (5% vs. 15%) were lower in the CW arm compared with the SSB arm (53.9 minutes), respectively. 4459 diary entries were completed, and of those 33% were recorded as removing the bandage or device. Of these, 78% were in the CW arm and 22% in the SSB arm. Common reasons for removal were for washing (72%) and pain (4%).	UK RCT (feasibility study) comparing CW with SSB.
Comparison of different types of 2-layer compression bandaging (n=1, Guest et al. (2017) is reported above in the 4LCB vs 2LCB section)				

2LCB, 2-layer compression bandage; 4LCB, 4-layer compression bandage; 2LCH, 2-layer compression hosiery; 2LSSB, 2-layer short stretch bandage; 4LSSB, 4-layer short stretch bandage; CH, compression hosiery; CW, compression wrap; GP, general practitioner; ITT, intention to treat; MOS, Medical Outcomes Study; Multi-layer compression system (MLCS); NR, not reported; NS, not significant; QALY, quality adjusted life year; RCT, randomised controlled trial; SD, standard deviation; SF-12, Short Form 12-item health questionnaire; SSB, short stretch bandage; VAS, visual analogue scale; VLU, venous leg ulcer; UK, United Kingdom; USA, United States of America

2.2 VenUS 6 study

VenUS 6 is an RCT of compression products for venous leg ulcers in a UK setting that completed data collection in August 2024. The EAG received academic in confidence results from an updated systematic review and network meta-analysis which includes VenUS 6 trial data. VenUS 6 is a pragmatic, parallel-group, three-arm RCT comparing three types of strong compression (40mmHg pressure at the ankle): i) compression wraps, ii) two-layer bandages, or iii) 'evidence-based compression' (2-layer compression hosiery or 4-layer compression bandages). Participants were followed up for between 4 and 12 months. The primary endpoint is time to healing, measured in days since randomisation. For further detail see section 5.5 in the EAR.

Results of the VenUS 6 study network meta-analysis

The EAG was sent unpublished results from a network meta-analysis (NMA) conducted alongside the VenUS 6 trial, which included relevant literature and the results of the VenUS 6 trial. This comprised tables of hazard ratios and uncertainty intervals and a CODA with correlated draws from the joint posterior distribution. The working NMA assumed equivalence between 4-layer compression bandages and 2-layer compression hosiery and conceptualised them as 'evidence-based compression' (EBC), as it saw them as current best evidence-based practice in the UK.

The NMA compared EBC with a range of strong compression treatment options, including several that are not used in the UK. This overview focuses on the comparison of EBC with the other 3 treatment options used in UK practice, but for further detail on the other treatment options used in the NMA, see section 5.5.1 of the EAR.

- EBC defined 4LCB as elastic systems consisting of orthopaedic wool plus three subsequent bandages and defined 2LCH as comprising a smooth first layer, or understocking, providing light compression over which a second overstocking i.e. UK class II or III depending on the understocking slips on.

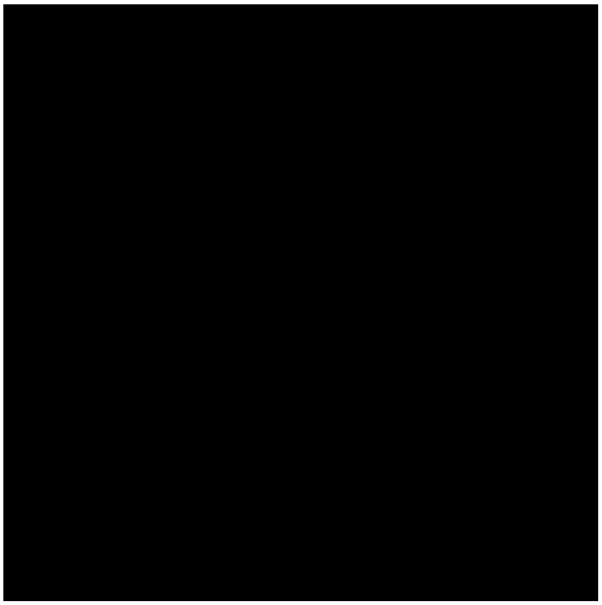
- Short stretch bandage (SSB) defined as an inelastic bandage system where one to three rolls of bandage are applied over orthopaedic wool.
- 2LCB systems defined as a bottom layer with cohesive compression bandage (which is the same as the 2-layer multicomponent bandages used in the EAG report)
- Compression wraps (CW) defined as adjustable hook-and-loop-fastened compression

As discussed in section 1, clinical experts advised was that SSB can typically be considered a type of 2LCB, which is the approach the EAG took in its clinical review, although they noted that it is possible for the number of layers in SSB to vary in practice. SSB was a separate treatment option in the NMA.

The outcome of the NMA was the number of individuals healed per arm (of a total number) over a certain follow-up. The NMA included results from 2 RCTs with individual patient data (VenUS IV and VenUS 6). It also included 19 RCTs with aggregate data. Of these, the EAG prioritised 9 studies for its clinical review. Further details of differences in the prioritisation criteria can be found in section 5.5.1 in the EAR. The use of prioritisation criteria is a key methodological difference between the EAG's review and the VenUS 6 NMA. For further detail, please see section 5.5.1 and table 6 and table 7 in the EAR.

VenUS IV results were not included in the base case NMA, because the two treatments it evaluates (4LCB and 2LCH) were assumed to have equivalent effectiveness as forms of EBC. However, at the request of the EAG, the VenUS 6 study team provided a scenario analysis that assessed 4LCB and 2LCH separately. The network diagram for the NMA scenario analysis can be found in figure 1. For the NMA base case network diagram, see figure 1 in section 5.5.1 of the EAR.

Figure 1: Network diagram for the scenario NMA



In these figures, 2LB = two-layer compression bandaging, 4LB = four-layer compression bandaging and HH = compression hosiery, as per the abbreviations used by VenUS 6.

Results from the base case VenUS 6 NMA, in the form of hazard ratios against the EBC reference treatment are presented in table 8 of the EAR, while the results from the scenario analysis are presented in table 9 of the EAR. Evidence from the VenUS 6 NMA suggests that

The EAG considered that the working NMA appeared generally well conducted

2.3 Ongoing studies

The EAG identified 1 ongoing study which is presented in table 3. Further details on the ongoing studies can be found in section 8.1 and table 20 of the external assessment report.

Table 3. Ongoing studies

Study name, status	Study type	Population	Compression products evaluated	Primary outcome
Evaluation of the efficacy of multilayer	NR	People with VLUs	Multi-layer compression (UrgoK2) plus an	12-week wound

Study name, status	Study type	Population	Compression products evaluated	Primary outcome
compression & UrgoStart Plus, 1 year study duration (approved 7.08.23)			interactive wound dressing (UrgoStart plus)	healing rates

3. Health economic evidence

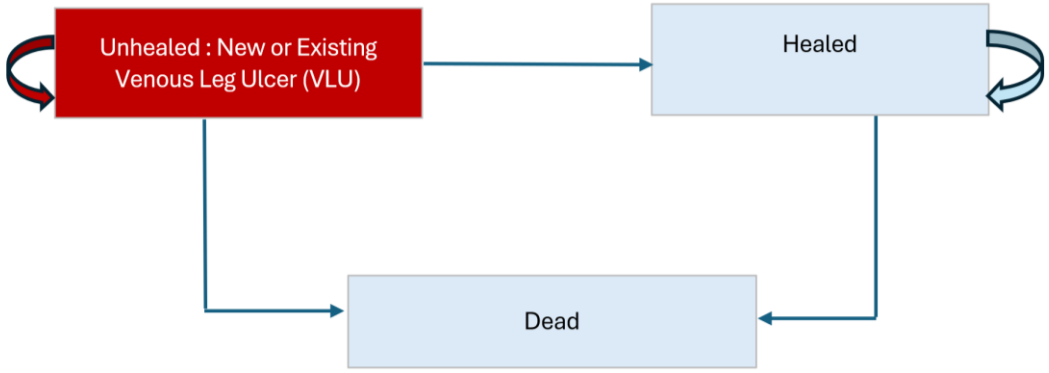
The external assessment group (EAG) did a review to identify suitable health economic models. They found 2 systematic reviews of previous economic evaluations, 3 trial-based economic evaluations and 7 model based economic evaluations (cost-utility analyses). However, none of the models were meeting the exact needs for this evaluation, so the EAG constructed a *de* novo model. An overview of these 12 economic evaluations is in section 7.1 of the external assessment report (EAR).

3.1 Health economic model

The EAG developed a state-transition (Markov) model (Figure 2) of 3 health states:

- Unhealed
- Healed
- Dead

Figure 2. Model structure



The model estimated the expected costs and QALYs accrued over a time horizon of 5 years with each of the 4 compression product types. Patients entered the model with an unhealed venous leg ulcer and at the point of

consultation with a medical care professional, where one of the 4 compression product types is applied. Each cycle, a patient has a probability of transitioning to the healed, or dead state. Based on healing rates observed in the clinical data, a transition period of 1 week was considered to capture costs and outcomes with sufficient granularity. While the venous leg ulcer was unhealed, patients were assumed to remain on the same compression product. However, treatment switching has been observed, even in controlled clinical trials, so this is a limitation of the model. The EAG also noted that recurrence of leg ulcers was not included in the model because the focus is on treating VLUs rather than prevention and because of available data limitations. The EAG's base case assumed cost differences for ankle size (i.e. published product price) and ambulatory status, but no difference in time to healing by either factor because of data limitations. Further details of the economic modelling and discussion are in section 7 and section 9 of the EAR, respectively.

Population

The EAG base case modelled a 65-year-old person with venous leg ulcers as VLUs are more common in people who are older. There is no source evidence to suggest a difference in outcome from treatment based on gender, so the only difference in the model is in general mortality (life expectancy). The EAG assumed an average risk of death by age between males and females.

3.2 Model inputs

Clinical inputs

Time to healing

The key input to the decision model was time to healing by compression product type, which were drawn from the VenUS 6 network meta-analysis (NMA) (see table 4). For further detail on survival curves for time to healing for the 4-layer compression bandages, see section 7.2.4.1 of the EAR.

Table 4: Hazard ratios of time to healing by compression product type

Compression product	Hazard ratio	95% equal-tailed credible interval
Four-layer compression bandage	1 (reference)	—
Two-layer compression bandage	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]
Compression wrap	[redacted]	[redacted]

Source: Means and 95% credible intervals estimated from scenario analysis CODA of 5,000 samples supplied to the EAG by the VenUS 6 study team.

Mortality

Probability of death was based on the UK life tables based on data for the years 2017 to 2019, as 2020 life tables are not recommended due to the impact of COVID-19 (Wailoo, 2024). This was then adjusted by a hazard ratio of 1.36 to reflect the increased mortality in people with VLUs compared with the general population (Ashby et al. 2014).

Resource use

Unhealed

Initially, Guest et al. (2017) was used to estimate usage of healthcare resources. The paper reported costs over a 6-month period for 2 different 2-layer compression systems and a 4-layer compression system, derived from a primary care research database (The Health Improvement Network, THIN database). However, because the EAG's decision model needed resource use disaggregated by healed and unhealed state, the EAG adjusted the resource use counts based on the likely pathway of people with VLUs.

Following discussions with clinical experts, the EAG identified 3 significant drivers for resource use and costs:

1. The number of contacts (visits) with healthcare professionals
2. Setting: at home, in a wound clinic or GP surgery
3. The salary band for the healthcare professionals

The EAG was unable to locate a reliable source for the average number of dressing changes per week for unhealed VLUs. The distribution of the number

of dressing changes was expected to be skewed, with a small proportion of patients needing a lot more dressing changes than the 'average' patient. As this is a key statistic for the economic evaluation, the EAG constructed a plausible but uncertain distribution for the number of dressing changes needed each fortnight, see Figure 6 in the EAR.

These assumptions led to a mean number of dressing changes per week of 1.60 (95% CrI 1.36–1.88) for 2-layer and 4-layer compression bandages (2LCB and 4LCB). For 2-layer compression hosiery (2LCH) and compression wraps (CW), the EAG assumed that some dressing changes would be done by someone other than a healthcare professional, estimating that such patients would need on average 1.11 healthcare professional contacts per week. Table 5 presents the weekly healthcare resource use while an ulcer is unhealed. For further detail on resource use for unhealed VLUs see section 7.2.5.1 of the EAR.

Table 5: Weekly healthcare resource use while ulcer unhealed

Resource	Four-/two-layer compression bandage	Two-layer compression hosiery/compression wraps
Community healthcare		
GP [a]	0.01	
Band 5 nurse [b]	1.60	—
Band 3 /4 healthcare staff [b]	—	1.11
Podiatrist	0.10	
Consumables		
Compression kit	1.60	2.0/26 (~0.08 pw) [c] 1.0/26 (~0.04 pw) [d]
Dressings	1.60	

Notes: [a] In surgery if patient ambulatory, home visit otherwise; [b] In wound clinic or GP surgery if patient ambulatory, home visit otherwise; [c] Two-layer compression hosiery only; [d] Compression wraps only

Upon healing of ulcer

Clinical experts advised that when a VLU has healed, a doppler ABPI test is undertaken, so this was incorporated as a one-off cost associated with transitions from the Unhealed to the Healed state in the Markov model.

Healed

Clinical experts advised that after healing, patients would typically be placed on maintenance compression, which would be compression hosiery though at a pressure lower than 40mmHg. Contacts with healthcare professionals would be infrequent, typically once per year. The EAG assumed that the maintenance compression hosiery would be replaced twice per year.

Costs

Technology costs and other consumables such as dressings

Unit costs of the intervention products were based on prices listed on the NHS Drug Tariff in June 2024 (see table 6). For the economic evaluation and the economically justifiable price (eJP) analysis, the lowest cost product was selected for each of the 4 compression product types for each product size. Products for ankle widths of 30cm or more were excluded from the costing. The EAG noted that in some cases price was insensitive to size and in others a smaller product was more expensive than the medium size.

Table 6: Unit costs for product type by size

	Product type			
Size	**4LCB**	**2LCB**	**2LCH**	**CW**
Medium (18-25cm)	£4.81	£7.26	£15.67	£105.10
Narrow (below 18cm)	£6.48	£7.26	£15.67	£105.10
Wide (25-30cm or 25-32cm)	£7.40	£8.30	£15.67	£105.10

4LCB: 4-layer compression bandage, 2LCB: 2-layer compression bandage, 2LCH: 2-layer compression hosiery, CW: compression wrap. Source: Drug Tariff Part IX, June 2024[3]

The confidential appendix from the external assessment report extracted the combined lowest cost price from both NHS Drug Tariff (publicly available) and Supply chain costs (confidential), which considers confidential discounts off the list prices offered to the NHS by suppliers.

Dressings were assumed to cost £0.57 each (BNF).

Community healthcare costs

These were estimated based on the PSSRU Unit Costs of Health and Social Care (2023). All these costs were assumed to be uncertain and were drawn from log-normal distributions with standard deviation equal to 10% of the mean. The costs for healthcare resource are in table 7. Further detail is reported in section 7.2.5.2 of the EAR.

Table 7. Community healthcare costs

	In surgery or wound clinic	At home
GP	£77 for 10 minutes	£117 for 30 minutes
Band 3 or 4 HCP	£19.50 for 32.5 minutes	£36.50 for 32.5 minutes plus 20 minutes of travel and £5 allowance for travel
Band 5 HCP	£28.71 for 32.5 minutes	£51.38 for 32.5 minutes plus 20 minutes of travel and £5 allowance for travel

Other costs

Ankle brachial pressure index testing was assumed to cost £22.48 (£20.48 in 2020/2021 prices) based on NICE Diagnostic Guidance 52. This was distributed log-normally with standard deviation equal to 20% of the mean.

Health-related quality of life

The EAG identified Iglesias et al. (2005) as the most appropriate study and assumed utility of 0.62 for an unhealed ulcer and 0.75 for a healed ulcer. This represents a significant improvement in quality of life. Other, less well-suited studies to answer the question, suggested a much less consequential difference. Therefore, the EAG did a scenario analysis in which the utility difference was set to 0.03 (Jull et al. 2010).

3.3 Model results

Base case

The EAG used fixed costs for each product type and undertook a probabilistic cost-effectiveness analysis. For the full results table, including different sizes,

see table 16 in section 7.1.3 of the EAR. All four product types are associated with very similar outcomes, with between 3.235 to 3.254 QALYs accrued over 5 years, with a range of 0.019 which is equivalent to 5 to 6 days of perfect health. On average, compression wraps (CW), and 2-layer compression hosiery (2LCH) incur the lowest (almost identical costs) but CWs yield the highest net monetary benefit. CWs dominated 2LCH and 4-layer compression bandages (4LCB) as these 2 compression types are more expensive and less effective. The added cost per extra QALY gained from 2-layer compression bandages (2LCB) is above NICE's willingness to pay threshold (£76,804 per QALY gained). Use of the NHS Supply Chain prices did not affect the results of the analysis, see confidential appendix.

The cost-effectiveness acceptability frontier for all analyses shows that CW have the highest probability of being cost-effective (~60%), at a willingness to pay of £20,000 per QALY. This is followed by 2LCH (~40%). As the willingness to pay rises the probability of the 2LCB becoming cost-effective increases. There is almost zero possibility of the 4LCB being cost-effective at any plausible willingness to pay threshold (Figure 3).

Figure 3: Cost-effectiveness acceptability curve/frontier

FLCB: four layer compression bandage; TLCB two layer compression bandage; TLCH two layer compression hosiery; CW compression wrap. Base case (medium ankle width, ambulatory person) shown. As optimal decision does not change with the threshold, the frontier coincides with the CW CEAC. Scenario analyses generated similar results.

A breakdown of costs is presented in table 17 of the EAR. Costs accrued in the 'healed' health state are broadly similar, which is consistent with the

comparators being of similar effectiveness. The overall cost differences are driven by the requirement for a Band 5 nurse for 4LCB and 2LCB, and compression product price which is higher for these 2 compression types compared with 2LCH and CW.

The parameter contributing most to decision uncertainty, was the relative treatment effect (hazard ratios) of the 4 compression product types. Further detail on this is reported in section 7.3.1.1 in the EAR.

Economically justifiable price (eJP) analyses

In the cost-effectiveness analysis, the compression wraps yielded the highest net monetary (and therefore health) benefit. Furthermore, it dominated 2LCH and 4LCB. As a result of this, the maximum eJP for the 4LCB, 2LCB and 2LCH was below zero, which means that they are not cost-effective at any price. The maximum eJP for CWs simplifies to the lowest priced product on the market (£105.10). Economically justified price analyses are in section 7.3.2 of the EAR.

Scenario analyses

The EAG repeated the decision analysis with an assumed lower utility benefit from a healed ulcer. This did not materially affect the cost-effectiveness results or the eJP. They also repeated the decision analysis with a scenario that assumed that a Band 3 nurse rather than Band 5 nurse administers 4LCB and 2LCB. This scenario also did not materially affect the results, and still showed lower costs associated with CW and 2LCH compared with 4LCB and 2LCB. All the scenario analysis results are described in section 7.3.3 of the EAR. The scenario analysis exploring different time horizons gave different results. Over a shorter time horizon (12 weeks), 2LCH is the most cost-effective product type and as the time horizon is lengthened, CWs become the preferred option (see table 10). Table 11 presents the eJP analysis for the shorter time horizon scenario.

Table 10: Scenario analysis results - shorter time horizon (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory, 12-week time horizon							
Two-layer compression hosiery	£323	0.148		£2,629	0.131	£710	0.101
Compression wrap	£346	0.148	£54,987	£2,614	0.131	£690	0.099
Four-layer compression bandage	£630	0.147	Dominated	£2,318	0.116	£402	0.057
Two-layer compression bandage	£645	0.148	£741,341	£2,323	0.116	£394	0.056
Medium ankle circumference, ambulatory, 24-week time horizon							
Two-layer compression hosiery	£492	0.306		£5,619	0.281	£1,647	0.235
Compression wrap	£516	0.307	£16,750	£5,624	0.281	£1,633	0.233
Four-layer compression bandage	£935	0.308	Dominated	£5,231	0.262	£1,223	0.175
Two-layer compression bandage	£961	0.305	£318,623	£5,138	0.257	£1,174	0.168
Medium ankle circumference, ambulatory, 52-week time horizon							
Two-layer compression hosiery	£703	0.681		£12,923	0.646	£4,066	0.581
Compression wrap	£716	0.685	£3,863	£12,979	0.649	£4,077	0.582
Two-layer compression bandage	£1,249	0.688	£175,580	£12,507	0.625	£3,566	0.509
Four-layer compression bandage	£1,372	0.680	Dominated	£12,225	0.611	£3,387	0.484

Table 11: Maximum eJP by population sub-group (shorter time horizon scenarios)

Analysis	4LCB	2LCB	2LCH	CW
medium ankle, ambulatory, 12 weeks	£0	£0	£15.67	£65.70
medium ankle, ambulatory, 24 weeks	£0	£0	£15.67	£65.70
medium ankle, ambulatory, 52 weeks	£0	£0	£0	£105.10

Comparison of results with those of VenUS 6

The comparison of the VenUS 6 and EAG's model structures and inputs are presented in table 12. A key structural difference was that the VenUS 6 model allowed for recurrence. A key methodological difference was in the estimation of transition probabilities.

[redacted]

Table 12: Comparison of VenUS 6 and EAG economic model structures and inputs

Key element	VenUS 6 economic model	EAG economic model
Time Horizon	Lifetime	5 years
Model structure	3-state Markov (state-transition) model; unhealed, healed, dead	3-state Markov (state-transition) model; unhealed, healed, dead
Allow for recurrence?	Yes (back transition from healed to unhealed)	No
Transition period	1 month	1 week
Estimation of transition probabilities	Estimation of survival function for EBC (including ulcer duration and size as covariates). HRs for other products applied from NMA. Monthly transition probabilities estimated from survival functions.	Estimation of survival function for 4LCB from published data (VenUS IV), not adjusted for ulcer duration and size. HRs for other products applied from NMA. Weekly transition probabilities estimated from survival functions.
Source of resource use	VenUS 6 study	protocol driven / expert opinion
Source of health state utilities	VenUS 6 study	Published literature

Table 13: VenUS 6 economic evaluation results (scenario analysis requested by EAG)

Treatment	Total costs £	Total QALYs	Inc. costs £	Inc. QALYs	ICER	NMB*
2LCH	[redacted]	[redacted]				[redacted]
CW	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
2LB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
4LB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Adapted from scenario analysis of VenUS 6 economic evaluation results. NMB, net monetary benefit.

4. User preferences

Eleven participants took part in the user preference assessment to identify what is important to users when choosing a compression product for treating venous leg ulcers (VLUs). Most participants were vascular or tissue viability nurses. A total of 7 criteria independent of clinical presentation were identified, defined, ranked in order of importance and weighted. The top 3 criteria included comfort of product, use of product by healthcare professional, patient or carer and bulkiness of product had a combined weighting of 70.9%. In addition, 3 criteria related to clinical presentation were identified. These highlighted the importance of clinical presentation such as wound condition, patient characteristics and for people with recurrent or non-progressing VLUs, previous treatment regimen and treatment efficacy, which can vary greatly between patients. Therefore, these criteria were not ranked, weighted or had performance rules developed because what may be important for one person with a specific clinical presentation may not be important for someone else. Both sets of criteria are closely related and thus there may be some overlap between them.

Details on the identified user preferences are in section 4.1 of the user preference report.

4.1 Survey of people with lived experience

Eighteen people completed the patient survey. The survey highlighted that venous leg ulcers have a big impact on people's lives including physical and emotional effects. It also highlighted that comfort and ease of use and bulkiness of the products were the most important criteria when choosing a compression product. The criteria ranking from the patient survey were in the same order as the ranking from the healthcare professionals.

Further details on the patient survey results are in section 4.2 of the user preference report.

5. Equality considerations

The final scope and the scoping equality impact assessment describe equality considerations for this assessment. The key studies in this assessment did not report subgroup data or study participant information on people with conditions that may limit self-care, people with low or high exudate wounds, people with very fragile skin, or people with irregular leg shapes. The EAG identified some additional equality issues, including venous leg ulcers are more common in intravenous drug users, who may have difficulty with morning appointments and appointment-based rather than drop-in clinics. Furthermore, a high proportion of people within prisons, remand centres and detention centres are former or current intravenous drug users. Finally, inequity of care provision depends on locality, including district nurse shortages and GPs in some areas not being contracted to provide lower limb management.

6. Key points, limitations and considerations

6.1 Clinical effectiveness

Key points

- The EAG included 32 studies and presented a narrative synthesis of 15 prioritised studies of which 14 were RCTs comparing the different

compression product types against each other. The clinical evidence was generally considered to be good quality and supports all compression product types evaluated as viable treatment options.

- Results from the VenUS 6 NMA suggested that [redacted]

Limitations

- Prioritised evidence did not present evidence specifically for any scoped subgroups.
- There was limited or no evidence for patient reported outcomes such as ease of treatment use and mobility.

Considerations for committee:

- What can the published studies and VenUS 6 network meta-analysis tell us about the comparative effectiveness between the different compression product types?

6.2 Health economic evidence

Key points:

- There is enough clinical evidence for cost-effectiveness. Compression wraps (CW) are most cost-effective in the EAG's base case; they are on average less expensive and more effective than the other compression product types. CW and 2-layer compression hosiery (2LCH) appear to be of equal, and lowest cost and may be considered to offer better value for money compared with 2-layer and 4-layer compression bandages as they are more expensive.
- The EAG regards the differences in outcomes as minor, with the difference between the most and least effective product type totalling 0.019 QALYs, the equivalent of 1 week of perfect health accrued over 5 years This is driven by the clinical evidence suggesting broad equivalence.

- Over a shorter time horizon (12 and 24 weeks), 2LCH is the most cost-effective product type. As the time horizon is lengthened, CWs become the preferred option.

Limitations:

- There was no data to do health economic analyses in the scoped subgroups
- There was considerable uncertainty in the model results:
    - The model assumed that individual products within product types were identical in effect
    - The model assumed that time to healing was unaffected by patient co-morbidity, BMI, ankle circumference, wound size and ambulatory status
    - The quality of resource use data was generally very low

Considerations for committee:

- Are the economic model structure, assumptions and clinical and cost parameters suitable for this assessment?
    - Are the estimated number of dressing changes reflective of current practice?
    - Which time horizon is most appropriate for this assessment?
- What can the model results tell us about the comparative cost-effectiveness of the different compression product types?

6.3 User preferences and patient survey

Key points:

- Compression product choice can be influenced by clinical presentation and preferences. Comfort, ease of use and bulkiness of the product were the most important factors when choosing a compression product.
- Clinical presentation of venous leg ulcers is very important in the choice of compression product used, so not all compression products are suitable for all types of venous leg ulcers.

Limitations:

- A potential limitation of the user preference assessment and patient survey is volunteer bias, so it is likely that the sample is not representative of the wider population. Most users were vascular nurse practitioners and tissue viability nurses but users that worked in the community were included.

Considerations for committee:

- What conclusions can be drawn from the user preference assessment?
- Are certain compression product types unsuitable for certain clinical presentations?

Appendix A Abbreviations

2LCB	2-layer compression bandage
4LCB	4-layer compression bandage
2LCH	2-layer compression hosiery
CW	Compression wrap
EAG	External assessment group
EAR	External assessment report
HR	Hazard ratio
ICER	Incremental cost-effectiveness ratio
LSA	Late-stage assessment
NMA	Network meta-analysis
NMB	Net monetary benefit
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
SSB	Short stretch bandage

Compression products for treating venous leg ulcers: late-stage assessment [GID-HTE10048]

EAG assessment report

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Maxwell S. Barnish	Project manager. Clinical effectiveness lead reviewer. Contributed to report writing and editing.
Daim Syukriyah	Led the EAG model development. Contributed to review of economic evaluations. Contributed to report writing and editing.
Alan Lovell	Led the EAG's literature searches and information management. Contributed to clinical and economic reviews. Contributed to report writing and editing.
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Aoi Nakayama	Contributed to review of clinical evidence.
G.J. Melendez-Torres	Contributed to review of clinical evidence.
Edward C.F. Wilson	Contributed to review of economic evidence. Guarantor.

This report should be referenced as follows. Barnish et al. Compression products for treating venous leg ulcers: late-stage assessment [GID-HTE10048]: EAG assessment report. Peninsula Technology Assessment Group (PenTAG), 2025. This report is accompanied by five appendices.

Confidential information

Confidential information contained within this report is shown in Table 1.

Table 1: Confidential information included in the report

Brief description	AIC/CIC	Page number(s)	Source
Summary of unpublished VenUS 6 NMA results	AIC	11	VenUS 6 team
Unpublished VenUS 6 trial results	AIC	55	VenUS 6 team
Unpublished VenUS 6 NMA results	AIC	58-59	VenUS 6 team
EAG interpretation of unpublished VenUS 6 NMA results	AIC	60-61	VenUS 6 team
Model inputs from unpublished VenUS 6 NMA results	AIC	71	VenUS 6 team
Information about changes to NHS Supply Chain prices	CIC	81	NHS Supply Chain
EAG interpretation of unpublished VenUS 6 NMA results	AIC	101	VenUS 6 team
VenUS 6 economic evaluation results and discussion related to these	AIC	111-112	VenUS 6 team
Analysis using NHS Supply Chain Prices	CIC/cPAS	cPAS appendix Model File (redacted version also supplied)	NHS Supply Chain
NMA inputs to model	AIC	Model file (redacted version also supplied)	VenUS 6 team

Abbreviations: AIC, academic in confidence; CIC, commercial in confidence; NA, not applicable; NMA, network meta-analysis.

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Abbreviations

Term	Definition
2LCB	Two-layer compression bandage
2LCH	Two-layer compression hosiery
4LCB	Four-layer compression bandaging/bandage systems
ABPI	Ankle brachial pressure index
AE	Adverse event
AIC	Academic in confidence
Ba	Adhesive bandage
BzeaH	Combination of bandage and hosiery, elastic, zinc paste and adhesive
BHeH	Combination of bandage and hosiery, elastic
CASP	Critical Appraisal Skills Programme
CI	Confidence interval
CIC	Commercial in confidence
CODA	Convergence diagnosis and output analysis
CW	Compression wrap
DCE	Discrete choice experiment
EAG	External Assessment Group
EBC	Evidence-based compression
eJP	Economically justifiable price
GP	General practitioner
HR	Hazard ratio
HRQoL	Health Related Quality of Life
HV	Hosiery with Velcro device
ICTRP	International Clinical Trials Registry Platform
INAHTA	International Network of Agencies for Health Technology Assessment
IPD	Individual patient data
IQR	Interquartile range
ITT	Intention-to-treat
L&R	Lohmann & Rauscher
LSA	Late-stage assessment
MCS	Mental component score
mmHg	Millimetres of mercury
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NMA	Network meta-analysis
NR	Not reported

Term	Definition
NS	Non-significant
Paste	Paste banding product
PCS	Physical component score
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSS	Personal Social Services
QALY	Quality-adjusted life year
r2LB	Reusable two-layer bandaging
RCT	Randomised controlled trial
RFI	Request for Information
RWE	Real-world evidence
SD	Standard deviation
SF-12	Short form health questionnaire 12 items
SOC	Standard of care
SSB	Short-stretch bandaging
TTO	Time-to-outcome
UI	User interface
UK	United Kingdom
VLU	Venous leg ulcer

Executive Summary

Introduction

This late-stage assessment (LSA) aimed to investigate the evidence base for compression products for treating venous leg ulcers to assess whether price variations are explained by differences in features and whether technologies represent value for money in the NHS. The assessment protocol outlined the evaluation to be conducted by the External Assessment Group (EAG), in its role as an independent, academic group supporting NICE. This report provides a description of the assessment undertaken by the EAG and its findings.

In brief, the EAG conducted systematic evidence searches to identify and synthesise evidence that provided insight into the clinical and cost effectiveness of compression products for treating venous leg ulcers using the eligibility criteria set in the review protocol. Economic analyses, including the development of a de novo economic model and additional exploratory analyses were conducted to establish the link between the features of compression products and price. As part of its report, the EAG provides an overview of contextual considerations that surround the assessment of compression products for treating venous leg ulcers. Finally, the implications for decision-makers and for future research are provided.

Clinical and technological evidence

The systematic review of published and unpublished evidence, including information provided by companies that produce compression products for venous leg ulcers, identified 17 prioritised studies that evaluated the clinical effectiveness of compression products for treating venous leg ulcers. These 17 studies provided evidence for all four scoped features of interest: 4-layer compression bandages, 2-layer compression bandages, 2-layer compression hosiery and compression wraps. Six prioritised studies were conducted exclusively in the UK, one further study included UK sites and all but two prioritised studies were conducted in a European setting. Head-to-head comparisons were available for many combinations of scoped features.

As the different types of compression product listed in the final scope for this appraisal were themselves the key features of interest, it was not indicated to conduct an intervention components analysis (to explore the relationship between product features and scoped outcomes). The EAG consequently conducted a narrative synthesis to explore potential patterns across the evidence that could be used to draw conclusions about the clinical effectiveness of

product features. The most commonly undertaken comparison was between 4-layer and 2-layer compression bandaging. Studies showed that 2-layer bandaging was at least as good as 4-layer, with some evidence 2-layer may be better. Hosiery and wraps (noting there was only one study on wraps for this comparison) were shown to be equivalent to 4-layer bandaging. There was some evidence that wraps may be better than 2-layer bandaging for % wounds healed, but there were only two studies and one used short stretch 2-layer bandaging. Hosiery was shown to be better than 2-layer bandaging – at first this appears contradictory but may be explained by all 2-layer products for this comparison being short stretch and therefore not the same products that were typically compared with 4-layer bandaging. There was some evidence that the type of 2-layer bandaging may influence outcomes, i.e. this feature is not necessarily unitary.

Evidence from the VenUS 6 NMA suggests that [redacted]

Economic evidence and analysis

The EAG developed a *de novo* model estimating the costs and QALYs accrued from the four types of compression product. The initial analysis followed the NICE reference case identifying the most cost-effective product type with a fully incremental analysis (termed the 'referent'). The price of each product type was set at the lowest price product available on the Drug Tariff (June 2024). Following this, the eJP for all other product types was set such that the ICER of that product type relative to the referent was just equal to the threshold (£20,000 per QALY).

The results of the analysis suggested that over five years, the differences in QALYs accrued between the four compression product types were very small, but compression wraps and compression hosiery appear to be associated with lower costs. This is the case for all ankle circumferences and whether or not the person with VLU is ambulatory or not. The difference in cost between product types is driven to a large part by the requirement for a band 5 nurse to apply 2LCB and 4LCB, but a band 3 or 4 for CW and CH. Based on expected values, due to the relative costs and consequences of the four compression product types, there is no maximum economically justified price for any compression product except for CW, which defaults to the minimum priced CW product. However, the EAG urges caution in the interpretation due to the limitations of the analysis, and the small absolute differences in outcomes between product types.

Key points for decision-makers

2-layer compression bandaging may be as effective as 4-layer compression bandaging or more effective, based on study results. Compression hosiery and wraps also may show comparable effectiveness. A key uncertainty is that results of studies using 2-layer compression bandaging were quite variable and this may relate to the type of two-later compression bandaging used.

Based on this rapid overview economic modelling, compression wraps are the most cost-effective option at the lowest priced product available. However, CW and CH may be considered broadly equivalent in terms of cost-effectiveness. Other product types should only be recommended where 2LCH is not appropriate for the person with VLU.

Research recommendations

Due to lack of data, the decision model assumed that time to healing was unaffected by leg size, BMI, co-morbidities, ambulatory status and wound size. Such data would increase the accuracy and precision of time to healing in different patient groups. The key model input with the greatest impact on decision uncertainty was the treatment effect (i.e. hazard ratio of time to healing with the different product classes). There was very little impact of uncertainty in health state utilities or in resource use / cost estimates in the quantitative analysis of value of information. However, overall the EAG rated the quality of resource use data in general very low and good quality studies in this area would be valuable.

It was noted that the VenUS 6 study will address many of the uncertainties in the evidence base once finalised results for all outcomes are published in the peer-reviewed literature. Therefore, it may be appropriate for research recommendations to focus on addressing matters of user preference and subgroups as well as how to overcome any implementation issues. However, one key area for effectiveness research may be understanding the different results observed in 2-layer bandaging studies and how these may relate to different types of 2-layer bandaging, including tubular and short stretch systems. Furthermore, it should be noted that the study design of VenUS 6 assumes clinical equivalence between four-layer compression bandaging and 2-layer compression hosiery. This may be a limitation, although the VenUS-IV trial[1] showed these two treatments to be of relatively similar effectiveness.

1. DECISION PROBLEM

The decision problem is described in the scope[1] and EAG comments are included in the protocol.[2] Following the initiation of the EAG assessment, the following changes and clarifications were made to the decision problem:

- **Broadening of definition of 'strong compression'**: In the final scope for the appraisal, strong compression was defined as a pressure of ≥ 40 mmHg. However, review of company Request for Information (RFI) forms found some products classed as strong compression delivered between 30 and 40 mmHg. The EAG considered that it would be preferable to include evidence for these products where the evidence is otherwise eligible.
- **Study settings**: Products in use in the UK were preferred where possible. However, as this is a features-based assessment, products that are not in UK use could be considered in certain circumstances. Specifically, where studies using these products address a comparison for which there was a relative lack of prioritised evidence or otherwise offer a unique perspective.

2. TECHNOLOGIES

Details of the technologies evaluated in this assessment are provided in the NICE scope.[2] At the time of the assessment, 717 compression products for venous leg ulcers were listed on the NHS Drug Tariff,[3] plus any additional products on NHS Supply Chain. The EAG was advised that about 80% of prescribing of compression products on the NHS is in community settings through the Drug Tariff with the remainder prescribed in hospital settings through NHS Supply Chain.

Late-stage assessments can focus on the innovative features that individual products may possess or the products in their entirety.[4] In this case, the 'features' for this appraisal were agreed to be the four types of compression product as listed on the final scope. Any product of one of these four types used in the NHS was eligible for inclusion. RFI forms were received from nine companies: Creed Health, Essity, Haddenham, L&R Medical, medi UK, SIGVARIS, Smith and Nephew, Solventum and Urgo. For technologies that met the eligibility criteria, but no RFI was provided, the EAG assessment was based on publicly available information. Anticipated benefits of different features are shown in Table 2.

Table 2: The anticipated benefits of features of compression products for people with venous leg ulcers

Features	How are they intended to benefit people with venous leg ulcers?	Groups of people who may use these
4-layer compression bandage systems and kits	This is the traditional approach to compression in the UK.	Most suitable where people can readily access clinical services and staff with sufficient training to apply 4-layer bandaging are available.
2-layer compression bandage systems and kits (these include 2-layer inelastic systems and 2-layer multi-component systems)	Can be changed by staff with less specialist training, such as nursing associates (Band 4). Increased mobility. Able to wear own footwear.	People in care homes. People living in locations where there are challenges with access to staff with sufficient training to apply 4-layer bandaging.
2-layer compression hosiery	Patient or carer can change the product. Increased mobility. Able to wear own footwear. More discreet. Promote self-care.	People living in settings where they have access to help changing products, or people who are mobile enough to change their own products, and do not have access to staff with sufficient training to apply 4-layer bandaging. More active patients who would benefit from a product that is less restrictive of mobility. Younger people who may not accept bandaging for cosmetic or psychological reasons.
Compression wraps	Patient or carer can change the product. Increased mobility. Able to wear own footwear. Promote self-care.	People living in settings where they have access to help changing products and do not have access to staff with sufficient training to apply 4-layer bandaging.

3. CLINICAL CONTEXT

The clinical care pathway is presented in the protocol. As part of its assessment, the EAG also sought clinical input and gained the following additional understanding that provides context to understanding the effectiveness of compression products for venous leg ulcers:

- **Standard of care**. During the assessment, the EAG learnt that traditionally, 4-layer compression bandages have been the standard of care. In recent years, there has been increasing acceptance of 2-layer compression products, 2-layer compression hosiery, and compression wraps, provided that the wound is small enough.

- **Service organisation**. During the assessment, the EAG gained insight into how services for treating people with venous leg ulcers are organised. Broadly, care is sub-divided into community services and hospital services. Within community services, there are clinics for ambulatory patients as well as district nursing team home-visiting services for patients who are housebound. This would include those in supported living and care homes. Some differences between Trusts were noted in how services are structured, the extent of community clinic services and how care is subdivided between hospital and community settings. The EAG was advised that in some localities GP services are not contracted to provide lower limb management, with care located in minor injuries units instead. Within hospital services, expertise in compression bandaging is primarily in vascular services and dermatology clinics. Advice from experts indicates that other hospital staff may not have the training to know about different compression products.

- **Resource use**. The EAG learnt that there were differences in appointment duration between Trusts, as well as between hospital and community settings. In hospital settings, appointment duration may be 30 minutes for the initial assessment and 10 minutes for follow-ups, whereas in community settings, 90 and 30 minutes respectively may be more common. The intention is to achieve healing in 12 weeks, but there was considerable variation in whether this was achieved. Frequency of appointments may be greater in community settings, home visits can be several times a week, but will depend on clinical need, in particular levels of exudate. Initial appointments need to be conducted by at least Band 5 staff, while follow-up appointments can be Band 3 or above.

- **Clinically relevant outcomes**. The EAG was advised that the most clinically relevant outcomes were healing rate / time to healing, time to compression, comfort, ease of

application, ability to undertake normal activities and wear normal footwear, quality of life, and cost effectiveness. The EAG considered that most of these were captured by the final scope for this appraisal.

- **Generalisability of international evidence**. The EAG was advised that studies in Europe would be broadly applicable, although venous leg ulcer care in other developed countries may be ahead of the UK and compression levels in Europe tend to be higher for hosiery. Therefore, benefits in European studies may overestimate expected benefits in an NHS setting. In the UK, only specialist nurses would tend to use compression at levels of >= 40 mmHg. There may also be differences in healthcare system organisation, where for example in New Zealand, the EAG was advised that the standard of care can generally be higher as there are fewer patients per clinic due to population differences.

4. EQUALITY ISSUES

The EAG identified the following equality issues in this assessment, based on expert advice:

- Venous leg ulcers are more common in older people.
- Venous leg ulcers are more common in ethnic minorities due to co-morbidities
- Venous leg ulcers are more common in women than men and can be pregnancy related (though some clinical experts felt that gender was fairly balanced in their experience).
- Rural living, homeless and Traveller populations may face additional challenges accessing appointments.
- Venous leg ulcers are more common in intravenous drug users, who may have difficulty with morning appointments and appointment-based rather than drop-in clinics.
- Inequity of care provision depending on locality, including district nurse shortages and GPs in some areas not being contracted to provide lower limb management.
- Socioeconomic status – some people cannot afford to take time off work to attend appointments or cannot afford travel costs.
- People within prisons, remand centres and detention centres. There are a high proportion of former/current IV drug users within these environments

5. CLINICAL AND TECHNOLOGICAL EVIDENCE REVIEW

The EAG identified 14 prior systematic reviews broadly relevant to the topic of venous leg ulcers (listed in Table 2 of the protocol). The EAG reflected upon the viability of updating one of these reviews instead of conducting its own review of the clinical effectiveness evidence. However, the EAG concluded that none of the available systematic reviews were recent enough to offer sufficient efficiency savings versus conducting our own review and sufficiently aligned to the decision problem for this appraisal. Of the eight systematic reviews since 2020, three[5-7] did not consider 2-layer compression hosiery or compression wraps, one[8] focused on comparing compression with no compression, one[9] only considered studies with healing as an outcome, one[10] was focused on recurrence, one[11] only considered studies with HRQoL and pain outcomes and one[12] focused on clinical decision making rationales. The Mauck et al.[13] review listed in Table 2 of the protocol was published in 2014 and focused on healing and recurrence outcomes. Finally, the VenUS-IV network meta-analysis[1] was based on a Cochrane review[14] with a search cut-off in 2012 and did not consider compression wraps. Therefore, there was no existing systematic review suitable for the EAG's clinical review purposes.

The EAG conducted the evidence review consistent with the decision problem, allowing for the additional considerations described in Section 1, and the review methods outlined in the review protocol,[15] subject to the minor protocol variation to the decision problem regarding the definition of strong compression as discussed above and one further variation as described below. Due to the volume of clinical evidence identified, including several randomised controlled trials (RCTs), it was decided to only consider full-text articles for inclusion rather than conference abstracts, which provide far less detailed information about the studies and are not subject to the same degree of peer-review as full text publications.

5.1. Evidence search strategies and study selection

The clinical evidence searches sought to identify reports of the effectiveness and safety of the features of compression products for treating people with a venous leg ulcer. Database searches were performed in Medline, Embase, Cochrane CENTRAL, Cochrane Database of Systematic Reviews, and CINAHL. Trial protocols were identified from searches in ClinicalTrials.gov,[16] the International Clinical Trials Registry Platform (ICTRP),[17] and Cochrane Protocols.[18] All evidence sources submitted by companies during the RFI process were assessed against the inclusion criteria – those that met these criteria were added to the screening process.

The search is fully described in the published protocol.[15] No amendments to the planned search were made. Details of the search approach, including lists of databases, search strategies and outcomes can be found in Appendix A.

Screening took place in Rayyan[19] and was performed using the inclusion and exclusion criteria described in the published protocol.[15] Following the identification of eligible studies, the EAG conducted a process of prioritisation, in line with the methods and process statement for late-stage assessment,[4] to select the evidence most pertinent to decision-making. In the prioritisation process, factors including study design, study setting and location, as well as sample size, were taken into account. Prioritisation was also conducted based on the technologies in the studies to ensure all technologies were captured.

Overall, the EAG included studies in adults with venous leg ulcers that compared a scoped strong compression product used in the NHS with either 4-layer compression bandages or another compression product considered to represent standard of care in the NHS and assessed at least one scoped outcome.

5.2. Included and excluded studies

A total of 1,757 records were retrieved by the database searches. Of these, 674 records were removed as duplicates, leaving 1083 to be screened at title and abstract, after which 119 were identified for full text retrieval. All 119 full texts were successfully retrieved. Six further studies were added to the full text database from the RFI received from companies – leaving a total of 125 studies to appraise at full text. From these, 34 studies were included. The EAG identified 106 records through trial protocol searches. Of these, 87 were excluded as not relevant to the present decision problem and 19 evaluated for consideration in the ongoing studies list (Table 26). From these, the EAG identified one further record that relates to an ongoing study pertinent to the present decision problem. A PRISMA diagram of the search and screen process is provided in Appendix B. A list of studies excluded at full text along with their reason for exclusion is provided in Appendix C. The EAG identified 17 prioritised studies from its systematic review and company RFIs (see Appendix D for the rationale). Table 3 is a 'landscape map' showing the evidence that was available for each feature of interest. Table 4 summarises the characteristics of the prioritised studies.

Sixteen of the identified prioritised studies were RCTs – the other[20,21] was a large UK retrospective cohort study comparing different forms of compression for venous leg ulcers in the

context of routine NHS practice. Six were conducted exclusively in the UK, while one further study[22] included some UK sites. With the exception of one study in the USA[23] and one in Australia,[24] the remaining studies were conducted in Europe. Clinical input to the EAG was that European studies would typically generalise best to UK practice, noting that compression used in Europe may typically be stronger than used in UK practice, while differences in service organisation in North America and Australia may reduce generalisability. Evidence covered all four compression product features listed in the scope – 4-layer bandaging, 2-layer bandaging, 2-layer compression hosiery and compression wraps. Head-to-head RCT evidence was available directly comparing features with each other. Quality appraisal of the includes studies is described in Section 5.3. Results and synthesis are presented in Section 5.4. Furthermore, information about the ongoing VenUS 6 trial, for which results are not yet published, is provided in Section 5.5.

Table 3: Landscape map of in-scope clinical studies identified for each feature

Feature	Randomised trial evidence	Observational study evidence
4-layer compression bandage systems and kits	Adderley et al (2014) **Ashby et al (2014a)** Ashby et al (2014b) **Blecken et al (2005)** **Dolibog et al (2014)** **Finlayson et al (2014)** **Franks et al (2004)** **Gillet et al (2019)** **Iglesias et al (2004)** **Karanikolic et al (2018)** **Lazareth et al (2012)** Moffatt et al (2008) **Moffatt et al (2003)** Scriven et al (1998) Szewczyk et al (2010) Ukat et al (2003) Wong et al (2012)	Cameron et al (1996)[c] **Guest et al (2017)** Guest et al (2015) Lane et al (2001) Meaume et al (2023)

Feature	Randomised trial evidence	Observational study evidence
2-layer compression bandage systems and kits	Coull et al (2006)[a] **Dolibog et al (2014)** Dolibog et al (2013) **Franks et al (2004)** **Gillet et al (2019)** **Iglesias et al (2004)** **Junger et al (2004a)** **Junger et al (2004b)** **Lazareth et al (2012)** **Mariani et al (2008)[b]** Milic et al (2007) Moffatt et al (2008) **Moffatt et al (2003)** **Mosti et al (2020)** **Polignano et al (2004)** Scriven et al (1998) **Stather et al (2021)** Szewczyk et al (2010) Ukat et al (2003) Wong et al (2012)	Brizzio et al (2006)[d] **Guest et al (2017)** Guest et al (2015) Meaume et al (2023)
2-layer compression hosiery	Adderley et al (2014) **Ashby et al (2014a)** Ashby et al (2014b) **Dolibog et al (2014)** Dolibog et al (2013) **Finlayson et al (2014)** **Junger et al (2004a)** **Mariani et al (2008)** Nelson et al (2006) **Polignano et al (2004)** Szewczyk et al (2010)	Brizzio et al (2006)
Compression wraps	**Blecken et al (2005)** **Mosti et al (2020)** **Stather et al (2021)**	None identified

a = bandage can be used with different amount of layers, this study used 2 layers including padding, b = two or more layers, c = vs single-layer bandage consider NHS SOC at the time; d = short-stretch 'multilayer bandage', taken to be 2-layer based on expert advice. Studies in bold are prioritised.

Short Stretch Bandaging (SSB) was identified as a particular sub-type of compression bandaging that featured frequently in the identified studies. It was not listed as a separate intervention category on the NICE final scope for the appraisal. However, through discussion with clinical experts, it became clear that it was an important intervention and should not just be excluded. It was noted that the number of layers used in SSB can vary in clinical practice and

indeed clinical trials between one and three layers. However, following discussion with clinical experts, it was clear that SSB are most frequently used as 2-layer bandages and the best place to categorise them in the clinical review for this appraisal is alongside 2LCB. This fits with the features-based approach to LSAs, even if some studies used SSB with for example an additional top layer for particularly oedematous limbs or in cases of slippage. However, noting SSB are a sub-type of bandage, differing in its features from multi-component 2LCB systems, we ensured that we specifically discussed in our results where studies used SSB. Furthermore, given their different cost properties, the economics team considered SSB separately. Clinical expert advice was that cohesiveness is not a particularly important feature in describing compression products. Clinical expert advice was that tubular bandages are not typically used for compression in the UK, and they do not offer graduated compression. Therefore, while studies including a tubular bandaging arm may be useful for facilitating comparisons where there is limited other evidence, given the pragmatic nature of an LSA, these studies should still be seen as limited in terms of the information they can offer. Further clinical expert advice to the EAG after the prioritisation process indicated that studies using tubular compression are not the most relevant to this appraisal as they offer graduated compression rather than strong compression.

Table 4: Prioritised studies with clinical and technological evidence

Study name, design and location	Intervention(s) and comparator **Note: exact pressure values are shown where available**	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Ashby et al, 2014,[1] VenUS IV, RCT, UK	Compression hosiery (at least 40 mmHg) (Carolon Multi-Layer Compression System (H&R Healthcare); Clini Duo40 (CliniSupplies); Mediven Ulcer kit (medi UK); Activa leg ulcer hosiery kit (Activa Healthcare); Jobst UlcerCARE (BSN medical) or VenoTrain ulcertec (Bauerfeind UK)) vs 4-layer bandaging (various UK products delivering 40mmHg pressure at the ankle, per clinical nurse choice).	457 people with venous leg ulcers (of which 453 were analysed). Recruited from community nursing teams, GP practices and leg ulcer clinics. Follow up for 12 months. Analysis sample size per arm: 230; 223.	• **% wounds healed** was similar in the compression hosiery (76.1%) and 4-layer bandaging (79.3%) arms. • Median **time to healing** was similar in the compression hosiery (99 days) and 4-layer bandaging (98 days) arms – adjusted model HR 0.99 (95% CI 0.79, 1.25). • **Quality of life** was similar in the compression hosiery (SF-12 PCS baseline mean 38.1 (SD 10.8), 12 months 39.1 (11.9); SF-12 MCS baseline 48.6 (12.0), 12 months 49.3 (10.8) and 4-layer bandaging (SF-12 PCS baseline 38.8 (11.7), 12 months 38.5 (12.4); SF-12 MCS baseline 50.5 (10.4), 12 months 50.9 (11.6)) arms – there was no significant evidence of difference in LLMs. • **Ulcer-related pain** in the past 24 hours was similar in the compression hosiery (baseline mean 28.0 (SD 27.1), 12 months 18.0 (24.6)) and 4-layer bandaging (baseline 35.5 (30.4), 12 months 18.6 (27.6)) arms.	Large UK RCT that is likely to provide some of the most valuable results besides VenUS 6. However, it does not include 2-layer bandages.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			• **Change to a non-trial treatment** was more common in the compression hosiery (38.3%) than the 4-layer bandaging (27.8%) arm. • **Daytime adherence** (wearing every day) was high in both the compression hosiery (90.7%) and 4-layer bandaging (96.9%) arms. • **% participants with a serious adverse event** was similar in the compression hosiery (14.3%) and 4-layer bandaging (14.7%) arms. • **Death** was more common in the compression hosiery (20.9%) than the 4-layer bandaging (7.1%) arm. • **Hospitalisation** (required or prolonged) rates were similar in the compression hosiery (74.4%) and 4-layer bandaging (76.2%) arms. • **Non-serious adverse events** were more common in the compression hosiery (67.0%) than the 4-layer bandaging (58.0%) arm. • **Infection** rates were similar in the compression hosiery (5.7%) and 4-layer bandaging (6.9%) arms.	

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Blecken et al, 2005,[23] RCT, USA	Wrap (CircAid (medi UK)) vs 4-layer bandaging (various).	12 people with bilateral venous leg ulcers. Recruited from a hospital setting. Follow up for 12 weeks. Analysis sample size per arm: 12;12	• **% wounds healed** was the same in the wrap and 4-layer bandaging groups (both 33%). • **Adherence to treatment** was reported as 100% in both groups. • **Wound size reduction** (cm2 per week) was similar in the wrap (change -35.16) and 4-layer bandaging (change -27.6) arms – p = 0.369.	Small scale RCT, however it assesses wraps, for which the evidence base is generally more limited. The American context should be noted with regard to generalisability.
Dolibog et al, 2014,[25] RCT, Poland	Compression hosiery (Ulcer X (SIGVARIS) – 60 mmHg) vs 4-layer bandaging (SIGVARIS products delivering at least 45 mmHg) vs 2-layer bandaging (SIGVARIS products delivering 20-30 mmHg – i.e. reduced compression).	147 people with venous leg ulcers. Recruited from a hospital setting. Follow up for 2 months. Analysis sample size per arm: 30; 29; 30	• **% wounds healed** was similar in the hosiery (56.66%) and 4-layer bandaging (58.62%) arms, but lower in the 2-layer bandaging (16.66%) arm (p=0.03 for both comparisons vs 2-layer bandaging). • **Adherence to treatment** was reported as 100% in all groups. • **Wound size reduction** was similar in the hosiery (change -14.74) and 4-layer bandaging (-13.97) arms, but smaller in the 2-layer bandaging (-6.17) arm.	European RCT that compares 5 types of compression, although not all arms are within scope. It should be noted that the 2-layer arm delivers reduced compression. While in scope, compression hosiery at 60 mmHg is stronger than
Finlayson et al, 2014,[24] RCT, Australia	4-layer bandaging (various) vs class 3 (i.e. 30-40 mmHg) compression hosiery (various).	103 people with venous leg ulcers. Recruited from outpatient clinics. Follow up for 24 months. Analysis sample size per arm: 53; 50	• **% wounds healed** was higher in the 4-layer bandaging (84%) than compression hosiery (72%) arm, but the difference was not statistically significant (p=0.14). • Median **time to healing** was shorter in the 4-layer bandaging	RCT comparing compression hosiery with 4-layer bandages. Compares product features rather than specific products. It is understood that the product range in

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			(10 weeks) than compression hosiery (15 weeks) arm, p=0.003. • **Quality of life** (QL Index) scores were similar in the 4-layer bandaging (baseline mean (SD) 7·56 (2·20); 24 weeks 8·00 (2·36)) and compression hosiery (baseline 8.33 (1·72); 24 weeks 8·36 (2·43)) arms, p=0.223. • **MOS Pain Measures Pain Severity Scale**: Mean (SD) for 4-layer bandaging was 51·8 (28·3) at baseline and 23·0 (22·1) at 24 weeks. Mean (SD) for compression hosiery was 50·0 (26·4) at baseline and 34·0 (23·3) at 24 weeks, p<0.001 for main effect. • **Adherence** (at least three quarters of the time) was similar in both groups (88% 4-layer bandaging; 85% compression hosiery). • **Reduction in ulcer area** was similar in both groups (mean (SD) 96% (15.6%) 4-layer bandaging; 93% (14.6%) compression hosiery), p=0.27. • Few people in either group experienced an **adverse event** (6% 4-layer bandaging vs 4% compression hosiery).	Australia is generally comparable with the UK.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Franks et al, 2004,[26] RCT, UK	2-layer short stretch bandaging (Flexiban (Activa Healthcare) vs 4-layer bandaging (composed of Flexiban (Activa Healthcare), Setocrepe and Elset (SSL), and Coban (3M).	159 people with venous leg ulcers (of which 156 were analysed). Recruited from clinical centres. Follow up for 24 weeks. Analysis sample size per arm: 82; 74	• **% wounds healed** was similar in the ITT population for short stretch bandaging (75.6%) and 4-layer bandaging (79.7%), adjusted HR 1.08 (95% CI 0.63-1.85, p=0.79). • **Discontinuation** rates were similar in both groups (short stretch bandaging 20.7%; 4-layer 21.6%). • **% participants with an adverse event** were higher in the 4-layer bandaging (31.1%) than the short stretch bandaging (26.8%) arm. • **Tissue damage/new ulcers** were numerically more common in the short stretch bandaging (3.7%) than the 4-layer bandaging (2.7%) arm, though significance of this difference was NR. • **Pain** was equally common in the short stretch (2.4%) and 4-layer bandaging (2.7%) arms. • **Maceration** was equally common in the short stretch (2.4%) and 4-layer bandaging (2.7%) arms.	UK RCT comparing 4-layer with short stretch bandaging (Actico plus underlay).

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Gillet et al, 2019,[27] RCT (non-inferiority), France	2-layer bandaging (BIFLEX (Thuasne)) vs 4-layer bandaging (PROFORE (Smith & Nephew).	92 people with venous leg ulcers (of which 88 formed the full analysis set). Recruited from medical centres. Follow up for 16 weeks. Analysis sample size per arm: 47; 41	• **More wounds were healed** in the 2-layer bandaging (48.9%) vs 4-layer bandaging (24.4%) arm, p=0.02. • **Mean change in SF-12** by week 16 was not statistically significantly different between the arms, though was numerically greater in the 2-layer bandaging (+1.95 (SD 1.51) compared to the 4-layer bandaging arm (+0.76 (1.46)). • **Adjusted mean change in wound-related pain** was not statistically significantly different between groups – 2-layer bandaging -13.83 (SD 3.68) vs 4-layer bandaging -15.68 (4.0). • **Participants** reported significantly greater **satisfaction** with the softness (p=0.024), breathability (p=0.010), thickness (p=0.011) and putting shoes on simplicity (p=0.033) of 2-layer bandaging vs 4=layer bandaging. • **Physicians** indicated significantly higher **satisfaction** with 2-layer bandaging vs 4-layer bandaging for: application simplicity (p=0.024); application time (p=0.003); practicality of the system (p=0.002) and comfort	European RCT comparing 2-layer and 4-layer bandaging. This is considered a relevant prioritised study, as this is a features-based appraisal, though the specific 2-layer product does not appear on the Drug Tariff or Supply Chain.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			during handling (p=0.002). No difference in slippage along the leg was reported between groups (p=NS). • % of participants experiencing any **adverse event** was similar between arms (8.2% 2-layer bandaging vs 9.3% 4-layer bandaging). • % of participants experiencing **pain in extremity** was similar between arms (2% 2-layer bandaging vs 2.3% 4-layer).	
Guest et al, 2017,[21] retrospective cohort study, UK	2-layer bandaging (Coban 2 (3M)) vs 2-layer bandaging (Ktwo (Urgo)) vs 4-layer bandaging (PROFORE (Smith and Nephew).	600 people with venous leg ulcers. Routine database from GP settings. Follow up for 6 months. Analysis sample size per arm: 200; 200; 2000	• **More wounds were healed** in the cohesive 2-layer compression (Coban 2, 76%) than the 2-layer compression system (70%) than the 4-layer compression (64%) arm, overall effect p<0.05. • **Time to complete healing** was similar in the three groups – cohesive 2-layer compression mean 1.6 (SD 1.8) months, 2-layer compression system 2.0 (1.7), 4-layer compression 2.1 (1.9), but there was a statistically significant effect (p<0.003). • **QALY gain** 0.413 (SD 0.059) for cohesive 2-layer compression, 0.404 (0.057) for 2-layer compression system and 0.396	This is the only non-randomised study considered to be prioritised; however, this is because it is a large retrospective analysis of clinical outcomes by type of compression in routine NHS practice.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			(0.056) for 4-layer compression, overall effect p=0.006. • **% who switched treatment** 23% in the 4-layer compression arm compared to 8% for cohesive 2-layer compression and 3% for 2-layer compression system. • **Wound size reduction** was similar in all three arms (65% cohesive 2-layer, 68% 2-layer compression system, 62% 4-layer compression). • **Mean number of dressings** over a 6-month period was higher for 4-later compression bandaging (69.3) than cohesive 2-layer compression (41.9) or 2-layer compression system (44).	
Iglesias et al, 2004,[28] VenUS-I, RCT, UK	4-layer bandaging (various: PROFORE (Smith and Nephew), System 4 (SSL), original 4-layer bandaging (products from Smith and Nephew, Johnson & Johnson, 3M)) vs short stretch bandaging (Comprilan (Beirsdorf) or Rosidal	387 people with venous leg ulcers. Recruited from a variety of modes of leg ulcer service. Follow up for 12 weeks. Analysis sample size per arm: 195; 192	• **% of wounds healed** was similar in the 4-layer bandaging (80.5%) and short stretch (76.5%) arms – the difference was not statistically significant. • Median (95% CI) **time to healing** was shorter for 4-layer bandaging (92 (71-113) days) than short stretch bandaging (126 (95-157) days), although the difference was not statistically significant (p=0.12).	Large UK RCT comparing 4-layer and short stretch bandaging (noting that an additional layer on top of the two-layer short stretch bandage was allowed in case of slippage).

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
	K (Lohmann & Rauscher) with additional Coban (3M) layer if slippage occurs.		• For the **SF-12** PCS: 4-layer bandage baseline Mean (SD) 36.1 (8.30), 4th quarter Mean SD 35.0 (8.03); SSB baseline Mean (SD) 35.6 (7.62), 4th quarter Mean (SD) 34.2 (7.60). For the SF-12 MCS: 4-layer bandage baseline Mean (SD) 48.6 (12.34), 4th quarter Mean (SD) 51.7 (11.76); SSB baseline Mean (SD) 48.4 (12.28), 4th quarter Mean (SD) 49.1 (11.43). • **Discontinuation of intervention** was more common in the short stretch (34.38%) than the 4-layer bandaging arm (22.56%). • % of participants with any **adverse event** were similar in the 4-layer bandaging (17.00%) and short stretch bandaging (20.31%) arms. • **Death** rates were 7.69% in the 4-layer bandaging arm and 10.42% for short stretch bandaging. • **Occurrence of new ulcers** was similar in the 4-layer bandaging (5.64%) and short stretch bandaging (6.77%). • **Skin damage** was similar in the 4-layer bandaging (25.13%) and	

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			short-stretch bandaging (28.65%) arms. • **Maceration** was similar in the 4-layer bandaging (9.23%) and short-stretch bandaging (8.85%) • Mean adjusted **QALYs** from the economics section of the report, based on EQ-5D scores, were 0.69 (95% CI 0.66 to 0.74) for four-layer bandaging and 0.67 (0.63 to 0.72) for short-stretch bandaging.	
Junger et al, 2004 (Wounds),[29] RCT (non-inferiority), France, Germany, Austria, Switzerland	Tubular compression (Tubulcus (Laboratoires Innothera) 30-40mmHg vs short stretch bandaging (Rosidal K (Lohmann & Rauscher) .	191 people with venous leg ulcers (3 not randomised, 178 in per protocol analysis). Ambulatory patients. Follow up for 12 weeks. Analysis sample size per arm: 88, 90	• **% wounds healed** were similar in the tubular (58%) and short stretch (56.7%) compression arms – within the limits of non-inferiority. • Mean (SD) **time to healing** was similar for the tubular (43 (18.3) days) and short stretch (43.6 (18.3) days) arms. • **Compliance** (number of days compression was worn) was similar for the tubular (96.80%) and short stretch (96.40%), p=0.42. • **Wound size reduction** (in not healed individuals) was greater in the tubular (67.6%) than the short stretch (59%) group – statistical significance NR.	European RCT comparing 2-layer tubular compression bandaging and short stretch bandaging. This is considered a relevant prioritised study, as this is a features-based appraisal, though the specific tubular compression bandage does not appear on the Drug Tariff or NHS Supply Chain.

Study name, design and location	Intervention(s) and comparator **Note: exact pressure values are shown where available**	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Junger et al, 2004 (Curr Med Res Opin),[30] RCT, Netherlands and Germany	Compression hosiery (U-Stocking (Venotrain ulcertec)) vs short-stretch bandaging (Roselastic 530 (KOB)).	131 Caucasian people with venous leg ulcers (121 eligible for primary efficacy analysis). Recruited from phlebology outpatient clinics. Follow up for 12 weeks. Analysis sample size per arm: 61; 60	• **% wounds healed** was higher in the compression hosiery (47.5%) than short stretch (31.7%) arms, p = 0.0129. • Mean (SD) **time to healing** was similar in the compression hosiery (46 (20) days) and short stretch (46 (22) days). • Early **study discontinuation** was more common in the short stretch (8.33%) than the compression hosiery (3.27%) arm. • There was greater nursing **staff satisfaction** with compression hosiery than short stretch bandaging (p=0.0123). • **Regression in the ulcer surface** was more common in the compression hosiery (74.8%) than the short stretch (51.4%) arm, although statistical significance was not reached (p=0.0679). • % participants with any **adverse event** was numerically higher in the short stretch (39%) than the compression hosiery (31%) arm. • There was a tendency (p=0.07) for those in the compression hosiery arm to have more **pain in the leg.**	European RCT comparing compression hosiery and short stretch bandaging. This is considered a relevant prioritised study, as this is a features-based appraisal, though the specific hosiery does not appear on the Drug Tariff or NHS Supply Chain.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Karanikolic et al, 2018,[31] RCT, Serbia	High pressure multilayer system including Tubulcus (Laboratoires Innothera) with another layer over vs moderate pressure multilayer system including Tubulcus (Laboratoires Innothera)	109 people with venous leg ulcers (of which 102 were analysed). Recruited from an outpatient clinic. Follow up for 24 weeks. Analysis sample size per arm: 52; 50	• Among those aged 65 and over, high pressure (57.6%) was more effective than moderate pressure (28%) in **wound healing**, p<0.05. • **Paresthesias** were more common on high (38.46%) than moderate (12%) in those aged 65 and older, though statistical significance was not reached. • **Superficial necrosis of the skin** in those aged 65 and over, was more common on high (19.23%) than moderate (8%) pressure, though statistical significance was not reached.	European RCT comparing 2-layer tubular compression bandaging and a moderate pressure bandaging system that represents a form of standard of care. This is considered a relevant prioritised study, as this is a features-based appraisal, though the specific tubular compression bandage does not appear on the Drug Tariff or NHS Supply Chain.
Lazareth et al, 2012, RCT[22] (non-inferiority), France, UK and Germany	2-layer bandaging (KTech and Kpress (Urgo)) vs 4-layer bandaging (PROFORE (Smith and Nephew).	187 people with venous leg ulcers. 98% were recruited from outpatient clinics, the remainder from inpatient clinics. Follow up for 12 weeks. Analysis sample size per arm: 93; 93	• **% wounds healed** (with complete re-epithelialisation) were higher in the 2-layer (44%) than 4-layer (39%) bandaging arms, one-sided p=0.0165. • Median **time to healing** was 91 days in both arms. • **Discontinuation prior to week 12** was numerically higher in the 4-layer (16.13%) than the 2-layer (11.83%) arm. • More participants in the 2-layer arm (62%) than the 4-layer bandaging arm (47%) found **application** 'very easy', p=0.038.	European RCT (including UK sites) comparing 2-layer and 4-layer bandaging.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			• **Relative wound area reduction** was similar in the 2-layer (89.23%) and 4-layer (81.82%) bandaging arms, p=0.353. • There was a 6%-point increase in **healthy peri-lesional skin condition** from baseline to completion for the 2-layer arm and 3% points for the 4-layer bandaging arm. • **Median number of compression systems used per week** was comparable for the 2-layer (2.08) and 4-layer (2.13) bandaging arms – it was noted that these were both lower (1.2; 1.1) for UK participants. • **% participants with any AE** was 12% on 2-layer and 17% on 4-layer bandaging, p=0.99. • Pain was similar on 2-layer (5.40%) and 4-layer (6.40%) bandaging. • **De novo ulceration** was lower on 2-layer (4.30%) than 4-layer (6.40%) bandaging, although statistical significance was NR.	
Mariani et al, 2008, RCT,[32] Italy	Compression hosiery (Ulcer X (SIGVARIS)) vs short-stretch bandaging (details NR).	60 people with venous leg ulcers (of which 4 were excluded within a week of randomisation). Recruited from centres specialised in leg ulcer	• **% wounds healed** was higher in the compression hosiery (96.2%) than short-stretch bandaging (70.0%) arm, p=0.011.	European RCT comparing compression hosiery and short stretch bandaging.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
		care. Follow up period 4 months. Analysis sample size per arm: 26; 30	• Mean (SD) **time to healing** was comparable for the compression hosiery (56 (29.1)) and short-stretch bandaging (61.1 (22.7)) arms, p=0.52. • Venous Leg Ulcer Questionnaire scores showed that there was statistically significantly more **pain** in the short-stretch bandaging than the compression hosiery arm when applied, when removed and when walking, with a trend (p=0.06) for when wearing shoes. • **Inhibition of activities** was more common in the short-stretch (0.73%) than compression hosiery (0.49%) arm, p=0.025. • Mean (SD**) interval between visits** was longer for compression hosiery (8.2 (1.8) days) than short-stretch bandaging (6.7 (1.0) days), p=0.002. • Venous Leg Ulcer Questionnaire '**number of problems**' was greater for short-stretch bandaging than compression hosiery, p<0.001.	

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Moffatt et al, 2003,[33] RCT, UK	4-layer bandaging (PROFORE (Smith and Nephew)) vs 2-layer bandaging (SurePress (ConvaTec)).	112 people with venous leg ulcers (of which 109 formed the ITT population). Recruited from community leg ulcer clinics. Follow up for 24 weeks (or until closure of all areas of ulceration on reference limb). Analysis sample size per arm: 57; 52	• **% wounds healed** at 24 weeks was numerically higher in the 4-layer (88%) than 2-layer bandaging (77%) arm, although this difference was not statistically significant (p=0.55). A statistically significant (p=0.02) difference was found at 12 weeks but was not sustained. • Mean **time to closure** was similar in the 4-layer (8.2 weeks) and 2-layer (8.6 weeks) bandaging arms. • Study **withdrawal** was lower in the 4-layer (14%) than 2-layer (56%) bandaging arms. • Mean **frequency of compression change** was lower in the 4-layer (1.1 per week) than the 2-layer (1.5 per week) bandaging arms, p=0.0002. • Fewer people had an **AE** in the 4-layer (12%) than the 2-layer (35%) bandaging arms. • Fewer participants had **tissue breakdown** in the 4-layer (1.75%) than the 2-layer (5.77%) arms. • Fewer participants **had pain or discomfort** in the 4-layer (1.75%) than the 2-layer (13.46%) arms.	UK RCT comparing 2-layer and 4-layer bandaging.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
Mosti et al, 2020,[34] RCT, Italy	Wrap (CircAid JuxtaCures (medi)) vs 2-layer bandaging (Coban (3M)).	66 people with venous leg ulcers. Recruited from wound care clinics. Follow up for 12 weeks. Analysis sample size per arm: 33; 33	• **% wounds healed** was numerically higher in the wrap (78.7%) than the 2-layer bandaging (69.6%) group, although it was not statistically significant. • There was no statistically significant difference in **pain VAS scores** between groups. • **Wound size reduction** in not healed participants was numerically higher in the wrap (80%) than the 2-layer bandaging (71.2%) arms, but the difference was not statistically significant. • Median (IQR) **itching scores** were 1 (0–2) for the wrap group and 2 (0–3) for 2-layer bandaging, reported as p<0.5 (unclear if there may be a reporting error).	European RCT comparing wraps with short stretch bandaging (consists of a comfort and compression layer).
Polignano et al, 2004,[35] RCT, Italy	Compression hosiery (SurePress Comfort (ConvaTec)) vs short stretch bandaging (Comprilan (BSN)).	56 people with venous leg ulcers (of whom 2 were excluded). Recruited from medical centres. Follow up for 12 weeks. Analysis sample size per arm: 27; 29	• **% wounds healed** was higher in the compression hosiery (44%) than short stretch (17.2%) arm, p=0.027. • Mean (SD) **time to healing** was longer in the short stretch (101 (7) days) than the compression hosiery (72 (5) days) arm, p=0.0265. • Mean (SD) **pain VAS** score was higher in the short stretch	European RCT comparing compression hosiery with short stretch bandaging.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			(33.4mm (31.8)) than the compression hosiery (29.5mm (34)) arm, p=0.017. • **Adherence** was higher in the compression hosiery (92.3-100% good adherence) than the short stretch (80.8%-92.9% good adherence) arm. • Compression hosiery was 'significantly **easier to apply**' than short stretch bandaging (p=0.0439). • **% with any adverse event** was higher on short stretch bandaging (24.14%) than compression hosiery (11.11%)	
Stather et al, 2021,[36] RCT, UK	Wrap (JuxtaCures (medi UK) vs short stretch bandaging (Actico Short Stretch (Lohmann & Rauscher) or K2 (Urgo)).	40 people with venous leg ulcers. Recruited through a single clinical trials unit with patients recruited from primary care, vascular clinics and leg ulcer clinics. Follow up for 26 weeks. Analysis sample size per arm: 20; 20	• **% wounds healed** was comparable in the wrap (60%) and short stretch bandaging (55%) arms. • Mean (SD) **time to healing** was comparable in the wrap (12.67 (6.11) weeks) and short stretch bandaging (13.64 (6.98)) weeks, no statistically significant difference. • There was no statistically mean significant difference in **EQ-5D** scores at 1 month (-0.07 95% CI -0.21, -0.06; p=0.27), there was a statistically significant difference favouring wraps at 3 months (-0.14 95% CI -0.28,	UK RCT comparing wraps with short stretch bandaging.

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			0.01, p=0.04), and no statistically significant difference at 6 months (-0.06 95% CI -0.21, -0.08; p=0.49). • There were 219 **episodes** in the wrap group **where dressings were not changed** compared to 8 episodes in the short stretch bandaging group. • Of those who reported **removal of compression**, 78% were in the wrap arm and 22% in the short stretch arm. The most common reason for removal was washing (72%), followed by pain (4%). • **Discontinuation** was higher in the short stretch group (15%) compared to the wrap group (5%). • **Wound size reduction** was greater in the wrap than the short stretch arm, tending to statistical significance (p=0.06). • Mean (SD) **nursing time duration** was greater in the short stretch (53.9 (SD 6.6 minutes)) than the wrap (41.7 (SD 13.1 minutes)) arm, p=0.003. • The publication indicated that **adverse event** results were in an appendix. This was not	

Study name, design and location	Intervention(s) and comparator Note: exact pressure values are shown where available	Participants, setting and length of follow-up	Relevant outcomes and key results	EAG comments
			available on the journal website. The EAG contacted the corresponding author but as yet has not received a response.	

Abbreviations: AE, Adverse event; GP, General practitioner; ITT, intention to treat; NR, not reported; RCT, randomised controlled trial; UK, United Kingdom; SD, standard deviation; SF-12, Short Form 12-item health questionnaire; MCS, mental component score; PCS, physical component score; QALY, quality-adjusted life year; VAS, visual analogue scale. This table shows product names as displayed in the trial publications – any name changes are noted in section 5.2.2.

5.2.1. Study populations

Prioritised studies were broadly comparable in their populations. One study[23] required participants to have bilateral ulceration but was included as a prioritised study due to relatively limited volume of evidence available for compression wraps, which are a newer technology. The mean population age for each prioritised study was in the 60s or 70s, reflecting a typically older population, in line with clinical input. Studies were typically well balanced for gender. Ethnicity was only reported in one study,[30] in which all participants were Caucasian. In all studies, only a minority of participants – e.g. 17.2% in the VenUS IV study[1] – had diabetes, while people with diabetes were excluded from two studies.[28,29] Prioritised evidence did not present evidence specifically for any scoped subgroups: people with conditions that may limit self-care, people with low or high exudate wounds, people with very fragile skin, or people with irregular leg shapes.

5.2.2. Technologies evaluated

This was a features-based assessment, so the focus was on the four classes of product identified as the features for this appraisal, rather than individual products that represent these features. There were different types of two-layer compression bandages assessed. In addition to more 'standard' types of two-layer compression bandaging, two studies[29,31] assessed tubular compression and seven studies[26,28-30,32,35,36] assessed short-stretch bandaging. Clinical input to the EAG was that short-stretch bandages are typically two-layer. However, in VenUS-I,[28] an additional layer was added in the event of bandage slippage. Table 5 summarises products, used to exemplify the different features, that were mentioned as strong compression products in the company RFIs and were included in prioritised studies. It should be noted that the RFI instructions to companies stated, "we do not need detailed information on each product within a range of products e.g. different size bandages". Therefore, while availability of different sizes may be a relevant consideration, available information may be incomplete.

Table 5. Summary of example technologies mentioned in company RFIs and included in prioritised studies.

4-layer compression bandaging	2-layer compression bandaging	Compression hosiery	Compression wraps
PROFORE Company: Smith & Nephew Latex-free multi-layer bandage system available in a range of sizes. Not suitable for those with ABPI <0.8. Not suitable for those with small vessel disease. Caution required with those with diabetes. Listed as a strong compression product (>40 mmHg).	Actico Short Stretch Company: Lohmann & Rauscher Cohesive inelastic compression bandage. Not suitable for those with ABPI <0.5, use with caution under strict medical or specialist supervision for ABPI 0. 5 – 0.8. Not suitable for ankle circumference <18cm unless padding is used. Listed as a strong compression product (>40 mmHg).	Activa leg ulcer hosiery kit Company: Activa Healthcare (now part of Lohmann & Rauscher). Leg ulcer hosiery kit for the treatment of limbs without oedema. May be unsuitable where there is heavy exudate and for large wounds. Not suitable for those with ABPI <0.8 unless after specialist referral and under strict supervision and regular follow up. Not suitable for diabetic patients (unless after specialist referral and under strict supervision), those with arterial insufficiency, arterial disease, ischaemia, congestive cardiac failure, peripheral neuropathy, rheumatoid arthritis or known sensitivity to the fabric of the stockings. Listed as a strong compression product (>40 mmHg).	CircAid (now called juxtacures) Company: medi UK Graduated compression wrap (can offer strong compression). 3 lengths available, adjustable spine, customisable circumference. Not suitable for those with severe peripheral arterial disease, decompensated congestive heart failure, septic phlebitis, pre-gangrenous conditions, or sepsis.
K-Four Company: Urgo Four-layer kit with sizes 18-25cm, 25-30cm, greater than 30cm	Coban 2 (referred to just as Coban in some papers) Company: 3M (now called Solventum) Two-layer bandage system available both in kit form and as individual components.	JOBST UlcerCARE Company: BSN medical (now called Essity) Two-layer ulcer kit. Contains a range of options, including ready to wear and custom fit.	

	Not suitable for people with decompensated heart insufficiency, septic phlebitis, Phlegmasia coerulea dolens and other conditions contraindicated according to established guidelines or local procedures, known sensitivity to the materials, or ABPI <0.8. One kit size. Delivers 40 mmHg resting pressure.	7 sizes are available. Not suitable for those with ischaemia, untreated septic phlebitis, uncontrolled congestive heart failure, phlegmasia cerulea dolens or incompatibility with the fabric. Full kit achieves 40 mmHg pressure.	
	KTwo (now called UrgoKTwo) Company: Urgo UrgoKTwo contains multi-component 2-layer kit, containing K Tech (inelastic bandage) and K Press (elastic) bandages. A range of sizes is available. Pressure indicators are provided. Not suitable for those with moderate or severe arterial conditions, notably with ABPI <0.8, phlegmatia coerilea dolens, septic phlebitis, oedema from congestive heart failure, epifascial arterial bypass, or known hypersensitivity to any of the components, notably latex (although a separate latex free	mediven Ulcer Kit Company: medi UK 2-layer ulcer kit. Kit contains two liners and one outer. Top layer can be removed at night for comfort. Reduced fabric around tendon. Available in 7 sizes and 2 lengths. Not suitable for those with severe peripheral arterial disease, decompensated congestive heart failure, septic phlebitis, pre-gangrenous conditions and sepsis. Each layer offers 20 mmHg compression, for combined pressure of 40 mmHg.	

	version is available). Listed as a strong compression product (>40 mmHg).		
		Ulcer X Company: SIGVARIS Compression hosiery kit. Includes 2 liners (15-20 mmHg) plus a top garment. Top garment is 30% latex. Available in 4 sizes. Not suitable for those with severe cardiac insufficiency, phlegmasia coerulea dolens, severe peripheral arterial occlusive disease (with any of ABPI <0.6; ankle pressure <60mmHg; toe pressure <30mmHg), severe diabetic neuropathy with sensory loss or microangiopathy with the risk of skin necrosis, compression of an existing arterial bypass, or allergy to compression material. Total compression is 34-46 mmHg.	

Abbreviations: ABPI, ankle brachial pressure index; mmHg, millimetres of mercury.

5.2.3. Outcomes of the included studies

Outcomes assessed in each prioritised study are shown in Table 4. All of the prioritised studies reported at least some data on the percentage of wounds healed and time to healing was reported in eleven of these studies.[1,21,22,24,28-30,32,33,35,36] With regards to intermediate outcomes, nine studies[21-25,29,30,34,36] reported on wound size reduction, five[21,22,32,33,36] reported on either frequency of compression changes, interval between visits or nursing time, and one[22] reported on peri-wound skin condition. None of the prioritised studies reported on wound bed condition or oedema after the baseline assessment.

Assessment of patient reported outcomes varied across studies, with seven studies[1,21,24,27,28,36] reporting HRQoL (mobility was reported as part of this), ten[1,24,27,32,34,35] reporting pain-related outcomes, eleven[1,22,23,25,26,28-30,33,35,36] reporting data relevant to treatment adherence, and four[22,27,30,35] reporting data relevant to ease of treatment use.

Of the 17 prioritised studies, eleven[1,22,24,26-28,30,32-35] reported at least some adverse events data. For one further study,[36] the publication indicated that adverse event results were in an appendix, but this was not available on the journal website. The EAG contacted the corresponding author but at the time of writing had not received a response.

5.3. Quality appraisal of studies

A formal quality appraisal was conducted to assess the quality of the included evidence. For seven studies[23,26,28-30,32,35] included in the VenUS IV network meta-analysis by Ashby et al,[1] the EAG used the risk of bias results from Ashby et al, which in turn were based on a Cochrane review.[14] These ratings were based on an adapted version of the original Cochrane risk of bias tool,[37] further adapted in the Cochrane review to only include ratings for the following five domains: sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data and comparability of groups on baseline prognostic factors. The EAG's rationale for using these ratings, where available, was to prevent duplication of work, noting that these risk of bias scores were used to inform a Cochrane review.

To ensure consistency across studies, the EAG used the same adapted tool as the Cochrane review to conduct its own risk of bias assessments for studies not part of the Ashby et al review. This included eight studies[1,22,24,25,27,31,34,36] published after 2011, and one study[33] that was published in 2003 but not included in the Ashby et al review. One of the prioritised studies was not an RCT.[21] The risk of bias in this study was not assessed because it cannot be reasonably

compared with the prioritised RCTs. Instead, the EAG highlight that this study is, by design, at higher risk of bias than the other prioritised studies, and that this should be considered when interpreting the study results.

A full risk of bias table is provided in Appendix F. The prioritised RCTs were generally at low risk of bias, although this varied according to domain. Two[23,35] of the RCTs did not give sufficient details about the generation of the randomisation sequence. These two studies, and a further five studies,[22,31-34] also did not provide sufficient information on allocation concealment. Even though all but one[31] of these seven RCTs appeared to have a reasonable between-group baseline balance with regards to prognostic indicators, the EAG note that baseline imbalances on unmeasured characteristics may have been present in the other six RCTs (as well as the non-randomised study[21]) due to the lack of clarity regarding selection bias.

For the RCT that did not report allocation concealment and had a between-group baseline imbalance,[31] the baseline characteristic that differed between groups was ulcer size. This is a key prognostic factor, and therefore may impact upon study results, including the primary outcomes. Another RCT[27] had a baseline imbalance between groups in ulcer size (also in duration of ulcer and mobility). Reasons for this are unclear (randomisation processes appeared to be adequate). Again, this may impact upon all study outcomes. In a further RCT[36] there appeared to be differences between groups at baseline in ulcer size, patient sex, and smoking status, but this was unclear and likely due to the small sample size in this feasibility study.

Four of the RCTs[1,22,24,30] provided assessor blinded results, whereas in the majority of studies it was unclear whether outcome assessors were blinded to study group (although the EAG think it unlikely that assessors were blinded and then this not be reported). Blinding of patients and clinicians is not possible for these technologies, but it should be possible to produce assessor blinded results for several key outcomes. The EAG note, therefore, that for the majority of the prioritised RCTs, it is unclear whether researcher bias may have impacted upon study results.

5.4. Results from the evidence base and evidence synthesis

The EAG did not conduct its own network meta-analysis, due to the availability of the VenUS-IV meta-analysis[1] and the agreement that the appraisal would be paused to await availability of VenUS 6 network meta-analysis results. Therefore, the EAG produced a narrative synthesis. Due to the relatively large number of prioritised studies, stemming from the presence of four key features and seeking where possible to identify evidence for each comparison, results are

presented organised by feature (compression product type), rather than study-by-study. Tabulated results are provided in Table 4.

5.4.1. 4-layer bandaging vs 2-layer bandaging

Seven prioritised studies[21,22,25-28,33] compared 4-layer and 2-layer bandaging. All of these were RCTs except for one large retrospective cohort study conducted in a UK clinical practice setting. All six prioritised RCTs for this comparison were conducted in European settings, while three[26,28,33] were conducted exclusively in a UK setting and one further study[22] also included UK participants.

The one available UK RWE study[21] in a clinical practice setting showed greater wound healing in the 2-layer bandaging arms (especially the cohesive 2-layer compression) than the 4-layer bandaging arm, although time-to-healing and wound size reduction were fairly comparable across groups. A statistically significant difference across the two different 2-layer arms and the 4-layer bandaging arms was observed for time-to-healing, which may be explained by a mean difference of 0.4-0.5 months between the cohesive 2-layer compression bandaging arm and the other two arms. There was a greater QALY gain for the 2-layer bandaging arms (especially the cohesive 2-layer compression) than the 4-layer bandaging arm. Resource use in terms of number of dressings per month was higher for 4-layer than 2-layer bandaging.

RCT evidence showed that wound healing was lower for 4-layer compared to 2-layer bandaging in two studies,[22,27] higher in one study[25] and similar in three studies,[26,28,33] including one[33] which showed a statistically non-significant numerical difference in favour of 4-layer bandaging. Time to healing was assessed by three studies[22,28,33], none of which showed a statistically significant difference between these arms. While two studies[25,26] found adherence to be similar across arms, Lazareth[22] found discontinuation to be higher in the 4-layer bandaging arm while two studies[28,33] found the opposite effect. Two studies[22,27] assessed tolerability, ease of use and/or acceptability and both found a benefit for two-layer over four-layer bandaging. Two studies assessed wound size reduction - one[22] finding the arms to be similar with a statistically non-significant difference in favour of 2-layer bandaging and the other[25] finding wound size reduction to be smaller in the 2-layer bandaging arm. Two studies assessed quality of life, one[28] finding similar results between arms and the other[27] finding a numerical but not statistically effect in favour of 2-layer bandaging. One study[22] found that frequency of compression change was comparable across arms, while another found that frequency of compression change was statistically significantly lower on 4-layer than 2-layer bandages. Three studies[22,27,28] found

similar adverse event rates across arms, one study[26] showed a 4.3%-point higher rate in the 4-layer group (significance not assessed), and another showed much lower (12% vs 35%) adverse event rates in the 4-layer than 2-layer bandaging group. Numerical results, along with more details on specific types of adverse events, are shown in Table 4.

5.4.2. 4-layer bandaging vs compression hosiery

Two prioritised studies[1,24] compared 4-layer bandaging and compression hosiery. Both were RCTs – one[1] in the UK and one[24] in an Australian context. Wound healing rates were relatively similar between arms in both studies – in the Australian study[24] there was a 12%-point difference in favour of 4-layer bandaging, but it was not statistically significant. This study found statistically significant shorter time to healing in the 4-layer bandaging group, although this was not replicated in the UK study.[1] In both studies, quality of life was similar across arms. Reduction in ulcer size was assessed by one study[24] and showed similar results for both groups. Adherence was high and comparable across groups in both studies, while one study[1] found change to a non-trial treatment was more common in the compression hosiery group. Serious adverse events[1] were uncommon and comparable between groups. Finlayson et al[24] found that adverse events were rare in both groups but higher in the 4-layer bandaging arm (6% vs 4%). In contrast, Ashby et al[1] found that non-serious adverse events were common in both groups but higher in the compression hosiery group (67% vs 58%).

5.4.3. 4-layer bandaging vs compression wraps

Only one prioritised study compared 4-layer bandaging and compression wraps. This was a small (n=12 per arm) RCT[23] conducted in the USA. There was no other evidence available for this comparison. The groups were not shown to differ in wound healing rates, wound size reduction or adherence to treatment.

5.4.4. 2-layer bandaging vs compression hosiery

Three prioritised studies[30,32,35] compared 2-layer bandaging with compression hosiery – all were RCTs conducted in non-UK European settings. It is important to note that the type of 2-layer bandaging used in all three studies was short stretch. Clinical input to the EAG was that this should be classified alongside other 2-layer bandaging systems, and it is also not listed as a separate feature on the NICE scope for this appraisal.[2] All three studies showed compression hosiery to offer better wound healing than (short-stretch) 2-layer bandaging. Time-to-healing was comparable for two studies and longer for 2-layer bandaging than compression hosiery in

one study.[35] One study[30] assessed reduction in ulcer area and found a numerical but not statistically significant benefit in favour of compression hosiery. Adherence was better for compression hosiery in the two studies that assessed this – one in terms of % wear time[35] and the other in terms of discontinuation rates.[30] Ease of application[35] and staff satisfaction[30] were both greater for the compression hosiery arm. All studies showed greater adverse events/problems on short-stretch 2-layer bandaging than compression hosiery. Interval between visits[32] was longer for compression hosiery.

5.4.5. 2-layer bandaging vs compression wraps

Two prioritised studies[34,36] compared 2-layer bandaging and compression wraps. Both were RCTs – one in a UK context[36] and one in Europe.[34] The 2-layer bandage in Stather et al.[36] was short stretch. In both studies, wound healing rates were higher for the compression wrap group – for Mosti *et al* it was reported that the difference was not statistically significant. Wound size reduction was comparable across arms in one study[34] and numerically greater for the compression wrap group in the other study,[36] tending to statistical significance (p=0.06). Time-to-healing and quality of life were reported in one study[36] and shown to be comparable across arms. Discontinuation was higher for the 2-layer bandaging group and this group required more nursing time.[36] No overall adverse event data were available, just more specific pain and itching results for Mosti et al.,[34] which appeared comparable across arms.

5.4.6. Compression hosiery vs compression wraps

No identified studies compared compression hosiery and compression wraps.

5.4.7. Comparison of different types of 2-layer bandaging

Two prioritised studies[21,29] compared different types of 2-layer bandaging – one[21] a retrospective cohort study in the UK and one RCT[29] in a European context. Additionally, one European RCT[31] compared the same 2-layer compression system with and without an additional layer to strengthen compression. All three studies make different comparisons, so they cannot be synthesised. As noted above, the results of studies using tubular compression[29,31] are not shown. Guest et al.[21] found that more wounds were healed on cohesive 2-layer compression than the 2-layer compression system (76% vs 70%) but statistical significance is only reported for the 3-way comparison including 4-layer bandaging. Time to healing and wound size reduction were similar across arms. QALY gain was higher for cohesive 2-layer compression (0.413 (SD 0.059) vs 0.404 (0.057)). Dressing change frequency was similar for these two arms.

Treatment switching was 8% for the cohesive 2-layer compression group vs 3% for the 2-layer compression system.

5.5. The VenUS 6 study

VenUS 6 is an ongoing RCT of compression products for venous leg ulcers in a UK setting. Information about the study design and aims is publicly available from the protocol.[38] However, at the time of the EAG's clinical review, there were no publicly available results from this trial. Academic in confidence results from an updated systematic review and network meta-analysis including VenUS 6 are presented in the economic section of the final report and are used to inform the EAG model. The EAG considers that VenUS 6 is likely to be the most pivotal trial to inform this appraisal, subject to availability of sufficient clinical data.

VenUS 6[38] is a pragmatic, parallel-group, three-arm RCT comparing three types of strong compression (40mmHg pressure at the ankle): i) compression wraps, ii) two-layer bandage, or iii) 'evidence-based compression' (two-layer hosiery or four-layer bandage). Participants will be followed up for between 4 and 12 months. The primary endpoint is time to healing, measured in days since randomisation. Secondary endpoints include healing of the reference leg, ulcer recurrence, ulcer/skin deterioration, amputation, admission/discharge, surgery to close/remove incompetent superficial veins, infection, death, treatment changes, adherence and ease of use, ulcer-related pain, health-related quality of life and resource use. Only publicly available information from the published protocol is included in this section.

5.5.1. VenUS 6 network meta-analysis

The EAG was sent unpublished results from a network meta-analysis (NMA) conducted alongside the VenUS 6 trial. This comprised tables of hazard ratios and uncertainty intervals and a CODA with correlated draws from the joint posterior distribution. The working NMA assumed equivalence between four-layer compression bandage and two-layer compression hosiery, since this assumption underpins the design of the VenUS 6 study. Methodological details are available publicly in the Health Economics Analysis Plan (HEAP) on clinicaltrials.gov.[39,40]

The NMA conceptualised 2-layer compression hosiery (2LCH) and 4-layer compression bandaging (4LCB) as 'evidence-based compression' (EBC), as it saw them as current best practice in the UK. It should be noted that clinical experts consulted by the EAG also saw 2-layer compression bandaging (2LCB) as part of current NHS standard of care as well as best

practice. Therefore, there may be limitations in the extent to which this EBC concept generalises to UK clinical practice.

Within EBC, the NMA defined four-layer compression bandage systems (4LCB) as elastic systems consisting of orthopaedic wool plus three subsequent bandages and defined two-layer compression hosiery (2LCH) as comprising a smooth first layer, or understocking, providing light compression over which a second overstocking i.e. UK class II or III depending on the understocking slips on.

The NMA compared EBC with a range of high-pressure compression treatment options, including several that are not used in the UK. We focus commentary on the comparison with the three other treatment options used in UK practice:

- Short-stretch bandage (SSB) - an inelastic bandage system where one to three rolls of bandage are applied over orthopaedic wool.
- Two-layer compression bandage systems (2LCB) - bottom layer with cohesive compression bandage - sub-compression wadding layer and cohesive bandage
- Compression wraps (CW) - adjustable hook-and-loop-fastened compression

The other treatments in the NMA were:

- Zinc paste bandage (ZPB) – an inelastic system consisting of a paste bandage often with a support bandage on top)
- Adhesive bandage (Ba)
- Hosiery with Velcro device (HV)
- Combination of bandage and hosiery, elastic (BheH)
- Combination of bandage and hosiery, elastic, zinc paste and adhesive (BzeaH)
- Choice of SSB and 2LCB, or mixed SSB/2LCB
- Reusable 2LCB (r2LCB)

As discussed earlier, clinical expert advice to the EAG was that SSB can typically be considered a type of 2LCB, which is the approach the EAG took in its clinical review, although the EAG noted that it is possible for the number of layers in SSB to vary in practice.

The outcome of the NMA was the number of individuals healed per arm (of a total number) over a certain follow-up. This summary data (available for most studies) was synthesised together with the individual-patient data for VenUS 6 and VenUS 1 and modelled assuming that time to

healing followed a fully parametric survival distribution. The link between the individual and summary data was done via parameter sharing within the NMA model. A Bayesian analytical approach was used. Non-informative priors were used to inform the analysis. The EAG considered this to be appropriate. Analyses were conducted in WINBUGS, linked to R, using a 5000 run 'burn-in' followed by a further 5000 iterations, upon which iterations were based. Chain convergence and absence of autocorrelation were assessed by running different chains, and by inspecting density, history, and Gelman-Rubin graphic outputs for each model.

Both fixed effects and random effects models were assessed for suitability. Both models showed satisfactory performance. The fixed effects model was preferred because three of the contrasts contained moderate-to-high risk of bias studies. It would be a strong assumption to generalise the heterogeneity of the studies informing them to the rest of the network, as would be required using a random effects model.

The NMA included results from 2 RCTs with IPD and 19 with aggregate data. The two trials with IPD available were VenUS-1 and VenUS 6.[28,38] Of the 20 published studies in the VenUS 6 working NMA, eight were included as prioritised studies by the EAG. These differences largely relate to the prioritisation process.

Figure 1: Network diagram for the base case NMA

Figure 2: Network diagram for the scenario NMA

In these figures, 2LB = two-layer compression bandaging, 4LB = four-layer compression bandaging and HH = compression hosiery, as per the abbreviations used by VenUS 6.

Table 6. Studies with IPD included in NMA

ID	Study	Treatment	Follow up (weeks)	Number of participants	Mean ulcer duration (months)	Mean ulcer size at baseline (cm^2)	Number of participants with healed reference ulcers during follow-up	Included in EAG clinical review?
1	VenUS I[28]	4LCB	52	195	3	3.81	107	Yes (Iglesias et al, 2004)
		SSB	52	192	3	3.82	86	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	Only in this additional NMA section*

Abbreviations: 4LCB, four-layer compression bandage; SSB, short-stretch bandage; EBC, evidence-based compression; 2LCB, two-layer compression bandage; CW, compression wrap. * as the study results were not available at the time of the search or provided through company RFIs.

Table 7. Studies with aggregate data included in NMA

ID	Study	Treatment	Follow up (weeks)	Number patients	Mean ulcer duration (months)	Mean ulcer size (cm2)	Number healed	Included in EAG clinical review?
1	Duby 1993[41]	4LCB	12	25	20.5	11.9	11	No
		SSB	12	25	26.7	13.1	10	
2	Scriven 1998[42]	4LCB	52	32	13	13.3	17.6	Not prioritised
		SSB	52	32	21	8.3	18.24	
3	Partsch 2001[43]	4LCB	16	53	1.25	1.5	33	No
		SSB	16	59	1	1.9	43	
4	Ukat 2003[44]	4LCB	12	44	--	17.7	13	Not prioritised
		SSB	12	45	--	12.2	10	
5	Franks 2004[26]	4LCB	24	74	2	5	59	Yes
		SSB	24	82	2	3.5	62	
6	Junger 2004[29]	SSB	12	60	5.57	5.95	19	Yes
		2LCH	12	61	4.14	5.62	29	
7	Kralj 1996[45]	4LCB	24	20	7.9	18.6	7	No

		Ba	24	20	6.9	17.2	8	
8	Polignano 2004[46]	4LCB	24	39	--	10.1	29	Yes
		ZPB	24	29	--	9.3	19	
9	Wilkinson 1997[47]	4LCB	12	17	--	11.2	8	No
		BHeH	12	18	--	8.6	8	
10	Colgan 1995[48]	4LCB	12	10	9.3	27.5	6	No
		BzeaH	12	10	66.5	48.5	7	
11	Blecken 2005[23]	4LCB	12	12	--	50.08	4	Yes
		HV	12	12	--	48.98	4	
12	Moffatt 2008[49]	4LCB	4	42	48.8	5.7	3	Yes
		2LCB	4	39	46.6	11.8	6	
13	Szewczyk 2010[50]	4LCB	12	15	--	6	9	Not prioritised
		2LCB	12	16	--	5.3	10	
14	Wong 2012[51]	4LCB	24	107	--	--	72	Not prioritised
		SSB	24	107	--	--	77	
15	Harrison 2011[52]	4LCB	52	215	11.7	3	178	No
		SSB	52	209	11.4	3.3	192	
16	Gillet 2019[27]	4LCB	16	43	6.5	--	10	Yes
		r2LCB	16	49	9.4	--	23	
17	Mosti 2020[34]	CW	12	33	9	16	26	Yes
		2LCB	12	33	8	12.5	23	
18	Stather 2021[36]	CW	26	20	--	--	12	Yes
		Mixed SSB/2LCB	26	20	--	--	11	
19	Lazareth 2012[22]	4LCB	12	93	6.81	10.29	78	Yes
		2LCB	12	94	6.42	9.75	82	

Abbreviations: 4LCB, four-layer compression bandage; SSB, short-stretch bandage; EBC, evidence-based compression; 2LCB, two-layer compression bandage; CW, compression wrap; Ba, adhesive bandage; BHEH, combination of bandage and hosiery, elastic; BzeaH - combination of bandage and hosiery, elastic, zinc paste and adhesive; r2LCB, reusable 2-layer compression bandage.

Of the 19 aggregate data studies in the NMA, 13 (68%) were included in the EAG clinical evidence review, although some were not prioritised for detailed presentation in the report. The use of prioritisation criteria due to the policy timeframe of this review is a key methodological difference between our review and the VenUS 6 NMA. Explanations for the six aggregate studies from the NMA that were not included in the EAG review follow below.

- Colgan et al. (1995),[48], Kralj et al. (1995),[45] and Duby et al. (1993),[41] were not retrieved in the database search as they were neither indexed by Medline nor Embase. Colgan and Kralji were both conference abstracts from the 1995 European Conference on Advances in Wound Management, which Embase does not index. Duby was a 1993 paper in the journal *Wounds*, a journal which neither Medline nor Embase indexed for that year (e.g. Medline started indexing it in 2007).

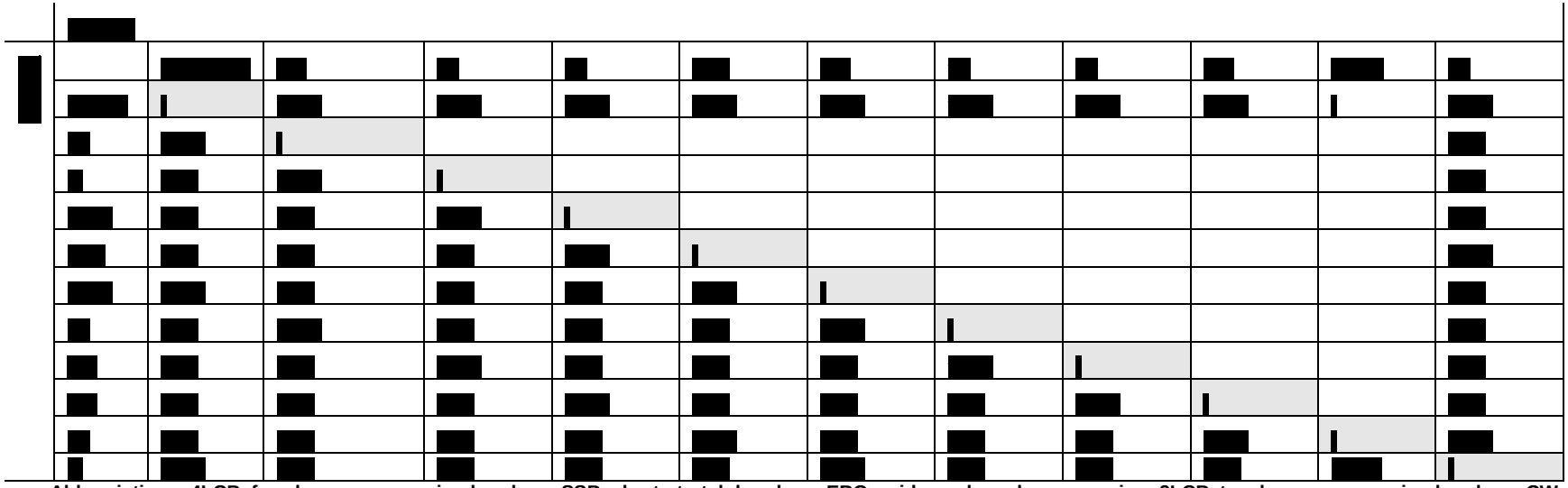
- Harrison et al. (2011)[52] was not retrieved in the database search because the abstract used "compression system" or "compression technology". Neither term was used in the EAG's search (the relevant line in the EAG search was (Compression adj2 (bandag* or dressing* or wrap* or sock* or stocking* or hosiery or garment* or sleeve* or clothes or clothing or suit)). Neither was the paper identified through MeSH, as no indexing terms have been assigned to the paper.

- Partsch et al.[43] was excluded at full-text screening because the pressure was reduced or full compression depending on leg circumference and therefore did not meet the intervention criterion.

- Wilkinson et al.[47] was excluded for suboptimal pressure not meeting the intervention criterion of full compression.

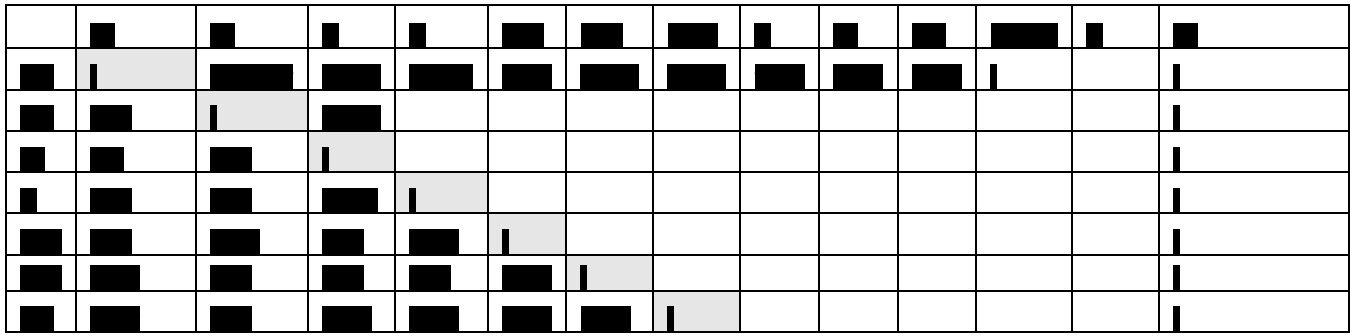
VenUS-IV results were not included in the base case NMA, because the two treatments it evaluates (4LCB and 2LCH) were assumed to have equivalent effectiveness as forms of EBC. However, at the request of the EAG, the VenUS 6 study team provided a scenario analysis that assessed 4LCB and 2LCH separately. Results from the base case VenUS 6 NMA, in the form of hazard ratios against the EBC reference treatment are presented below as Table 8, while results from the scenario analysis are shown in Table 9.

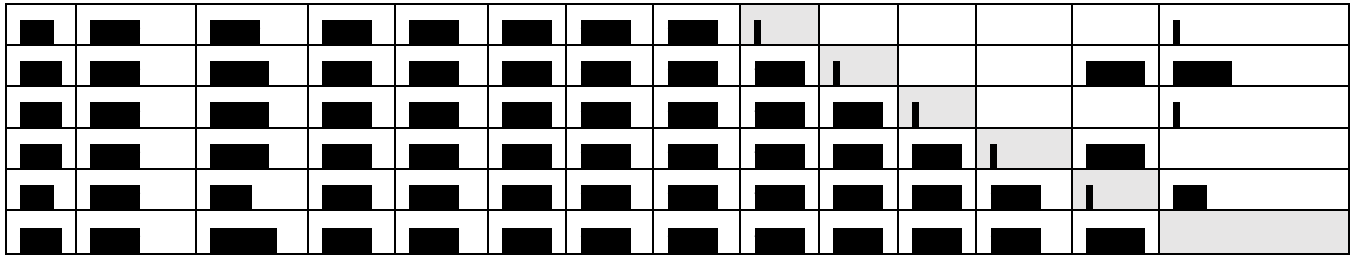
Table 8. Results from VenUS 6 base case NMA for number of individuals healed per arm (of a total number) over a certain follow-up



Abbreviations: 4LCB, four-layer compression bandage; SSB, short-stretch bandage; EBC, evidence-based compression; 2LCB, two-layer compression bandage; CW, compression wrap; Ba, adhesive bandage; BHEH, combination of bandage and hosiery, elastic; BzeaH, combination of bandage and hosiery, elastic, zinc paste and adhesive; r2LCB, reusable 2-layer compression bandage; ZPB, Zinc paste bandage; IPD, individual patient data. *, estimates from a meta-analysis with fixed-effect model, comprising of IPD and AD (log normal distribution), **, estimates from a single trial with IPD, *, estimates from a meta-analysis with fixed-effect model †, estimates from single trial with aggregated data, empty cells: direct evidence not available, HRs greater than 1 indicate better outcomes (i.e., reduced time to ulcer healing).**

Table 9. Results from VenUS 6 scenario NMA for number of individuals healed per arm (of a total number) over a certain follow-up





Abbreviations: 4LCB, four-layer compression bandage; SSB, short-stretch bandage; EBC, evidence-based compression; 2LCB, two-layer compression bandage; CW, compression wrap; Ba, adhesive bandage; BHEH, combination of bandage and hosiery, elastic; BzeaH - combination of bandage and hosiery, elastic, zinc paste and adhesive; r2LCB, reusable 2-layer compression bandage; ZPB, Zinc paste bandage; IPD, individual patient data.*, estimates from a meta-analysis with fixed-effect model, comprising of IPD and AD (log normal distribution), **, estimates from a single trial with IPD, ***, estimates from a meta-analysis with fixed-effect model, †, estimates from single trial with aggregated data empty cells: direct evidence not available, HRs greater than 1 indicate better outcomes (i.e., reduced time to ulcer healing).

[redacted]

The EAG considered that the working NMA appeared generally well conducted. The concept of EBC as used in the NMA is an assumption and relies on 4LCB and 2LCH being of equivalent effectiveness. This is based on VenUS-IV,1 which showed no statistically significant difference (HR 0.99, 95% CI 0.79 to 1.25; p = 0.96) in time-to-healing in the adjusted model between 4LCB and 2LCH. No formal feasibility assessment was presented.

[redacted]it is important for the uncertainty in the relative effectiveness of these products to be incorporated in the economic evaluation, thus the relevant hazard ratios from the scenario reported in Table 9 were used in the decision model.

5.6. Conclusions of the clinical and technological evidence review

At the time of the EAG assessment, there were a large range of compression products available on the NHS through the Drug Tariff[3] and NHS Supply Chain,[53] of which many fitted the scope of this appraisal, i.e. strong compression products that are either 4-layer compression bandaging, 2-layer compression bandaging, 2-layer compression hosiery or compression wraps. This was a feature-based assessment and the EAG sought to identify the best available prioritised evidence to represent these features with the greatest relevance to UK NHS practice.

The EAG identified 17 prioritised studies offering direct head-to-head comparisons between at least two of these features, drawing on evidence from a range of products. The focus was on the features rather than the products themselves. Among the prioritised studies, six were

exclusively UK studies, one further study included some UK sites, and all but two of the prioritised studies were conducted in a European context, which is beneficial for generalisability. All but one study, which was a large retrospective cohort study in the context of routine UK NHS practice, were RCTs, benefitting internal validity. The evidence was generally considered to be fairly high quality, although open label studies do pose an increased risk of bias. It is important to note that, in many cases, different types of compression products have different visual appearance, precluding blinding of patients and clinicians. The EAG note, however, that blinding of outcome assessors should be possible, but did not often occur. In addition, the EAG highlight that caution should be taken when interpreting the results of studies for which there were imbalances at baseline on prognostic indicators.

Studies showed that 2-layer bandaging was at least as good as 4-layer, with some evidence 2-layer may be better. Hosiery and wraps (noting there was only one study on wraps for this comparison) were shown to be equivalent to 4-layer bandaging. There was some evidence that wraps may be better than 2-layer bandaging for % wounds healed, but there were only two studies and one used short stretch 2-layer bandaging. Hosiery was shown to be better than 2-layer bandaging – at first this appears contradictory but may be explained by all 2-layer products for this comparison being short stretch and therefore not the same products that were typically compared with 4-layer bandaging. There was some evidence that the type of 2-layer bandaging may influence outcomes, i.e. this feature is not necessarily unitary.

Evidence from the VenUS 6 NMA suggests that [redacted]

6. ECONOMIC EVIDENCE SEARCHES AND SELECTION

6.1. Evidence search strategy and study selection

The economic searches sought to identify previously published economic evaluations, health-related quality of life (HRQoL) studies, and utility studies relevant to the decision problem. The population in the economic search was wider than the clinical search as studies that did not meet the criteria for inclusion in the effectiveness review may still be of value in informing elements of the decision model.

Database searches were performed in Medline, Embase, the Cochrane library, CINAHL, INAHTA and ICTRP and clinicaltrials.gov for ongoing trials. All evidence sources submitted by companies during the RFI process were assessed against the inclusion criteria – those that met these criteria were added to the screening process.

The search is fully described in the published protocol[15] – no amendments to the planned search were made. Details of the search approach, including lists of databases, search strategies and outcomes, can be found in Appendix A.

Screening was performed using the inclusion and exclusion criteria described in the published protocol.[15] In brief, the EAG included studies in adults with a venous leg ulcer, that assessed any compression product listed in the final scope, for which an economic evaluation or assessment of utility, HRQoL, costs or resource use was performed. Screening was conducted in Rayyan.[19]

6.2. Included and excluded studies

A total of 2,178 records were retrieved by the database searches. Of these, 569 were removed as duplicates, leaving 1,609 records to be screened at title and abstract. From the title and abstract screen, 78 were identified for full text retrieval. In total, 26 economic studies were included in the review. A list of studies excluded at full text along with the rationale for exclusion is provided in Appendix C. A PRISMA diagram of the search and screen process is provided in Appendix B. A review of previous economic analyses is presented in Section 7.1.

7. ECONOMIC ANALYSES

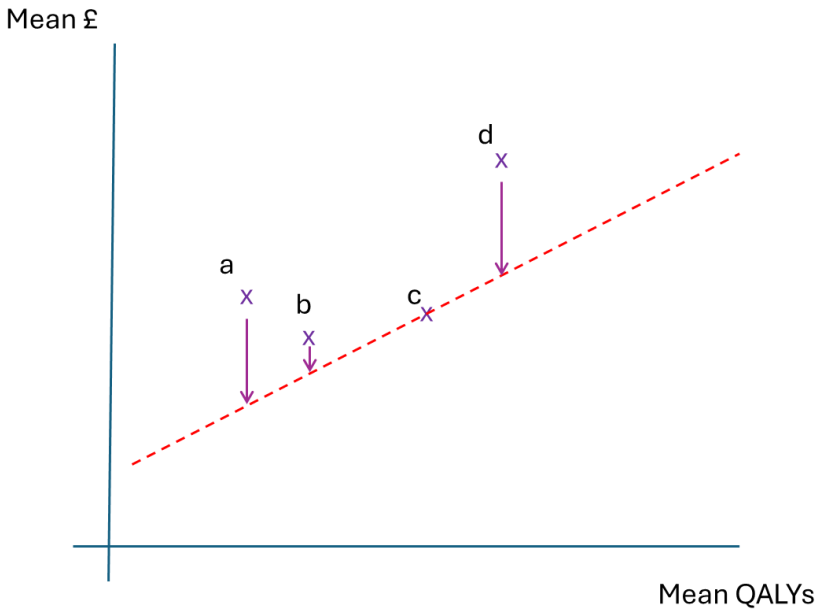
The EAG conducted a pragmatic economic evaluation of compression products in adults with venous leg ulcers from the perspective of the UK NHS and PSS, consistent with the methods recommended in the NICE reference case[4] and ISPOR Good Practices Report.[54]

As there are a large number of individual products under the four classes of compression bandage, a comparative estimate of the incremental cost effectiveness of each against each other was both infeasible and unnecessarily complicated. The EAG therefore calculated the maximum economically justifiable price (eJP) for each of the four product types and associated uncertainty. This is the price yielding an ICER equal to the maximum willingness to pay threshold.

To achieve this, the EAG conducted an initial analysis of the four classes of product with the lowest unit cost product in each class. The option yielding the highest net benefit at the willingness to pay threshold (£20,000) was declared the referent. The maximum eJP for all bandage types is a unit cost that generates an ICER of £20,000 compared with the referent. This is illustrated graphically in Figure 3 below where all four comparators lie on the dotted line. The eJP was then compared with the prices charged for different products.

Critical in this analysis is the assumption that all products within each class are identically effective in terms of health-related quality of life gains. To account for variations in this the EAG repeated the analysis but using the mid-price of the class of each product rather than the lowest. The EAG also conducted a further analysis using a willingness to pay threshold of £7,000, which is the estimate of the marginal cost per QALY of all NHS expenditure, and thus a plausible estimate of the health opportunity cost of NHS expenditure.[55]

Figure 3: Illustration of eJP analysis



In the figure product c is associated with the maximum net benefit at a willingness to pay of £20,000 per QALY. The dotted line has a gradient of £20,000 / QALY. The maximum eJP of each of a, b and d is that which leads to the point lying along the dotted line.

In summary, the EAG conducted an economic evaluation comparing the costs and QALYs gained from four classes of compression product from the perspective of the NHS and PSS, reporting results as the maximum economically justified price for each class required to achieve an incremental cost-effectiveness ratio of £20,000 per QALY gained, in line with the NICE reference case.

Section 7.1 summarises previous economic analyses that were reviewed to either identify existing models which would be suitable for adaptation to this decision problem, or, where such a model did not exist, to provide insight into development and data sources for a *de novo* model. The methods section (7.2) describes 1) the method for the regression analysis to determine whether there is any relationship between compression product features and price and 2) the approach to modelling. The results are presented in Section 7.3, a summary of elements not captured in the model in Section 0 and a discussion and interpretation in Section 7.5.

7.1. Review of previous economic analyses

7.1.1. Economic evaluations

The EAG conducted a pragmatic review of previous economic evaluations in this population to inform model inputs. Two systematic reviews of previous economic evaluations were identified.[6,56] Goka et al.[6] focused on the clinical and economic impact of a specific two-layer compression system (Coban, 3M) compared to other 2-layer and 4-layer compression systems in people with venous leg ulcers. Layer et al.[56] conducted a systematic review of treatments for venous leg ulcers, identifying 23 models, on a wide range of different treatment types.

Three trial-based economic evaluations were identified. A within-trial analysis of the VenUS-IV study[1,57] took a cost-utility approach from a UK NHS & PSS perspective. It compared 4-layer compression bandaging with 2-layer hosiery and found hosiery to be a viable alternative that is relatively less costly and provides marginally higher QALYs. VenUS-1[28] (also UK-based), compared 4-layer bandaging with short stretch 2-layer bandaging and found 4-layer to be the dominant strategy. One further cost-of-illness study in the northwest of England,[58] found the average 2-week per person cost of treating people where a venous leg ulcer was the most severe wound was estimated at £166.39 (95% CI £157.78-£175.00) with community staff time making up over half of this amount.

Seven model-based economic evaluations (cost–utility analyses) were identified. A decision model was developed based on the VenUS-IV study results[1] comprising a three-state state-transition model (unhealed, healed, dead), allowing back-transitions to unhealed reflecting recurrence. Two-layer bandaging appeared to be cost-effective, but this is driven by potentially low-quality clinical evidence of superiority vs 4-layer. If equivalence between 2-layer and 4-layer compression bandaging is assumed, hosiery becomes the most cost-effective option due to its protective effect against recurrence. Guest and Fuller[59] used a 4-state model (static, improved, infected or healed) with transitions between all states permitted, except out of healed which was the absorbing state. Two-layer cohesive compression bandaging was shown to be dominant in this model, but none of four-layer compression bandaging, two-layer compression hosiery or compression wraps was included as a competing option. The primary contributor to total costs was district nurse visits (50%), and the difference in district nurse visits also made up approximately half of the difference in costs. Health Quality Ontario,[60] in Canada, used a 4-state model (healed, recurred, infected (transient) or dead), and found that use of compression

hosiery is likely to slightly increase costs, but be cost-effective. The context of this assessment was prevention of venous leg ulcer

A pre-print by Tuson et al.[61] using a 4-state partitioned survival model (open (unhealed), closed (healed), infected or dead (with no transition between closed and infected, and dead being the only absorbing state) produced a scatterplot which may suggest an undeclared assumption of non-inferiority of the intervention has either been imposed on the model or used to reject samples with negative incremental QALYs. Therefore, the results of this model were not of use to the EAG. Guest and Fuller[62] compared the cost effectiveness of two reduced compression interventions and is therefore not considered by the EAG to be of direct relevance to this appraisal. Two further papers from the same group[20,21] were considered by the EAG to be likely superseded by Guest and Fuller.[59]

In January 2025 following completion of the EAG's analysis, the EAG was provided with an early draft of the decision model based economic evaluation of the VenUS VI study which included a scenario analysis requested by the EAG reflecting the decision question of this appraisal more closely. We compare and contrast the results of that analysis with ours in section 9.3.

In summary, the EAG identified a range of trial- and model-based economic evaluations related to venous leg ulcers. However, none offered the combination of UK NHS PSS context, an up-to-date review of the literature, and comparison of 4LCB, 2LCB, 2LCH and CW that the EAG required. Therefore, it was necessary for the EAG to construct a *de novo* model.

7.1.2. Studies on health state utilities

The EAG conducted a pragmatic review of utility values in this patient population to inform model inputs. Five previous systematic reviews on health-related quality of life in patients with venous leg ulcers were identified,[11,63-66] one of which didn't include preference-based utility values;[63] none of the identified systematic reviews included a quantitative synthesis of quality of life in people with VLU.

The review also incorporated additional primary sources of utility data identified by the EAG, comprising one abstract[67] and ten peer reviewed papers. Of these, five[68-72] were conducted in the UK, two[73,74] in Australia, two[75,76] in New Zealand, and one[77] in Portugal. Utility elicitation methods included the SF-6D and standard gamble, with the EQ-5D questionnaire being the

most commonly used. Appropriate value sets were cited in most cases, such as Devlin (2018)[78] for the England TTO + DCE, and Dolan (1997)[79] for the England TTO.

All studies were observational except for Jull (2020),[76] which was an RCT comparing wool-derived keratin dressings to usual care dressings, and Klonizakis (2018),[72] which compared exercise plus compression therapy versus compression alone in patients with VLU. Quality of life estimates were often reported using EQ-5D questionnaire completed by patients at multiple time points (e.g., baseline, 3 months, 6 months) to capture changes in utility over time. Several studies[69,71,75,77] divided people into healed and unhealed groups, with Palfreyman (2008)[68] further categorizing utility by age in both groups.

The EAG considered Iglesias (2005)[71] to be the most suitable source for utilities in the model as it includes the largest sample size (387 patients across nine UK regions), and used the EQ-5D-3L, which aligns with NICE's preferred instrument and value set (Dolan 1997), ensuring direct applicability and generalisability to the UK setting. Cheng et al. (2019)[74] provided detailed longitudinal utility data at multiple time points (baseline, 1 month, 3 months, and 6 months) and used the UK valuation of utility. Although this study is more recent, the use of the Devlin et al 2018 value set, which NICE has previously advised against, makes it less suitable to use in model.[80]

7.1.3. Learnings from previous economic analyses

Previous economic analyses described in section 7.1.1 mostly comprised state transition models, with health states consisting of healed and unhealed, and infection and death being included in some analyses. The EAG discussed potential model structures with clinical experts and the CI and lead economist of the VenUS 6 study.[38] Based on these, the EAG understood that all ulcers will carry infection to some degree, but this was only likely to be substantially impactful on either patient quality of life or resource use if develops cellulitis. The EAG therefore opted not to include a discrete 'infection' health state and was unable to identify sufficient quality data on the incidence, cost and quality of life impact of the condition to incorporate in the model.

The EAG considered whether death should be included as a health state. This is essential in models with a life-time horizon, but based on review of healing rates, the EAG felt that five years was sufficient to capture the majority of differences in cost and outcomes for the different product classes (indeed, a two- or three-year time horizon would also be fit for purpose).

Furthermore, the presence of or healing of ulcers were not considered to affect mortality *per se*, with any mortality effect being due to the underlying condition that led to the formation of ulcers. However, for completeness the EAG chose to include a 'dead' health state to more accurately model expected costs and outcomes, whilst understanding this is only likely to affect incremental comparisons where death occurs with an unhealed ulcer and that this will likely be relatively rare.

7.2. Economic analyses methods

7.2.1. Decision Model overview & expert input into design and analysis

The EAG developed a state-transition (Markov) model to estimate the expected costs and QALYs accrued over a time horizon of five years with each of the four compression product types. This information was used to report the maximum eJP as described in section 7.2.7.

The EAG considered whether to include recurrence of a leg ulcer within its analysis. This would provide a more comprehensive model of the patient pathway. However, the EAG opted not to include this for two reasons. Firstly, the remit of the scope was the treatment rather than prevention of venous leg ulcers and the EAG considered prevention of recurrent (or primary) ulcers a separate clinical question. Secondly, including recurrence would add a layer of complexity and data demands to the analysis which were infeasible within the resources and timescale for this study.

The EAG discussed the model structure and inputs with clinical experts (tissue viability nurses and community nurses with expertise in leg ulcers) at a meeting on 21st October 2024 to assess:

- the plausibility of the model structure and assumptions
- the plausibility of the modelled survival function representing time to healing with a 4-layer compression bandage, with a particular focus on modelled projections beyond the observed data
- whether the proposed resource use estimates reflect current care pathways for people with venous leg ulcers within primary and community care settings, both during treatment and after a person's ulcer is healed.

The clinical experts considered the model structure to be appropriate for the decision question, albeit within the limitations of the scope (i.e. excluding recurrence of ulcers). The median time to healing of approximately 12 weeks was consistent with experience as well as relevant guidelines (The NWSCP team, 2024),[81] whilst the extrapolations from the curve adequately reflected reality,

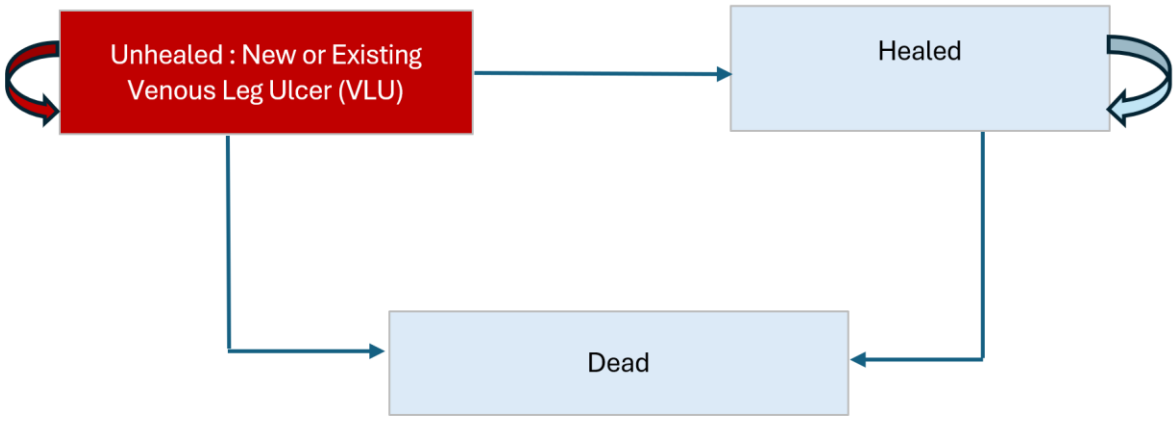
with a small number of people whose ulcers were very slow to heal, if at all. Whilst the experts were not able to provide precise numbers there was consensus that the survival function was fit for purpose. Several of the resource use items which had been drawn from the literature were considered somewhat different from routine practice in the experience of the experts. Therefore, the EAG modified its assumptions as described in section 7.2.5 below.

7.2.2. Decision Model structure

On the basis of review of previous studies (section 7.1.1) and consultation with clinical and economic experts (section 7.2.1), the EAG developed a state-transition (Markov) model of three health states: unhealed, healed and dead (Figure 4). Patients enter the model with an unhealed ulcer. One of the four compression products is applied and each cycle a patient has a probability of transitioning to the healed state, or dead. Based on healing rates observed in the data, a transition period of one week was considered to capture costs and outcomes with sufficient granularity.

While the ulcer was unhealed, patients were assumed to remain on the same compression product. Treatment switching has been observed even in controlled clinical trials,[1] so this assumption is a limitation which is discussed further in section 9.

Figure 4: Model structure



7.2.2.1. Time horizon

Patients entered the model at the point of consultation with a medical care professional where one of the four classes of compression product is applied to the person with venous leg ulcers.

A five-year time horizon was used for the analysis, representing a long enough time horizon to capture the majority of differences in cost and outcomes between products.

7.2.2.2. Perspective

An NHS and Personal Social Services perspective was adopted in line with the NICE reference case.[82]

7.2.3. Modelled population

The EAG base case modelled a 65-year-old person with venous leg ulcers. The EAG understands VLUs are more common in older persons and women. However, most of the source studies on which the model data are based comprised gender-balanced populations. There is no evidence to suggest a difference in outcome from treatment of VLUs between men and women. The only difference by gender within the model therefore is in general mortality (life expectancy). The EAG assumed an average risk of death by age between males and females.

Products are supplied in various sizes to account for variability in leg circumference (based on measurement of ankle circumference). These are associated with different prices and may be associated with different effectiveness. The EAG's base case reflected an 'average' / medium sized ankle, with sub-group analyses for smaller and larger ankles.

Patients with VLUs may have mobility difficulties, which could be associated with longer time to healing[83] (though a Cox proportional hazards regression in VenUS[1] IV found no association when also controlling for ulcer area and duration) and will generally result in patients getting their contacts with nurses and other healthcare providers in the community (i.e., in their home or at a residential/nursing home) rather than attending a GP surgery or wound clinic.

Due to data limitations, the EAG's base case assumed cost differences for ankle size (i.e. published product price) and ambulatory status, but no difference in time to healing by either factor. This is discussed further in section 9.

7.2.4. Effectiveness data

7.2.4.1. Time to healing

The key input to the decision model was time to healing by product type, which were drawn from the VenUS 6 NMA (Table 10).

Table 10: Hazard ratios of time to healing by compression product type

Compression product	Hazard ratio	95% equal-tailed credible interval
Four-layer compression bandage	1 (reference)	—
Two-layer compression bandage	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]
Compression wrap	[redacted]	[redacted]

Source: Means and 95% credible intervals estimated from scenario analysis CODA of 5,000 samples supplied to the EAG by the VenUS 6 study team.

[redacted]

Hazard ratios from the network meta-analysis in Table 10 were applied directly to a baseline survival curve for time to healing for the four-layer compression bandage.

Baseline time to healing was estimated for the four-layer compression bandage by reconstructing event and censoring times from a time to healing (cumulative risk, i.e., 1 − Kaplan–Meier survival) curve published from the VenUS IV study.[1] The curve was first digitised to (x, y) coordinates using the software DigitizeIt,[84] then individual patient data (IPD) were reconstructed from this using the web UI to the R package IPDfromKM.[85]

Graphical inspection of the log-cumulative hazard and related plots from the constructed IPD was undertaken; deviations from straight lines were observed which cast some doubt on the suitability of the Weibull, log-normal and log-logistic models. Reconstructed IPD were used to fit parametric survival curves by the maximum likelihood method. The following parametric models were explored: exponential, Weibull, Gompertz, log-normal, log-logistic, generalised gamma, and Weibull with gamma-distributed individual frailty. The optimal fit (generalised gamma) was determined using Akaike's information criterion and validated by visual inspection (see Table 11 and Figure 5).

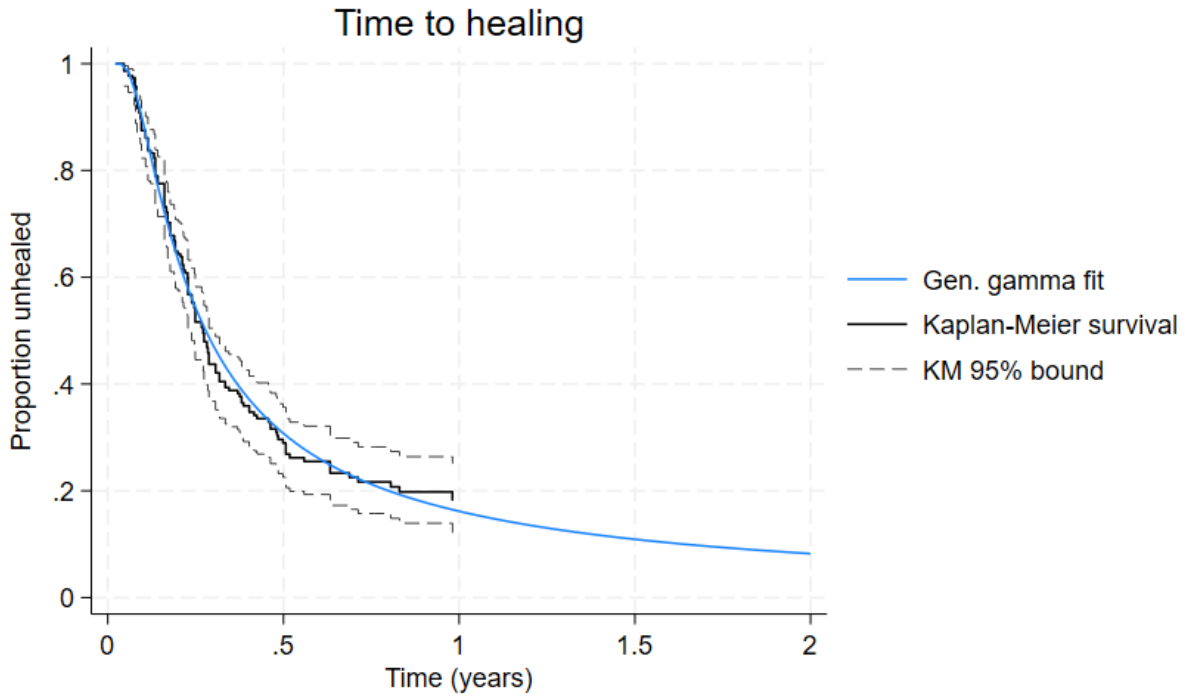
Table 11: Comparison of goodness of fit - time to healing, 4LCB

Parametric model	Log-likelihood[1]	Degrees of freedom	Akaike's information criterion[2]
Exponential	−284.2	1	570.3
Gompertz	−283.5	2	571.0
Weibull	−281.2	2	566.4
Log-logistic	−263.3	2	530.6

Log-normal	−260.8	2	525.7
Generalised gamma	−251.7	3	509.4
Weibull with gamma-distributed individual frailty	−252.2	3	510.4

1. *Higher number indicates better fit. 2. Lower number indicates better fit, taking into account parsimony.*

Figure 5: Comparison of empirical time-to-healing data (VenUS IV) and generalised gamma fitted to reconstructed IPD



7.2.4.2. Mortality

Probability of death was based on UK life tables based on data for the years 2017-2019 (2020 lifetables are not recommended due to the impact of Covid 19[86]), adjusted by a hazard ratio of 1.36 to reflect the increased mortality in people with VLU compared with the general population.[57]

7.2.5. Resource use and cost

Costs were considered from an NHS and Personal Social Services perspective as per the NICE manual.[82] Resource item categories included compression products, dressings, primary care contacts and podiatrist visits.

7.2.5.1. Resource use

Unhealed

Initially, the usage of healthcare resources was estimated from Guest et al. 2017,[21] who reported costs over a 6-month period for two different two-layer systems and a four-layer compression system as derived from a primary care research database (The Health Improvement Network, THIN database).[87] The EAG's decision model required resource use disaggregated by healed/unhealed state rather than a longitudinal cost estimate of a cohort whose ulcers healed at varying timepoints. We therefore adjusted the resource use counts based on the likely clinical pathway of people with VLUs. These estimates formed a starting point for discussions with clinical experts as described section 7.2.1 above.

Following this, it became clear that significant drivers of resource use and costs would be:

1. The number of contacts with healthcare professionals to change dressings (which would in turn depend on the number of dressing changes needed and whether these dressings could be changed by a family member or informal carer)
2. Whether patients needed to be visited in their home or could attend a wound clinic or a GP surgery
3. The salary band for the healthcare professionals changing the dressings

The number of dressing changes needed was stated to be at least once per week, with some patients needing more frequent dressing changes (even daily where ulcers were producing large quantities of exudate). For the four-layer and two-layer compression bandages, these would need to be replaced when dressings were changed, and a suitably experienced nurse (Band 5) would need to do this. For two-layer compression hosiery and compression wraps, some dressing changes could be done by a family member or informal carer, and the healthcare professional changing the dressing could be from a lower band (Band 3 or 4). For compression hosiery, we were advised that patients were often given two kits each 6 months ("one to wear, one to wash"), while for compression wraps, only a single kit would be given to last 6 months.

Reliable sources for the average number of dressing changes per week for an unhealed venous leg ulcer could not be located.[88,89] The distribution of the number of dressing changes per week is expected to be skewed, with a small proportion of patients requiring many more dressing changes than the "average" patient and making it challenging to estimate the mean number of dressing changes, which is the key statistic required for economic evaluation. We therefore

constructed a plausible but uncertain distribution for the number of dressing changes required each fortnight, as shown in Figure 6. This assumption led to a mean number of dressing changes *per week* of 1.60 (95% CrI 1.36–1.88). We then assumed that on average, for patients with compression hosiery or compression wraps, some dressing changes would be done by someone other than a healthcare professional (dressing changes done by someone other than a healthcare professional each fortnight/total dressing changes needed per fortnight: 0/2, 1/3, 2/4, 2/5, 3/6, 3.5/7), which meant that such patients would require on average 1.11 healthcare professional contacts for their VLU (95% CrI 1.04–1.20). To incorporate this into the model we sampled two correlated parameters: the first was the natural logarithm of the number of dressing changes needed per week, and the second was the proportion of dressing changes over and above one per week that would be undertaken by a healthcare professional for patients using compression hosiery or compression wraps.

For comparison, in the VenUS IV study,[1] there were an estimated mean 1.26 nurse visits per week (total number of visits, divided by number of weeks participating in the study with an unhealed ulcer) for compression hosiery and 1.31 nurse visits per week for four-layer compression bandage. These estimates are closer to the figures we have estimated than studies based on THIN database, and also represent a smaller difference in contacts than we have assumed. However The VenUS IV study was a clinical trial recruiting participants between 2009 and 2011 and so may have limited generalisability to current clinical practice for several reasons (e.g., performance bias, exclusion of patients with high levels of wound exudate, secular trends in care provision).

Figure 6: Distribution for number of dressing changes per fortnight (expected value and 95% credible interval)

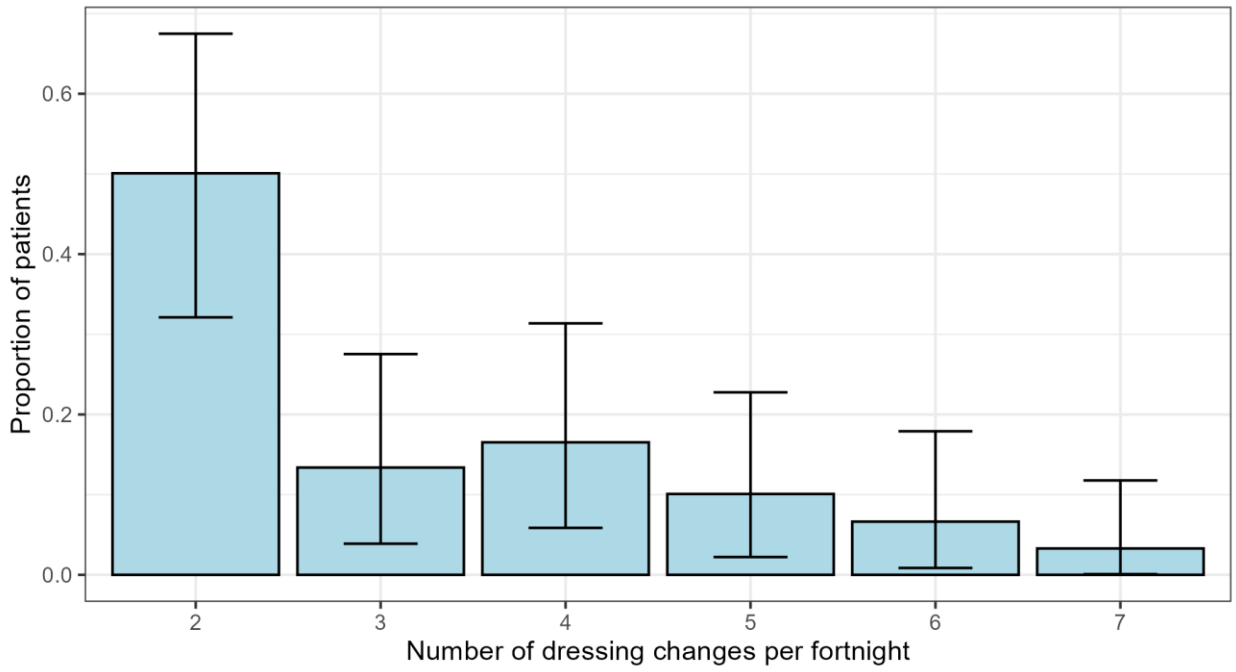


Table 12: Weekly healthcare resource use while ulcer unhealed

Resource	Four-/two-layer compression bandage	Two-layer compression hosiery/compression wraps
Community healthcare		
GP [a]	0.01	
Band 5 nurse [b]	1.60	—
Band 3 /4 healthcare staff [b]	—	1.11
Podiatrist	0.10	
Consumables		
Compression kit	1.60	2.0/26 (~0.08 pw) [c] 1.0/26 (~0.04 pw) [d]
Dressings	1.60	

Notes: [a] In surgery if patient ambulatory, home visit otherwise; [b] In wound clinic or GP surgery if patient ambulatory, home visit otherwise; [c] Two-layer compression hosiery only; [d] Compression wraps only

Upon healing of ulcer

Clinical experts advised that when a VLU has healed, a doppler ABPI test is undertaken, so this was incorporated as a one-off cost associated with transitions from the Unhealed to the Healed state in the Markov model.

Healed

Clinical experts advised that after healing, patients would typically be placed on maintenance compression, which would be compression hosiery though at lower than 40 mmHg pressure. We assumed that this would be replaced twice per year. Contacts with healthcare professionals would be infrequent, typically once per year.

7.2.5.2. Unit costs

Costs were uprated to 2022/23 prices, where appropriate, using the NHSCII Pay & Prices index.[90]

Community healthcare

These were estimated based on the PSSRU Unit Costs of Health and Social Care (2023).[90] All these costs were assumed to be uncertain and were drawn from log-normal distributions with standard deviation equal to 10% of the mean.

A GP appointment in a GP surgery was estimated to cost £77, which includes 10 minutes of face-to-face time, direct care staff costs, qualifications, and average prescription costs. A GP home visit was estimated to cost £117, which includes £89 for 30 minutes of GMS activity (assumed 10 minutes appointment plus 20 minutes travel) and average prescription costs.

A contact with a Band 3 / 4 healthcare professional in a surgery or wound clinic was estimated to cost £19.50, which is based on the costs of 32.5 minutes of Band 4 clinical staff time (including salary oncosts and overheads).[1] A home visit by a Band 3 / 4 healthcare professional was estimated to cost £36.50, which includes the 32.5 minutes above, plus 20 minutes of staff time and £5 allowance for travel.

A contact with a Band 5 nurse in a surgery or wound clinic was estimated to cost £28.71, again based on a 32.5-minute appointment duration. A home visit by a Band 5 nurse was estimated to cost £51.38, which includes the 32.5-minute appointment duration, plus 20 minutes of staff time and £5 allowance for travel.

Consumables

Consumables requiring unit costs were the compression products themselves and dressings.

Unit costs of the intervention products were based on prices listed in the drug tariff as at June 2024.[3] The EAG reviewed the individual products described as 'kits' in the name or product description (i.e. excluding individual bandages or components of systems). For the economic evaluation and eJP analysis, the lowest cost product was selected for each of the four product types for each product size. Product sizes were defined as medium for ankle width of 18-25cm, narrow for width below 18cm and wide for those described as 25cm or greater. The EAG noted that prices did not necessarily increase as the size of product increased: in some cases price was insensitive to size and in others a smaller product was more expensive than the medium.

The confidential appendix to this report extracts the combined lowest cost prices from both the (publicly available) drug tariff and commercial-in-confidence NHS Supply Chain costs, which takes into account confidential discounts off the list prices offered to the NHS by suppliers.

Dressings were assumed to cost £0.57 each (BNF).[91]

Table 13: Unit costs for product type by size

	Product type			
Size	**4LCB**	**2LCB**	**2LCH**	**CW**
Medium	£4.81	£7.26	£15.67	£105.10
Narrow	£6.48	£7.26	£15.67	£105.10
Wide	£7.40	£8.30	£15.67	£105.10

4LCB: 4-layer compression bandage, 2LCB: 2-layer compression bandage, 2LCH: 2-layer compression hosiery, CW: compression wrap. Source: Drug Tariff Part IX, June 2024[3]

Other

ABPI testing was assumed to cost £22.48 (£20.48 in 2020/21 prices) based on NICE Diagnostic Guidance 52.[92] This was distributed log-normally with standard deviation equal to 20% of the mean.

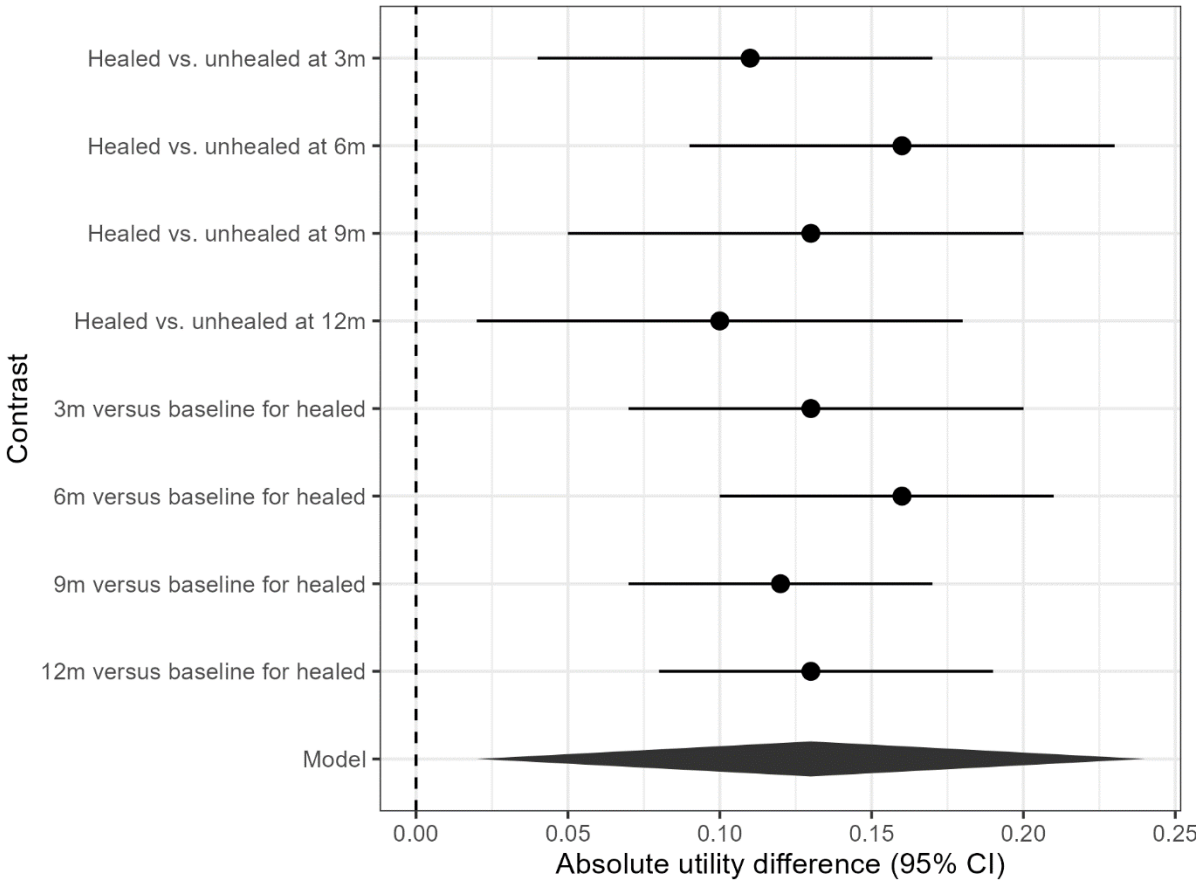
7.2.6. Health state utilities

Several studies reported health state utilities (Table 14).

Of these, Iglesias et al. (2005) was judged to be the most relevant. Iglesias et al. collected quality of life data from participants in the VenUS I study, including with the EQ-5D-3L instrument. The Measuring and Valuing Health (MVH) value set (Dolan 1997[79]) was applied to determine utility values, which was derived from a time trade-off exercise in a representative sample of the UK general population. At the time of entry to the study (baseline), mean utility was 0.62 (standard error 0.02).

Various contrasts were presented: comparisons at each timepoint (3 months, 6 months, 9 months and 12 months post-baseline) between those with a healed and unhealed ulcer at that timepoint, and differences from baseline within the groups with healed and unhealed ulcers. The first of these could be at risk of bias because individuals with better overall health might have faster ulcer healing and therefore be overrepresented in the healed ulcer group. The second type of contrast is also potentially problematic because quality of life could improve over time regardless of healing. In fact, there was no evidence of any change in utility from baseline in individuals whose ulcer was unhealed. The absolute utility difference estimates ranged from 0.10 to 0.16 for the first type of contrast and from 0.12 to 0.16 for the second type of contrast. In the model, the EAG used a normally distributed parameter with mean 0.13 and standard error 0.056 such that 95% of the distribution lay between 0.02 and 0.26.

Figure 7: Absolute utility difference estimates from Iglesias et al. (2005) and EAG model parameter distribution



Therefore, the model assumed utility of 0.62 for an unhealed ulcer and 0.75 for a healed ulcer. This represents a very significant improvement in quality of life. Some other studies, though less well suited to answer the question, suggested a much less consequential difference. In a scenario analysis, the difference in utility was set to 0.03 (Jull et al. 2010).[75]

Table 14: Key HRQoL studies included

Author	**Iglesias**	**Jull**	**Cheng**
Year	2005	2010	2019
Funded by	NHS research and development	Health Research Council of New Zealand	Wound Management Innovation Cooperative Research centre
Countries	UK	New Zealand	Australia
Study type	Observational	Observational	Observational
Participant population	patients with VLU across 9 UK regions	Patients with VLU who don't have diabetes, rheumatoid arthritis or peripheral artery disease	Patients with VLU in Brisbane, Queensland, Australia.
Number of participants	387	368	80
Complications considered	Healed vs unhealed	Healed vs unhealed	Healed vs unhealed
Method of elicitation	SF-12 and EQ-5D-3L self-completed by participants	SF-12 and EQ-5D-3L self-completed by participants	EQ-5D-5L SPVU-5D
Method of evaluation	MVH (Dolan 1997 England TTO)	unclear	Devlin 2018 England (TTO + DCE)
Baseline utilities reported	0.62	NR	0.73
Relevant information contained	Utilities at 3, 6 and 12 months	Change in utilities after 12 weeks	Utilities baseline, 1-month, 3-month and 6-month
EAG subjective assessment of quality and relevance			

Abbreviations: EAG, external assessment group; HRQoL, health-related quality of life.

7.2.7. Approach to analysis & scenarios

The EAG's approach to determining the eJP for each class of product firstly assigned a price per unit equal to the lowest price out of all products within the class. The model was run probabilistically to estimate the mean cost and QALYs accrued for each of the four product classes. Parameters contributing to uncertainty were explored by presentation of the expected value of perfect parameter information[93] using the Sheffield Accelerated Value of Information (SAVI) tool.[94,95] This shows not only which model parameters' (or groups of parameters') uncertainty affects uncertainty in cost-effectiveness, but also places a monetary value on eliminating that uncertainty, thus helping to guide the allocation of finite research resources.

Estimated cost and QALYs were converted to net monetary and health benefit at a value of £20,000 per QALY (the willingness to pay threshold). The product class with the highest expected net monetary/health benefit was termed the referent. The eJP for the other three classes was calculated as that yielding an ICER of £20,000 per QALY gained compared with all others. Graphically, this is the price required for all four points to lie on a line of gradient £20,000/QALY that bisects the referent. The analyses were repeated for narrow, medium and wide ankle circumference products and for ambulatory and non-ambulatory patients, a total of 6 sub-populations for the base case. The EAG also explored a scenario under a lower utility gain from a healed ulcer. The base case was also modified to a 12 week, 24 week and 1 year time horizon. Finally a scenario assuming 4LCB and 2LCB were applied by a band 3 nurse was conducted. Analyses are summarised in Table 15. Results of each analysis are reported at willingness to pay thresholds of £20,000 and £7,000. Analyses are repeated using confidential NHS Supply chain prices in the accompanying confidential appendix, including an additional analysis comprising [redacted]

Table 15: Base case and scenario analyses

Scenario	Details
Base case 1	Medium ankle, ambulatory person with VLU
Base case 2	Medium ankle, non-ambulatory person with VLU
Base case 3	Narrow ankle, ambulatory person with VLU
Base case 4	Narrow ankle, non-ambulatory person with VLU
Base case 5	Wide ankle, ambulatory person with VLU
Base case 6	Wide ankle, non-ambulatory person with VLU
Scenario 1	Lower utility gain from healed ulcer, Medium ankle, ambulatory person with VLU

Scenario 2	Lower utility gain from healed ulcer, Medium ankle, non-ambulatory person with VLU
Scenario 3	Lower utility gain from healed ulcer, Narrow ankle, ambulatory person with VLU
Scenario 4	Lower utility gain from healed ulcer, Narrow ankle, non-ambulatory person with VLU
Scenario 5	Lower utility gain from healed ulcer, Wide ankle, ambulatory person with VLU
Scenario 6	Lower utility gain from healed ulcer, Wide ankle, non-ambulatory person with VLU
Scenario 7	Medium ankle, ambulatory person with VLU, 12 week time horizon
Scenario 8	Medium ankle, ambulatory person with VLU, 24 week time horizon
Scenario 9	Medium ankle, ambulatory person with VLU, 52 week time horizon
Scenario 10	Medium ankle, ambulatory person with VLU, Band 3 nurse applying 4LCB and 2LCB

7.3. Economic Analysis Results

This section presents the results of the economic analyses, beginning with cost-effectiveness analyses where the unit cost for each product group is estimated as the cheapest product on the market within that group, followed by economically justified price (eJP) analyses which indicate maximum prices for product groups in relation to the prices of one or more other products.

In this section a competing option demonstrates cost-effectiveness if and only if it provides the greatest (expected) net benefit among the set of all competing options. For the purposes of analysis, net benefit is calculated as net monetary benefit (costs subtracted from the product of QALYs and the willingness-to-pay for a QALY or the cost-effectiveness threshold). Results converted into net health benefit are presented alongside monetary benefit as per the NICE manual.[82]

7.3.1. Cost-effectiveness analyses

To allow a standard cost-effectiveness analysis, fixed costs for each product group were used, as shown in Table 13.

A probabilistic analysis was undertaken, sampling 2000 sets of parameter values from relevant distributions reflecting uncertainty in the parameters (Table 16). All four product types are associated with very similar outcomes, with between 3.235 to 3.254 QALYs accrued over five years (range 0.019, equivalent to 5 or 6 days of perfect health). Compression wraps and compression hosiery on average incur the lowest (almost identical) costs, with two and four layer compression bandages being approximately £700 (+~60%) and £1000 (+~83%) more expensive over five years respectively. Based on expected values, compression wraps yield the highest net monetary benefit: on average compression hosiery and four layer compression bandages are dominated by compression wraps (both more expensive and less effective), and the added cost per extra QALY gained from two-layer compression bandages is above NICE's willingness to pay threshold (at £76,804 / QALY gained). In summary, over five years, the differences in QALYs accrued between the four compression product types are very small, but compression wraps and compression hosiery appear to be associated with lower costs. This is the case for all ankle circumferences and whether or not the person with VLU is ambulatory or not. The cost-effectiveness acceptability frontier for all analyses shows that compression wraps have the highest probability of being cost-effective (around 60% at a willingness to pay of £20,000/QALY), followed by compression hosiery (around 40% at £20,000/QALY). As the

willingness to pay rises the probability of two layer compression bandages becoming cost-effective rises. There is almost zero probability of four layer compression bandages being cost-effective at any plausible willingness to pay (Figure 8).

A breakdown of costs is in Table 17. Costs accrued in the 'healed' health state are broadly similar, which is consistent with the comparators being of similar effectiveness. The overall cost differences are driven by the requirement for a Band 5 nurse to dress 4LCB and 2LCB, and compression product price (higher for 4LCB and 2LCB than CH or CW).

Table 16: Cost-effectiveness analysis results (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory							
Compression wrap	£1,255	3.245		£63,651	3.183	£21,462	3.066
Two-layer compression hosiery	£1,259	3.239	Dominated	£63,514	3.176	£21,411	3.059
Two-layer compression bandage	£1,942	3.254	£76,804	£63,143	3.157	£20,838	2.977
Four-layer compression bandage	£2,324	3.235	Dominated	£62,381	3.119	£20,323	2.903
Narrow ankle circumference, ambulatory							
Compression wrap	£1,257	3.254		£63,829	3.191	£21,523	3.075
Two-layer compression hosiery	£1,261	3.247	Dominated	£63,686	3.184	£21,470	3.067
Two-layer compression bandage	£1,947	3.264	£74,738	£63,323	3.166	£20,898	2.985
Four-layer compression bandage	£2,418	3.244	Dominated	£62,456	3.123	£20,288	2.898
Wide ankle circumference, ambulatory							
Compression wrap	£1,256	3.253		£63,812	3.191	£21,518	3.074
Two-layer compression hosiery	£1,260	3.246	Dominated	£63,664	3.183	£21,464	3.066
Two-layer compression bandage	£1,983	3.263	£78,381	£63,270	3.163	£20,856	2.979
Four-layer compression bandage	£2,459	3.243	Dominated	£62,400	3.120	£20,241	2.892
Medium ankle circumference, non-ambulatory							
Compression wrap	£1,908	3.242		£62,927	3.146	£20,784	2.969
Two-layer compression hosiery	£1,966	3.235	Dominated	£62,733	3.137	£20,678	2.954
Two-layer compression bandage	£2,971	3.251	£118,705	£62,043	3.102	£19,784	2.826
Four-layer compression bandage	£3,638	3.231	Dominated	£60,988	3.049	£18,981	2.712
Narrow ankle circumference, non- ambulatory							
Compression wrap	£1,908	3.252		£63,136	3.157	£20,857	2.980
Two-layer compression hosiery	£1,967	3.245	Dominated	£62,939	3.147	£20,750	2.964

Two-layer compression bandage	£2,983	3.261	£118,398	£62,243	3.112	£19,846	2.835
Four-layer compression bandage	£3,745	3.242	Dominated	£61,087	3.054	£18,946	2.707
Wide ankle circumference, non-ambulatory							
Compression wrap	£1,905	3.254		£63,172	3.159	£20,872	2.982
Two-layer compression hosiery	£1,962	3.247	Dominated	£62,971	3.149	£20,765	2.966
Two-layer compression bandage	£3,009	3.263	£119,002	£62,254	3.113	£19,833	2.833
Four-layer compression bandage	£3,772	3.243	Dominated	£61,091	3.055	£18,930	2.704

Abbreviations: QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; 2LCH, two-layer compression hosiery; 4LCB, four-layer compression bandage; 2LCB, two-layer compression bandage; CW, compression wrap. *Fully Incremental Analysis

Figure 8: Cost-effectiveness acceptability curve/frontier

FLCB: four layer compression bandage; TLCB two layer compression bandage; TLCH two layer compression hosiery; CW compression wrap. Base case (medium ankle width, ambulatory person) shown. As optimal decision doesn't change with the threshold, the frontier coincides with the CW CEAC. Scenario analyses generated similar results.

Table 17: Breakdown of costs by compression product

	4LCB	2LCB	CH	CW
Unhealed				
GP Visit	£33.82	£24.80	£31.97	£28.00
Band 3/4 healthcare staff	£0.00	£0.00	£679.85	£595.41
Band 5 nurse	£1,530.31	£1,122.29	£0.00	£0.00
Podiatrist visit	£260.11	£190.76	£245.84	£215.31
Total*	£1,824.24	£1,337.86	£957.66	£838.71
Healed				
Band 5 nurse	£108.91	£113.82	£109.92	£112.08
ABPI test	£21.21	£21.73	£21.32	£21.56
Total*	£130.12	£135.55	£131.25	£133.64
Total				
GP Visit	£33.82	£24.80	£31.97	£28.00
Band 3/4 healthcare staff	£0.00	£0.00	£679.85	£595.41
Band 5 nurse	£1,639.22	£1,236.12	£109.92	£112.08
Compression systems				
4 layer compression bandage	£256.38	£0.00	£0.00	£0.00
2 layer compression bandage	£0.00	£283.80	£0.00	£0.00
2 layer compression hosiery	£118.89	£124.25	£157.98	£122.35
Compression wraps	£0.00	£0.00	£0.00	£111.58
ABPI test	£21.21	£21.73	£21.32	£21.56
Podiatrist visit	£260.11	£190.76	£245.84	£215.31
Total*	£1,954.36	£1,473.40	£1,088.91	£972.35
Total Cost (Incl compression products)	£2,329.64	£1,881.45	£1,246.89	£1,206.29

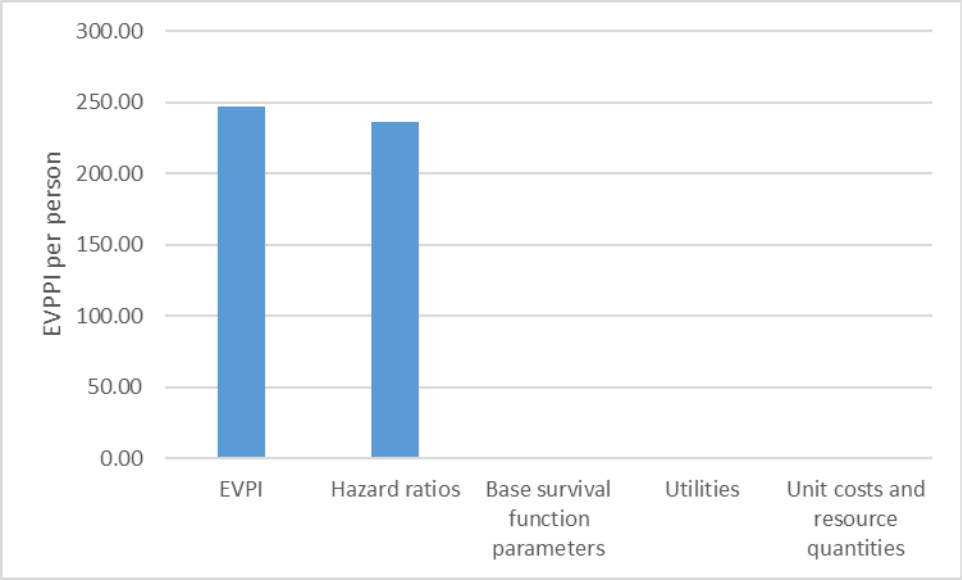
* Excluding compression product costs

7.3.1.1. Parameters contributing to decision uncertainty

Sampled inputs and outputs from the probabilistic analysis for base case 1 were input into the SAVI tool to generate estimates of the EVPPI per person for each model parameter. These were subsequently grouped together into logically linked parameters (relative treatment effect, base survival function parameters, utilities and costs). An EVPPI of greater than zero means there is value in reducing uncertainty in the relevant parameter / groups of parameters. For the purpose of this report, the relative size of the EVPPI can be interpreted as the relative impact on decision uncertainty of those parameters.

The total value per person of eliminating decision uncertainty is £247.30. This is almost entirely accounted for by uncertainty in the relative treatment effect of the four compression product types (hazard ratios).

Figure 9: Expected value of partial perfect information



Note the sum of the EVPPIs will generally not equal the EVPI due to interactions between parameters in the model.

7.3.2. Economically justified price (eJP) analyses

Based on the cost-effectiveness analysis reported in Section 7.3.1, we identified the referent product group which could produce maximum expected net benefit with the current range of prices, and then estimated the eJP for other products by determining the price for each product at which it would match the expected net benefit for the reference product group. The uncertainty in these eJPs was then explored by calculating the probability each product group would be cost-effective (provide maximal net benefit) across a range of prices including its eJP, assuming other products were costed at their eJP.

In the cost-effectiveness analysis (section 7.3.1) compression wraps yielded the highest net monetary (and therefore health) benefit. Further, it dominated two layer compression hosiery and four-layer compression bandages. Because of this, the maximum eJP for all product types except compression wraps was below zero (that is, they are not cost-effective at any price).

The maximum eJP for compression wraps simplifies to the lowest priced product on the market (Table 18).

Table 18: Maximum eJP by population sub-group

Analysis	4LCB	2LCB	2LCH	CW
Base case 1 (medium ankle, ambulatory)	£0	£0	£0	£105.10
Base case 2 (narrow ankle, ambulatory)	£0	£0	£0	£105.10
Base case 3 (wide ankle, ambulatory)	£0	£0	£0	£105.10
Base case 4 (medium ankle, non-ambulatory)	£0	£0	£0	£105.10
Base case 5 (narrow ankle, non-ambulatory)	£0	£0	£0	£105.10
Base case 6 (wide ankle, non-ambulatory)	£0	£0	£0	£105.10

7.3.3. Scenario analysis results

The EAG repeated the decision analysis with an assumed lower utility benefit from a healed ulcer. This did not materially affect the results or the eJP analyses (Table 19 and Table 20). However, over a shorter time horizon (12 weeks), compression hosiery is the most cost-effective product class. As the time horizon is lengthened, compression wraps become the preferred option (Table 21 & Table 22). Finally, a scenario assuming a Band 3 nurse rather than Band 5 nurse is required to administer 4LCB and 2LCB does not materially affect the results, with lower costs associated with CW and CH compared with 4LCB and 2LCB. CW remains the most cost-effective treatment, but a maximum eJP for 2LCB is observed at £3.22 per product (Table 23 and Table 24).

Table 19: Scenario analysis results- lower utility benefit from healed ulcer (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory							
Compression wrap	£1,259	2.867		£56,087	2.804	£18,812	2.687
Two-layer compression hosiery	£1,263	2.866	Dominated	£56,050	2.803	£18,797	2.685
Two-layer compression bandage	£1,949	2.869	£327,731	£55,440	2.772	£18,137	2.591
Four-layer compression bandage	£2,330	2.865	Dominated	£54,967	2.748	£17,724	2.532
Narrow ankle circumference, ambulatory							
Compression wrap	£1,257	2.866		£56,073	2.804	£18,808	2.687
Two-layer compression hosiery	£1,261	2.865	Dominated	£56,035	2.802	£18,793	2.685
Two-layer compression bandage	£1,944	2.869	£337,400	£55,426	2.771	£18,135	2.591
Four-layer compression bandage	£2,415	2.864	Dominated	£54,864	2.743	£17,633	2.519
Wide ankle circumference, ambulatory							
Compression wrap	£1,257	2.864		£56,025	2.801	£18,792	2.685

Two-layer compression hosiery	£1,262	2.863	Dominated	£55,989	2.799	£18,776	2.682
Two-layer compression bandage	£1,984	2.866	£348,659	£55,339	2.767	£18,079	2.583
Four-layer compression bandage	£2,465	2.862	Dominated	£54,769	2.738	£17,567	2.510
Medium ankle circumference, non-ambulatory							
Compression wrap	£1,907	2.864		£55,364	2.768	£18,138	2.591
Two-layer compression hosiery	£1,966	2.862	Dominated	£55,270	2.764	£18,067	2.581
Two-layer compression bandage	£2,972	2.866	£518,322	£54,340	2.717	£17,087	2.441
Four-layer compression bandage	£3,647	2.861	Dominated	£53,573	2.679	£16,380	2.340
Narrow ankle circumference, non-ambulatory							
Compression wrap	£1,907	2.867		£55,441	2.772	£18,165	2.595
Two-layer compression hosiery	£1,964	2.866	Dominated	£55,350	2.768	£18,096	2.585
Two-layer compression bandage	£2,983	2.869	£515,618	£54,407	2.720	£17,104	2.443
Four-layer compression bandage	£3,745	2.865	Dominated	£53,554	2.678	£16,310	2.330
Wide ankle circumference, non-ambulatory							
Four-layer compression bandage	£3,761	2.865		£53,536	2.677	£16,293	2.328
Two-layer compression bandage	£3,001	2.870	Dominated	£54,389	2.719	£17,086	2.441
Two-layer compression hosiery	£1,963	2.866	£518,375	£55,350	2.768	£18,097	2.585
Compression wrap	£1,906	2.867	Dominated	£55,442	2.772	£18,166	2.595

Abbreviations: QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; 2LCH, two-layer compression hosiery; 4LCB, four-layer compression bandage; 2LCB, two-layer compression bandage; CW, compression wrap. *Fully Incremental Analysis

Table 20: Maximum eJP by population sub-group (low utility gain scenario)

Analysis	4LCB	2LCB	2LCH	CW
Base case 1 (medium ankle, ambulatory)	£0	£0	£0	£105.10
Base case 2 (narrow ankle, ambulatory)	£0	£0	£0	£105.10
Base case 3 (wide ankle, ambulatory)	£0	£0	£0	£105.10
Base case 4 (medium ankle, non-ambulatory)	£0	£0	£0	£105.10
Base case 5 (narrow ankle, non-ambulatory)	£0	£0	£0	£105.10
Base case 6 (wide ankle, non-ambulatory)	£0	£0	£0	£105.10

Table 21: Scenario analysis results- shorter time horizon (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory, 12 week time horizon							
Two-layer compression hosiery	£323	0.148		£2,629	0.131	£710	0.101
Compression wrap	£346	0.148	£54,987	£2,614	0.131	£690	0.099
Four-layer compression bandage	£630	0.147	Dominated	£2,318	0.116	£402	0.057
Two-layer compression bandage	£645	0.148	£741,341	£2,323	0.116	£394	0.056
Medium ankle circumference, ambulatory, 24 week time horizon							
Two-layer compression hosiery	£492	0.306		£5,619	0.281	£1,647	0.235
Compression wrap	£516	0.307	£16,750	£5,624	0.281	£1,633	0.233
Two-layer compression bandage	£935	0.308	Dominated	£5,231	0.262	£1,223	0.175
Four-layer compression bandage	£961	0.305	£318,623	£5,138	0.257	£1,174	0.168
Medium ankle circumference, ambulatory, 52 week time horizon							
Two-layer compression hosiery	£703	0.681		£12,923	0.646	£4,066	0.581
Compression wrap	£716	0.685	£3,863	£12,979	0.649	£4,077	0.582
Two-layer compression bandage	£1,249	0.688	£175,580	£12,507	0.625	£3,566	0.509
Four-layer compression bandage	£1,372	0.680	Dominated	£12,225	0.611	£3,387	0.484

Table 22: Maximum eJP by population sub-group (shorter time horizon scenarios)

Analysis	4LCB	2LCB	2LCH	CW
medium ankle, ambulatory, 12 weeks	£0	£0	£15.67	£65.70
medium ankle, ambulatory, 24 weeks	£0	£0	£15.67	£65.70
medium ankle, ambulatory, 52 weeks	£0	£0	£0	£105.10

Table 23: Scenario analysis results- Band 3 nurse applying 4LCB and 2LCB (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory, 12 week time horizon							
Compression wrap	£1,206	3.257		£63,936	3.197	£21,594	3.085
Two-layer compression hosiery	£1,247	3.247	Dominated	£63,700	3.185	£21,484	3.069
Two-layer compression bandage	£1,521	3.265	£40,051	£63,779	3.189	£21,334	3.048
Four-layer compression bandage	£1,839	3.243	Dominated	£63,017	3.151	£20,861	2.980

Table 24: Maximum eJP by population sub-group (Band 3 nurse applying 4LCB & 2LCB)

Analysis	4LCB	2LCB	2LCH	CW
medium ankle, ambulatory, 12 weeks	0	£3.22	0	£105.10

7.4. Factors not included in the decision model

A number of elements were excluded from the model along with a number of simplifying assumptions. These included:

- The model assumes individual products within classes are identical in effect (time to healing of ulcer)
- The analysis does not take into account user preferences over differences between individual products within classes. The EAG emphasises the importance of considering the results presented here alongside the user preference report
- The analysis assumes time to healing is unaffected by patient co-morbidity, BMI, ankle circumference, wound size and ambulatory status. Source data are assumed to be

representative of the population, but subgroup analyses may lead to biased estimates of cost-effectiveness

7.5. Summary and interpretation of the economic evidence

The EAG's analysis found that compression wraps dominated other compression product types; they were on average less expensive and more effective than all other product types. The difference was such that there was no positive eJP for the other product types and the eJP for 2LCWs simplified to the lowest priced product in the range.

These results must be interpreted within the limitations and assumptions of the decision model described in sections 7.2, 0 above and 9 below. Specifically the EAG makes the following observations:

- Compression wraps and two-layer compression hosiery accrue approximately the same cost per patient over the five year time horizon (£1,255 vs £1,259, increment = -£3). Compression wraps accrue very slightly higher QALYs (3.245 vs 3.239, increment = 0.006).
- Two- and four-layer compression bandages are on average more expensive over the five year time horizon than compression wraps and compression hosiery. This is likely driven by the more frequent dressing changes with a more highly qualified nurse required for 2LCB and 4LCB compared with the CW or CH. QALYs accrued are very slightly higher with two-layer compression bandages (vs compression wraps and compression hosiery), and lower with four-layer, although it is questionable whether these differences are clinically meaningful.
- Due to the relative costs and consequences of the four product types, based on expected values, there is no positive eJP for any product except compression wraps, and that defaults to the lowest cost product within its class. However, given the similarity in cost and outcomes, the EAG considers the lowest priced compression wrap and lowest priced compression hosiery to represent the eJP for these two product types; two- and four-layer compression bandages represent relatively lower value for money investments for the NHS.

8. EVIDENCE GAPS AND RESEARCH RECOMMENDATIONS

8.1. Evidence gap analysis

An overview of the prioritised evidence base for the assessment of compression products for people with VLUs is shown in Table 25. The EAG highlight that this is a representation of the individual prioritised studies, for illustrative purposes, rather than a map of all available evidence on this topic. Table cells coloured red denote areas where no in-scope evidence was available in the prioritised studies, and amber denotes limited evidence (i.e. <5 studies).

There were six clinical outcomes with high quality evidence for at least one category of compression products: percentage of wounds healed, time to wound healing and wound-related pain (for 4LCB, 2LCB and 2LCH); reduction in wound size, adverse events and adherence (for 4LCB and 2LCB); or outcomes related to frequency of compression changes (only for 2LCB). For cost items, good data on prices of the technologies and cost of dressings were available (standard NHS price schedules), however data on the cost of supporting products and other resource use were extremely limited.

The table demonstrates large gaps in the prioritised evidence base, including areas where evidence was of insufficient quality to inform robust decision-making. These gaps are further discussed in section 8.2.

Table 25: Evidence gap analysis

		Compression Product Class / Type			
		4LCB	**2LCB**	**2LCH**	**CW**
Outcomes specified in the NICE scope	Reduction in wound size (9 studies)	**5**	**7 (8 arms)**	**2**	**4**
	Changed to wound bed condition (slough/biofilm/exudate/granulation/oedema)	**0**	**0**	**0**	**0**
	Condition of peri-wound skin (1 study)	**1**	**1**	**0**	**0**
	Levels and reduction of oedema	**0**	**0**	**0**	**0**
	Frequency of compression product changes (or interval between visits or nursing time; 5 studies)	**3**	**5**	**1**	**1**
	Percentage of wounds healed (all studies)	**10**	**14 (16 arms)**	**5**	**4**
	Time to complete wound healing (11 studies)	**6**	**9 (10 arms)**	**5**	**1**
	Intervention-related adverse events (11 studies)	**7**	**9 (10 arms)**	**4**	**1**
	HRQoL (6 studies)	**4**	**4**	**3**	**1**
	Wound-related pain (10 studies)	**6**	**8**	**5**	**1**
	Adherence (11 studies)	**7**	**8 (9 arms)**	**4**	**3**
	Ease of treatment use (4 studies)	**2**	**4**	**2**	**0**
	Mobility outside of HRQoL measures	**0**	**0**	**0**	**0**
	Cost of technologies	**2**	**2**	**2**	**1**
	Cost of supporting products	**1**	**1**	**1**	**1**
	Cost of dressings	**1**	**1**	**1**	**1**
	Cost of other resource use (NHS & social care contacts, staff band and time, staff training, clinical waste disposal)	**1**	**1**	**1**	**1**

Abbreviations: HRQoL, health-related quality of life; NHS, National Health Service; 4LCB, four-layer compression bandage; 2LCB, two-layer compression bandage; 2LCH, two-layer compression hosiery; CW, compression wrap.Ongoing studies

The pivotal ongoing study is VenUS 6, an RCT of compression products for venous leg ulcers in a UK setting,[38] as described in Section 5.5. RFIs from the following companies did not list any ongoing studies: Creed Medical Limited/OVIK Health, Haddenham Healthcare, L&R Medical UK, medi UK, SIGVARIS Britain, Solventum and Urgo Limited. The RFI from Smith and Nephew included completed, terminated and withdrawn studies in the ongoing studies list. The EAG noted studies in the RFI publication list for potential inclusion. The only ongoing study noted by this company was in diabetic foot ulcers and therefore outside of the scope of this appraisal and not included in Table 26 below. The only relevant ongoing study listed in the company RFIs is VenUS 6, which was listed in the Essity RFI. The EAG also conducted trial registry searches to identify any other relevant ongoing studies not identified in the RFIs. From these searches, the EAG identified one further ongoing study from Gloucestershire Hospitals NHS Foundation Trust in the UK that potentially addresses the decision problem. One further study[96] that otherwise appeared relevant was excluded due to lack of a control arm to make a comparison with standard of care.

Table 26: Ongoing studies

Name, sponsor and registry number	Date and country	Study type and population	Research objective	Outcomes
Evaluation of the efficacy of multilayer compression & UrgoStart Plus, Gloucestershire Hospitals NHS Foundation Trust, NR – listed on https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/evaluation-of-the-efficacy-of-multilayer-compression-urgostart-plus/	Approval date 7 Aug 2023, 1 year planned duration, UK	NR, people with venous leg ulcers	To evaluate the 12-week healing rates in patients with venous leg ulcers treated with compression system using UrgoStart Plus as the wound contact layer. This can be compared with 12-week healing for a similar cohort of patients treated with the same compression system and a simple low adherent non-interactive dressing.	12-week wound healing rates
VenUS 6, NIHR HTA programme, ISRCTN67321719. Included on Essity RFI	2021-2024 (according to protocol), UK. Essity RFI states expected completion 2025/2026.	RCT, adults with a venous leg ulcer with ABPI >=0.8 and able to tolerate strong compression.	To compare compression-wraps with 'evidence-based compression' for time-to-healing of venous leg ulcers. To determine whether two-layer bandage systems are non-inferior to 'evidence-based compression' for time to healing of venous leg ulcers. To determine which strong compression treatment for venous leg ulcers is most cost-effective.	Primary outcome: time-to-healing. Secondary outcome: Clinical events – healing of the reference leg, ulcer recurrence, ulcer/skin deterioration, amputation, admission/discharge, planned treatment to close/remove incompetent superficial veins (e.g. via endovenous ablation, sclerotherapy) within 28 days, infection, new ulcer occurrence or death. Changes to allocated treatment and reasons for change. HRQoL using VEINES-QoL and EQ-5D-5L.

Name, sponsor and registry number	Date and country	Study type and population	Research objective	Outcomes
				Adherence to treatment and ease of use questionnaires. Ulcer-related pain using 21-point Box Scale. Resource use.

Abbreviations: HRQoL, health-related quality of life.

8.2. Key areas for evidence generation

The EAG identified several key needs for future research. A summary of the key gaps and needs is presented in this section. This takes into account both the prioritised evidence and identified ongoing studies. A selection of key research recommendations relevant to this assessment are then described in Section 8.3.

8.2.1. Population gaps

The EAG highlight that the prioritised evidence did not report data specifically for scoped subgroups (i.e. people with conditions that may limit self-care, people with low or high exudate wounds, people with very fragile skin, or people with irregular leg shapes). This is a gap in the evidence across all categories of compression products.

Population data was not well reported across the included evidence. Notably, ethnicity was only reported in one study,[30] in which all participants were Caucasian. It is, therefore, uncertain whether the available evidence is derived from populations that represent the ethnic diversity of patients seen in UK clinical practice.

8.2.2. Intervention gaps

There was less evidence overall for compression wraps (evidence came from fewer than five prioritised studies for all outcomes). The products with the most prioritised evidence fell into the 2LCB category, followed by 4LCB, and then 2LCH. The EAG note that this is largely representative of the overall amount of evidence available for these products; larger numbers of both prioritised and deprioritised studies were available for 2LCB and 4LCB, whereas it was necessary to prioritise all of the available evidence for compression wraps.

The ongoing VenUS 6 RCT[38] and NMA address some of the evidence gaps for compression wraps. [redacted] However, the EAG note that the total amount of evidence for compression wraps, and to a lesser extent 2LCH, remain notably lower than for 2LCB and 4LCB.

8.2.3. Outcome gaps

In the prioritised studies, there were no data reported on changes to wound bed condition or reduction of oedema. There were also no data found in these studies on changes to mobility

(although for all categories of compression products this was covered by limited HRQoL data). Indeed, it is notable that HRQoL data was limited for all product types.

There were also fewer studies, across all product types, that reported on ease of treatment use. The EAG highlight that patient experiences, including ease of use, are important to consider especially because they may impact upon the treatment of future ulcers in the same patients. Although adherence data were available for all types of compression products (albeit limited for 2LCH and compression wraps), this should not be taken as a proxy for ease of treatment use. This is because adherence to treatment within a study context may differ from that in routine clinical practice.

8.2.4. Other clinical considerations

Overall, the evidence base was of reasonable quality. However, the EAG reiterate that only four of the prioritised RCTs[1,22,24,30] provided assessor blinded results. As a result of this, researcher bias may have impacted upon the remaining study results.

The EAG also note that, due to the large body of studies identified, it was necessary to mostly prioritise RCT data. The strength in this approach is that biases associated with non-randomised studies were likely limited in the included evidence base. However, the EAG acknowledges that RWE can be particularly useful for evaluating some outcomes (e.g. patient and clinician experiences and adherence to treatment). It should be noted that fewer RWE studies were identified in comparison to RCTs, with no observational studies identified for compression wraps.

8.2.5. Economic evidence gaps

8.2.5.1. Structural assumptions

A number of structural assumptions and simplifications were made during development of the decision model. In particular, the model does not allow for ulcer recurrence and therefore the model represents an ‘episode’ of the management of an ulcer. The implicit assumption is that repeated ulcers are managed in an identical manner to the first ulcer with which a person presents for treatment. This may not be the case, and this therefore represents an evidence gap.

The EAG considered inclusion of infection and/or cellulitis in the model. Following discussions with clinical experts, the EAG determined that all ulcers would be colonised by bacteria to a

greater or lesser extent and that only if this progressed to cellulitis would this particularly impact a person's quality of life and incur costs of treatment. However, the EAG was unable to identify appropriate data to quantify the impact of this on health-related quality of life, time to healing of ulcer or cost to the NHS within the resources available for this analysis.

8.2.5.2. Model inputs

Clinical effectiveness

Due to lack of data the EAG assumed that leg size (as determined by ankle and/or calf circumference) and whether the person with VLE is ambulatory or non-ambulatory only affected cost (via differences in product price by sizing and requirement for home rather than clinic contacts with health care professionals) and not time to healing. It is plausible that ankle circumference may be linked to underlying co-morbidities which may influence time to healing, and that a non-ambulatory person may also experience longer time to healing. The model also did not differentiate time to healing by ulcer size. The time to healing and hazard ratios sourced from the network meta-analysis reflect the range of ankle sizes, ambulatory status and lesion size of participants enrolled in the underlying clinical trials. As these studies had varying protocols, inclusion/exclusion criteria, settings and were conducted at different times they may not be directly generalisable to the UK population. On publication, the NMA accompanying and incorporating the VenUS VI study results will partially resolve these uncertainties, but it is ultimately a matter of judgement as to the generalisability of the results.

Resource use

Use of healthcare resources while ulcers are unhealed is not informed by good quality contemporary evidence. A number of studies have been conducted using the THIN database[21,59,97] and these have suggested much higher levels of healthcare resource use and costs than those incorporated into the decision model. One possible explanation is that these studies include healthcare resource use which is not directly incurred due to a single VLU (i.e., patients could have multiple VLUs or have other health conditions with significant management requirements). The EAG's estimates, which were informed by discussion with clinical experts, suggest a similar number of contacts with healthcare professionals to those in the VenUS IV study,[1] but with more frequent contacts for those using compression bandaging (which could be because of high exudate levels; such patients would have been excluded from VenUS IV if exudate levels were too high for hosiery use) and less frequent contacts for those using

compression hosiery (in a trial context participants would have been less likely to be asked to partially self-manage and it is also possible that healthcare providers now ask more patients to partially self-manage due to resource constraints). A further source of uncertainty in the model was the frequency of dressing changes. Whilst a dressing is of minimal cost, this is normally undertaken by a nurse which has a greater cost implication.

Impact of healing on utility

It is clear that patients with VLU have relatively low health-related quality of life, but it is unclear how much their health-related quality of life is improved by VLU healing. Comparisons between groups of individuals based on healing status may be confounded by comorbidities, while comparisons within individuals between pre-healing and post-healing timepoints could be confounded by other factors (e.g., adaptation, feeling of being looked after). Although our best estimate is that utility improves by 0.13, other studies estimated significantly smaller improvements. However, our scenario analysis suggested that the results were insensitive to this.

8.3. Research recommendations and optimal research designs

It should be noted that the gaps in the prioritised evidence may not fully reflect the gaps in the entire evidence base. However, because studies were prioritised based upon key markers of quality and relevance (including study design, study setting and location, and sample size), the EAG believe that it is reasonably likely that these gaps hold true. Based on this, the EAG highlight the following research recommendations (with the caveat that some of these gaps may be covered by less relevant deprioritised evidence or may be partially addressed by the VenUS 6[38] final results).

- Even after the publication of the ongoing VenUS 6 RCT[38] and NMA, large-scale, multi-centre, UK-based RCTs that compare compression wraps with the other product categories (particularly with 2LCH) will likely be useful. These RCTs should consider blinding of outcome assessors, and present both blinded and unblinded results where possible. This will limit researcher bias in the study results. Future RCTs should also include important subgroups (people with conditions that may limit self-care, people with low or high exudate wounds, people with very fragile skin, or people with irregular leg shapes).

- A full range of outcomes should be evaluated in any further RCTs in this area, including HRQoL measures that include mobility, changes to wound bed condition, reduction of oedema, and assessment of peri-wound skin condition.
- Large-scale RWE studies are also recommended, particularly those that compare compression wraps with the other product categories. These studies would be well placed to collect data on patient and clinical experiences, including ease of use and adherence to treatment, and to be designed to represent the populations seen in UK clinical practice.

9. DISCUSSION

The EAG conducted a systematic review to identify evidence addressing the decision problem – that is to say comparing 4LCB, 2LCB, 2LCH and/or CW with either 4LCB or another product representing NHS SOC in the UK. Clinical evidence showed that 2-layer bandaging was at least as good as 4-layer, with some evidence 2-layer may be better. Hosiery and wraps (noting there was only one study on wraps for this comparison) were shown to be equivalent to 4-layer bandaging.

Further, we developed a decision model estimating the cost-effectiveness of four classes of compression products, 4LCB, 2LCB, 2LCH and CW, with the price of each set to the lowest available according to the Drug Tariff (June 2024), with a view to using the output to estimate the maximum economically justified price for all products.

The results showed that CW dominated all other compression product types except for 2LCB: it was on average both less costly and more effective than others. When comparing against 2LCB, 2LCB was not cost-effective, yielding an ICER of £76,804/QALY gained. The differences in cost and outcome were such that there was no positive price for any of the other three classes at which they became the most cost-effective option. Therefore, there was no positive economically justifiable price for these product types, and the maximum eJP for CW was equal to the minimum price currently on the market.

9.1. Interpretation of results

The clinical evidence supports all of 4LCB, 2LCB, 2LCH and CW as viable treatment options. The evidence was generally considered to be good quality. Furthermore, the vast majority of prioritised clinical studies were conducted in a UK or European setting, improving generalisability. However, open label studies do pose an increased risk of bias. It is important to note that, in many cases, different types of compression products have different visual appearance, precluding blinding of patients and clinicians. The EAG note, however, that blinding of outcome assessors should be possible, but did not often occur. In addition, the EAG highlight that caution should be taken when interpreting the results of studies for which there were imbalances at baseline on prognostic indicators.

The point estimate economic analysis results suggest that CW are the most cost-effective product class, and that there is no price at which any other product class becomes value for

money. However, as stated in section 7.5, the EAG regards the differences in outcomes as minor, with the difference between the most and least effective product type totalling 0.019 QALYs, the equivalent of one week of perfect health accrued over five years (3.254 – 3.235 QALYs, Table 16). This is driven by the clinical evidence suggesting broad equivalence, with some evidence favouring 2LCB over 4LCB. CW and CH appear to be of equal, and lowest, cost whilst 2LCB and 4LCB are more expensive. Therefore, CW and CH may be considered to offer better value for money than 2LCB or 4LCB, and the eJPs for each product class defaults to the lowest priced product within each class.

The EAG notes that the cost difference between 4LCB / 2LCB and CH/CW is driven primarily by the assumed difference in nurse band required to apply product types (as well as frequency of product changes). Clinical advice to the EAG was that a band 5 would typically be required to apply 4LCB and 2LCB, whilst a band 3 is required for CH and CW. Comments from manufacturers to the EAG suggested that 1) a lower band nurse may be able to apply 4LCB and 2LCB, and that 2) no nurse may be required for CH and CW as the patient can self-administer. The generalisability of the results and applicability to a particular setting therefore depends on the nursing policy in place in that setting. However, the EAG's scenario analysis assuming a Band 3 nurse applies 4LCB and 2LCB demonstrated that the results were broadly insensitive to this: the costs for these remain higher than CH or CW due to the higher number of procedures.

The economic results must be interpreted with caution. The analysis reported here was constrained by the resources and time allowed for a late-stage assessment evaluation. It therefore should be considered an approximate overview of the plausible costs and consequences of the different treatment modalities and a guide to reasonable product pricing, rather than a definitive assessment. The eJPs must also be interpreted with caution for a number of reasons.

Firstly, the eJPs assume no dressings are included in the kits – naturally the eJP of a kit with a dressing *which will actually be used* is equal to the sum of the eJP without the dressing plus the cheapest cost of acquiring the equivalent dressing (our analysis estimated a cost of 57p for a dressing). If the dressing is going to be disposed of, then there is no reason to pay more for the kit simply because it contains the unwanted dressing.

Secondly, the eJP will depend on the prices of comparator products. If the reference product increases (decreases) in price, this likely leads to an increase (decrease) in the eJP for other

products. As we have not modelled “no compression”, there is technically no maximum eJP for any one product except in relation to other products, and there is a reliance on market mechanisms to prevent an upwards spiral of prices and eJPs.

It may also be argued that the reference product has an eJP *higher* than its current market price, namely the maximum price to which it can be raised and still maximise expected net benefit (assuming other products do not change in price); market competition is again important to prevent an immediate transfer of surplus from consumers (i.e. NHS patients in this case) to producers if this alternative eJP is revealed and acted upon by the manufacturer.

Thirdly, the eJP depends on the characteristics of the patient and of the ulcer, because the market prices can vary according to these characteristics (i.e., bandages of different sizes are often priced differently) and because the provision of healthcare can also vary (e.g., non-ambulatory patients require home visits, which are more expensive as they result in travel time). Although the eJP is conditional on those patient characteristics, this does not mean all these characteristics are sensible bases for price discrimination; it is reasonable for prices to vary according to the size of the product, but it may not be considered reasonable for a manufacturer to charge different prices for the exact same product simply based on the end user. The conditional (or stratified) eJPs may be used by a decision maker to decide, for subgroups of patients and based on prices offered by manufacturers, which products should be routinely used. E.g., if the price offered by the market for a product group exceeds its eJP in patient subgroup A but is below its eJP in patient subgroup B, the NHS will purchase the product for patients in subgroup B but not in subgroup A.

It is not appropriate to attempt to calculate the “overall” eJP for a product group by, e.g., taking a weighted average across the stratified eJPs. When these factors are easily known at the time of the decision problem, they should be used to determine the economically optimal action. To do otherwise would be to discard the static value associated with optimising according to heterogeneity.[98]

9.2. Strengths and Weaknesses

This analysis draws on the best evidence available to the authors, including a good quality network meta-analysis with model inputs reviewed for clinical plausibility by relevant experts. However, the analysis has a number of limitations.

- It is a rapid overview of the economics of the market for compression products in the NHS and should therefore be considered an approximate guide to the costs and benefits rather than a definitive assessment.
- The model assumed there was no difference in effect between individual products within the four classes considered. Where manufacturers can demonstrate a superior outcome compared with their within class competitors, there would be an argument for a higher price.
- Pressure ranges treated as 'strong compression' differed between studies. Some products are in the 30-40 mmHg range, which is below the ideal target pressure in the scope. Other products are in the target 40+ mmHg range. Some studies are unclear on the pressure used. Furthermore, the required pressure varies from person to person. These pressure variations may have an impact on the clinical effectiveness and ultimately cost effectiveness of compression products.
- Two-layer compression bandages were listed as a feature on the NICE scope. However, during the assessment, it emerged that there were different types of two-layer compression bandages which may affect results. Short-stretch bandages were considered to be a type of two-layer compression bandage by experts. However, clinical results for short-stretch bandages generally did appear different than more standard two-layer compression bandage systems.

In addition, the decision model was subject to a number of simplifying assumptions. Firstly, when estimating time to healing, the model did not specifically take into account wound size, whether the person with VLU was ambulatory or not, ankle/calf size comorbidities or BMI. Implicitly, the time to healing estimated from the NMA represented the mix of patients enrolled in the source studies. Subgroup analyses adjusted for differences in cost between these groups, but not effectiveness, so should be interpreted with caution.

The model also did not account for treatment switching, providing an estimate of the costs and consequences of a single compression product modality. Treatment switching has been observed even in controlled clinical trials[1], so this assumption is a limitation. The EAG considers this may bias the analysis in favour of compression hosiery or compression wraps, since their higher unit cost means that wastage resulting from switching would have a greater cost impact.

Further limitations on the costings were that the model assumes that some dressing changes are handled through self-management or informal care. Personal social services may offer this in some cases, thus the cost may be underestimated in all treatment arms. The model also excluded any 'downstream' costs following ulcer healing; the model assumed that once healed, patients would receive an ABPI to check for vascular abnormalities requiring further investigation. The cost of these investigations and any subsequent vascular surgery was excluded. Finally the analysis only considered 'off the shelf' sized products and excluded made to measure compression products.

In summary compression wraps (CW) appear to be the most cost-effective form of compression product, generating higher QALYs at lower cost compared with any of the other three product types. The difference is such that there is no non-zero eJP for these product types and the maximum eJP for CW is simply equal to the lowest cost product. A logical policy conclusion would be to prioritise the prescription of CW, with other types recommended only where CWs are clinically unsuitable for an individual person with VLU.

9.3. Comparison of results with those of VenUS 6

Following conduct of this analysis, the EAG were provided with a final version of the CODA from the Venus 6 NMA, including an additional scenario analysis requested by the EAG that more closely matched the decision question for this review and economic evaluation. Specifically, the VenUS 6 base case assumed equivalence of effect between 'evidence based compression' (EBC), 4LCB and CH and therefore merged them in the analysis. However, the EAG's analysis required 4LCB and CH to be distinct product categories. The VenUS 6 study team provided a scenario analysis CODA with these two categories split out. The CODA was incorporated into the decision model and the results from the Venus 6 economic evaluation and the EAG's analysis compared here.

The VenUS 6 study compared EBC (physician and patient's choice between CH and 4LCB) with other compression products, namely short-stretch bandages (SSB), 2LCB and CW. The comparator set was chosen on the basis that time to healing with CH and 4LCB was equivalent. Analysis including the scenario requested by the EAG was also presented (where CH and 4LCB are separated rather than combined).

Both analyses structured the model as a 3-state state-transition model. However, the VenUS 6 model took a patient lifetime horizon and a 1-month transition period, compared with five years and weekly transitions in the EAG's approach (Table 27).

A key stuctural difference was that the VenUS 6 model allowed for recurrence. This was implemented in a series of 13 tunnel states allowing the risk of recurrence to decline with time, diminishing to zero after one year without recurrence (as per findings from VenUS IV and VenUS 6).

The key methodological difference was in estimation of transition probabilities from the NMA. The VenUS 6 analysis first estimated time to healing with EBC as a function of ulcer size and ulcer duration. This was the referent survival function. Hazard Ratios for other treatments were applied to this to estimate their respective survival functions, from which monthly transition probabilities were estimated. The EAG process was structurally similar, but with 4LCB as the referent, using data from the VenUS IV study. Hazard ratios from the VenUS 6 NMA were applied to this.

Resource use and health state utilities were sourced from the VenUS 6 study, whereas the EAG model resource counts were protocol driven with review by clinical experts, and health state utilities drawn from the literature.

Table 27: Comparison of VenUS 6 and EAG economic model structures and inputs

Key element	VenUS 6 economic evaluation	EAG analysis
Time Horizon	Lifetime	5 years
Model structure	3-state Markov (state-transition) model; unhealed, healed, dead	3-state Markov (state-transition) model; unhealed, healed, dead
Allow for recurrence?	Yes (back transition from healed to unhealed)	No
Transition period	1 month	1 week
Estimation of transition probabilities	Estimation of survival function for EBC (including ulcer duration and size as covariates). HRs for other products applied from NMA. Monthly transition probabilities estimated from survival functions.	Estimation of survival function for 4LCB from published data (VenUS IV), not adjusted for ulcer duration and size. HRs for other products applied from NMA. Weekly transition probabilities estimated from survival functions.
Source of resource use	VenUS 6 study	protocol driven / expert opinion
Source of health state utilities	VenUS 6 study	Published literature

[redacted]

Table 28: VenUS 6 economic evaluation results (scenario analysis requested by EAG)

Treatment	Total costs £	Total QALYs	Inc. costs £	Inc. QALYs	ICER	NMB*
CH	[redacted]	[redacted]				[redacted]
CW	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
2LB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
4LB	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Adapted from scenario analysis of VenUS 6 economic evaluation results. NMB, net monetary benefit.

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Appendix A – Evidence searches

Searches for clinical and economic evidence – summary

Database/search	Date	# hits
Clinical		
Medline clinical	22/08/2024	511
Embase clinical	22/08/2024	657
Cochrane Reviews	22/08/2024	10
Cochrane Trials	22/08/2024	274
CINAHL	23/08/2024	305
Total		**1757**
Deduped		**1083**
Economic		
Medline economic	22/08/2024	1081
Embase economic	22/08/2024	1086
HTA database	23/08/2024	11
Total		**2178**
Deduped		**1609**
Protocols		
Cochrane Protocols	22/08/2024	0
ICTRP	10/09/2024	67 (multiple searches – not deduped)
Clinicaltrials.gov	10/09/2024	156 (multiple searches – not deduped)
Deduped		**109**
Other sources		
MHRA	10/09/2024	0
MAUDE (FDA)	10/09/2024	0
NICE	10/09/2024	15
SIGN	10/09/2024	0

Clinical searches

Ovid MEDLINE(R) ALL 1946 to August 21, 2024

#	Searches	Results
1	compression bandages/ or stockings, compression/	2981
2	(Compression adj2 (bandag* or dressing* or wrap* or sock* or stocking* or hosiery or garment* or sleeve* or clothes or clothing or suit)).ab,ti,kw.	4207
3	(anti-embolic or antiembolic).ab,ti,kw.	87
4	or/1-3	5956
5	Varicose Ulcer/ or Leg Ulcer/	13595
6	((varicose* or venous* or leg* or crural or cruris or stasis) adj2 (ulcer* or ulcus)).ab,ti,kw.	11232
7	vlu.ab,ti,kw.	385
8	or/5-7	16970
9	4 and 8	1272
10	randomized controlled trial.pt.	619434
11	controlled clinical trial.pt.	95591
12	randomized.ab.	657345
13	placebo.ab.	250980
14	clinical trials as topic.sh.	203108
15	randomly.ab.	440250
16	trial.ti.	316024
17	or/10-16	1620993
18	Epidemiologic Methods/	31625
19	exp Epidemiologic Studies/	3328940
20	Observational Studies as Topic/	9981
21	Clinical Studies as Topic/	841
22	(Observational Study or Validation Studies or Clinical Study).pt.	166176
23	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	251590
24	cohort*.ti,ab,kf.	969733
25	(prospective adj7 (study or studies or design or analysis or analyses)).ti,ab,kf.	575309
26	((follow up or followup) adj7 (study or studies or design or analysis or analyses)).ti,ab,kf.	182425
27	((longitudinal or longterm or (long adj term)) adj7 (study or studies or design or analysis or analyses or data)).ti,ab,kf.	378602
28	(retrospective adj7 (study or studies or design or analysis or analyses or data or review)).ti,ab,kf.	766288
29	((case adj control) or (case adj comparison) or (case adj controlled)).ti,ab,kf.	170621
30	(case-referent adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	642
31	(population adj3 (study or studies or analysis or analyses)).ti,ab,kf.	253331
32	((multidimensional or (multi adj dimensional)) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	5465

#	Searches	Results
33	(quasi adj (experiment or experiments or experimental)).ti,ab,kf.	23274
34	(interrupt* time* series or (segment$2 adj3 regression) or (before adj2 after)).ti,ab,kf.	360858
35	("single-arm" or "single arm" or "non random*" or "non-random").ti,ab,kf.	43872
36	or/18-35	4776111
37	9 and (17 or 36)	512
38	exp animals/ not humans.sh.	5250817
39	37 not 38	511

Embase 1974 to 2024 August 21

#	Searches	Results
1	compression sleeve/ or compression stocking/ or exp compression bandage/	8396
2	(Compression adj2 (bandag* or dressing* or wrap* or sock* or stocking* or hosiery or garment* or sleeve* or clothes or clothing or suit)).ab,ti,kw.	6308
3	(anti-embolic or antiembolic).ab,ti,kw.	141
4	or/1-3	12116
5	leg ulcer/	15541
6	((varicose or venous or leg or crural or cruris or stasis) adj2 (ulcer* or ulcus)).ab,ti,kw.	13940
7	vlu.ab,ti,kw.	569
8	or/5-7	20454
9	4 and 8	1712
10	randomized controlled trial/	840522
11	controlled clinical trial/	473809
12	10 or 11	1036084
13	random$.ti,ab.	2112750
14	randomization/	99947
15	intermethod comparison/	308158
16	placebo.ti,ab.	382523
17	(compare or compared or comparison).ti.	633608
18	((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.	2986653
19	(open adj label).ti,ab.	118308
20	((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.	286450
21	double blind procedure/	222957
22	parallel group$1.ti,ab.	34171
23	(crossover or cross over).ti,ab.	130165

#	Searches	Results
24	((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab.	441296
25	(assigned or allocated).ti,ab.	521763
26	(controlled adj7 (study or design or trial)).ti,ab.	482034
27	(volunteer or volunteers).ti,ab.	292086
28	human experiment/	669253
29	trial.ti.	435304
30	or/13-29	6553870
31	30 not 12	5682077
32	(random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.)	10159
33	Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.)	406616
34	(((case adj control$) and random$) not randomi?ed controlled).ti,ab.	22794
35	(Systematic review not (trial or study)).ti.	297711
36	(nonrandom$ not random$).ti,ab.	19778
37	"Random field$".ti,ab.	3103
38	(random cluster adj3 sampl$).ti,ab.	1675
39	(review.ab. and review.pt.) not trial.ti.	1226036
40	"we searched".ab. and (review.ti. or review.pt.)	54592
41	"update review".ab.	145
42	(databases adj4 searched).ab.	70903
43	(rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/	1266228
44	Animal experiment/ not (human experiment/ or human/)	2663231
45	or/32-44	4619051
46	31 not 45	4906876
47	observational study/	388939
48	cohort analysis/	1210403
49	longitudinal study/	220027
50	follow up/	2236862
51	retrospective study/	1673221
52	exp case control study/	241173
53	cross-sectional study/	659450
54	quasi experimental study/	12913
55	prospective study/	937249

#	Searches	Results
56	(observational adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	392165
57	cohort*.ti,ab,kf.	1633041
58	(prospective adj7 (study or studies or design or analysis or analyses)).ti,ab,kf.	877174
59	((follow up or followup) adj7 (study or studies or design or analysis or analyses)).ti,ab,kf.	290388
60	((longitudinal or longterm or (long adj term)) adj7 (study or studies or design or analysis or analyses or data)).ti,ab,kf.	535786
61	(retrospective adj7 (study or studies or design or analysis or analyses or data or review)).ti,ab,kf.	1274290
62	((case adj control) or (case adj comparison) or (case adj controlled)).ti,ab,kf.	227136
63	(case-referent adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	712
64	(population adj3 (study or studies or analysis or analyses)).ti,ab,kf.	383998
65	(descriptive adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	187026
66	((multidimensional or (multi adj dimensional)) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	6346
67	(cross adj sectional adj7 (study or studies or design or research or analysis or analyses or survey or findings)).ti,ab,kf.	648433
68	((natural adj experiment) or (natural adj experiments)).ti,ab,kf.	4052
69	(quasi adj (experiment or experiments or experimental)).ti,ab,kf.	28504
70	((non experiment or nonexperiment or non experimental or nonexperimental) adj3 (study or studies or design or analysis or analyses)).ti,ab,kf.	2540
71	(interrupt* time* series or (segment$2 adj3 regression) or (before adj2 after)).ti,ab,kf.	505621
72	("single-arm" or "single arm" or "non random*" or "non-random").ti,ab,kf.	73370
73	or/47-72	7372502
74	9 and (46 or 73)	658
75	(exp animal/ or nonhuman/) not exp human/	7408349
76	74 not 75	657

Cochrane

#1 MeSH descriptor: [Compression Bandages] this term only 292

#2 MeSH descriptor: [Stockings, Compression] this term only 356

#3 (Compression NEAR/2 (bandag* or dressing* or wrap* or sock* or stocking* or hosiery or garment* or sleeve* or clothes or clothing or suit)):ti,kw 1645

#4 (anti-embolic or antiembolic):ti,kw 3

#5 #1 or #2 or #3 or #4 1647

#6 MeSH descriptor: [Varicose Ulcer] this term only 846

#7 MeSH descriptor: [Leg Ulcer] this term only 628

#8 ((varicose* or venous* or leg* or crural or cruris or stasis) NEAR/2 (ulcer* or ulcus)):ti,kw 2489

#9 vlu:ti,kw 15

#10 #6 or #7 or #8 or #9 2489

#11 #5 and #10 286

CINAHL

#	Query	Results
S4	(AB ((random* or control* or comparative* or trial* or observational or cohort* or prospective* or longitudinal or retrospective* or (before N1 after) or (interrupt* N1 time*) or (single N1 arm))) OR TI ((random* or control* or comparative* or trial* or observational or cohort* or prospective* or longitudinal or retrospective* or (before N1 after) or (interrupt* N1 time*) or (single N1 arm)))) AND (S1 AND S2 AND S3)	305
S3	AB ((random* or control* or comparative* or trial* or observational or cohort* or prospective* or longitudinal or retrospective* or (before N1 after) or (interrupt* N1 time*) or (single N1 arm))) OR TI ((random* or control* or comparative* or trial* or observational or cohort* or prospective* or longitudinal or retrospective* or (before N1 after) or (interrupt* N1 time*) or (single N1 arm)))	1,880,803
S2	((MM "Venous Ulcer") OR (MM "Leg Ulcer")) OR AB (((varicose* or venous* or leg* or crural or cruris or stasis) N2 (ulcer* or ulcus))) OR TI (((varicose* or venous* or leg* or crural or cruris or stasis) N2 (ulcer* or ulcus))) OR AB vlu OR TI vlu	6,701
S1	((MM "Elastic Bandages") OR (MM "Compression Therapy")) OR AB ((Compression N2 (bandag* or dressing* or wrap* or sock* or stocking* or hosiery or garment* or sleeve* or clothes or clothing or suit))) OR TI ((Compression N2 (bandag* or dressing* or wrap* or sock* or stocking* or hosiery or garment* or sleeve* or clothes or clothing or suit))) OR AB ((anti-embolic or antiembolic)) OR TI ((anti-embolic or antiembolic))	3,279

Economic searches

Ovid MEDLINE(R) ALL 1946 to August 21, 2024

#	Searches	Results
1	*Varicose Ulcer/ or *Leg Ulcer/	11050
2	((varicose* or venous* or leg* or crural or cruris or stasis) adj2 (ulcer* or ulcus)).ti,kw.	7340
3	vlu.ab,ti,kw.	385
4	or/1-3	12055
5	"Value of Life"/	5829
6	Quality of Life/	292172
7	quality of life.ti,kf.	128069
8	((instrument or instruments) adj3 quality of life).ab.	4101
9	Quality-Adjusted Life Years/	16716
10	quality adjusted life.ti,ab,kf.	18995
11	(qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf.	31138
12	disability adjusted life.ti,ab,kf.	6405
13	daly*.ti,ab,kf.	5765
14	(sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf.	32360
15	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf.	2818
16	(sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kf.	656
17	(sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf.	8253
18	(sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf.	43
19	(sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf.	468
20	(hql or hqol or h qol or hrqol or hr qol).ti,ab,kf.	26632
21	(hye or hyes).ti,ab,kf.	78
22	(health* adj2 year* adj2 equivalent*).ti,ab,kf.	48
23	(pqol or qls).ti,ab,kf.	484
24	(quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf.	773
25	nottingham health profile*.ti,ab,kf.	1267
26	sickness impact profile.ti,ab,kf.	1102
27	exp health status indicators/	350106
28	(health adj3 (utilit* or status)).ti,ab,kf.	99297

#	Searches	Results
29	(utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf.	17309
30	(preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf.	15693
31	disutilit*.ti,ab,kf.	692
32	rosser.ti,ab,kf.	112
33	willingness to pay.ti,ab,kf.	9724
34	standard gamble*.ti,ab,kf.	929
35	(time trade off or time tradeoff).ti,ab,kf.	1739
36	tto.ti,ab,kf.	1528
37	(hui or hui1 or hui2 or hui3).ti,ab,kf.	2126
38	(eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf.	25290
39	duke health profile.ti,ab,kf.	95
40	functional status questionnaire.ti,ab,kf.	134
41	dartmouth coop functional health assessment*.ti,ab,kf.	14
42	or/5-41	799084
43	exp "Costs and Cost Analysis"/	272540
44	(cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.	230636
45	(value adj2 (money or monetary)).ti,ab,kf.	3252
46	exp models, economic/	16471
47	economic model*.ab,kf.	4525
48	markov chains/	16374
49	markov.ti,ab,kf.	31321
50	monte carlo method/	33208
51	monte carlo.ti,ab,kf.	64099
52	exp Decision Theory/	13784
53	(decision* adj2 (tree* or analy* or model*)).ti,ab,kf.	44473
54	or/43-53	574601
55	afghanistan/ or africa/ or africa, northern/ or africa, central/ or africa, eastern/ or "africa south of the sahara"/ or africa, southern/ or africa, western/ or albania/ or algeria/ or andorra/ or angola/ or "antigua and barbuda"/ or argentina/ or armenia/ or azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or botswana/ or brazil/ or brunei/ or bulgaria/ or burkina faso/ or burundi/ or cabo verde/ or cambodia/ or cameroon/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cote d'ivoire/ or croatia/ or cuba/ or "democratic republic of the congo"/ or cyprus/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or egypt/ or el salvador/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or fiji/ or gabon/ or gambia/ or "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or independent	1363281

#	Searches	Results
	state of samoa/ or exp india/ or indian ocean islands/ or indochina/ or indonesia/ or iran/ or iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libya/ or madagascar/ or malaysia/ or malawi/ or mali/ or malta/ or mauritania/ or mauritius/ or mekong valley/ or melanesia/ or micronesia/ or monaco/ or mongolia/ or montenegro/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nepal/ or nicaragua/ or niger/ or nigeria/ or oman/ or pakistan/ or palau/ or exp panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or "republic of north macedonia"/ or romania/ or exp russia/ or rwanda/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "sao tome and principe"/ or saudi arabia/ or serbia/ or sierra leone/ or senegal/ or seychelles/ or singapore/ or somalia/ or south africa/ or south sudan/ or sri lanka/ or sudan/ or suriname/ or syria/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad and tobago"/ or tunisia/ or turkmenistan/ or uganda/ or ukraine/ or united arab emirates/ or uruguay/ or uzbekistan/ or vanuatu/ or venezuela/ or vietnam/ or west indies/ or yemen/ or zambia/ or zimbabwe/	
56	"Organisation for Economic Co-Operation and Development"/	621
57	australasia/ or exp australia/ or austria/ or baltic states/ or belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or exp denmark/ or estonia/ or europe/ or finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or portugal/ or exp "republic of korea"/ or "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or sweden/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/	3583638
58	European Union/	18134
59	Developed Countries/	21609
60	or/56-59	3600106
61	55 not 60	1271829
62	54 not 61	539684
63	4 and (42 or 62)	1096
64	limit 63 to yr="1994 -Current"	1081

Embase 1974 to 2024 August 21

#	Searches	Results
1	*leg ulcer/	8772
2	((varicose or venous or leg or crural or cruris or stasis) adj2 (ulcer* or ulcus)).ti,kw.	7933
3	vlu.ab,ti,kw.	569
4	or/1-3	11103

#	Searches	Results
5	socioeconomics/	169708
6	exp Quality of Life/	714026
7	quality of life.ti,kf.	195396
8	((instrument or instruments) adj3 quality of life).ab.	5690
9	Quality-Adjusted Life Year/	38267
10	quality adjusted life.ti,ab,kf.	28993
11	(qaly* or qald* or qale* or qtime* or life year or life years).ti,ab,kf.	49014
12	disability adjusted life.ti,ab,kf.	7701
13	daly*.ti,ab,kf.	7418
14	(sf36 or sf 36 or short form 36 or shortform 36 or short form36 or shortform36 or sf thirtysix or sfthirtysix or sfthirty six or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).ti,ab,kf.	52672
15	(sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six or shortform6 or short form6).ti,ab,kf.	3156
16	(sf8 or sf 8 or sf eight or sfeight or shortform 8 or shortform 8 or shortform8 or short form8 or shortform eight or short form eight).ti,ab,kf.	1082
17	(sf12 or sf 12 or short form 12 or shortform 12 or short form12 or shortform12 or sf twelve or sftwelve or shortform twelve or short form twelve).ti,ab,kf.	13085
18	(sf16 or sf 16 or short form 16 or shortform 16 or short form16 or shortform16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).ti,ab,kf.	73
19	(sf20 or sf 20 or short form 20 or shortform 20 or short form20 or shortform20 or sf twenty or sftwenty or shortform twenty or short form twenty).ti,ab,kf.	550
20	(hql or hqol or h qol or hrqol or hr qol).ti,ab,kf.	42798
21	(hye or hyes).ti,ab,kf.	199
22	(health* adj2 year* adj2 equivalent*).ti,ab,kf.	56
23	(pqol or qls).ti,ab,kf.	788
24	(quality of wellbeing or quality of well being or index of wellbeing or index of well being or qwb).ti,ab,kf.	950
25	nottingham health profile*.ti,ab,kf.	1710
26	nottingham health profile/	692
27	sickness impact profile.ti,ab,kf.	1304
28	sickness impact profile/	2414
29	health status indicator/	3616
30	(health adj3 (utilit* or status)).ti,ab,kf.	130506
31	(utilit* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or weight)).ti,ab,kf.	27654
32	(preference* adj3 (valu* or measur* or health or life or estimat* or elicit* or disease or score* or instrument or instruments)).ti,ab,kf.	20786
33	disutilit*.ti,ab,kf.	1392
34	rosser.ti,ab,kf.	148
35	willingness to pay.ti,ab,kf.	14532

#	Searches	Results
36	standard gamble*.ti,ab,kf.	1244
37	(time trade off or time tradeoff).ti,ab,kf.	2524
38	tto.ti,ab,kf.	2413
39	(hui or hui1 or hui2 or hui3).ti,ab,kf.	3407
40	(eq or euroqol or euro qol or eq5d or eq 5d or euroqual or euro qual).ti,ab,kf.	42131
41	duke health profile.ti,ab,kf.	123
42	functional status questionnaire.ti,ab,kf.	182
43	dartmouth coop functional health assessment*.ti,ab,kf.	14
44	(cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf.	317164
45	(value adj2 (money or monetary)).ti,ab,kf.	4386
46	or/5-45	1336588
47	Statistical Model/	178823
48	economic model*.ab,kf.	6789
49	Probability/	158065
50	markov.ti,ab,kf.	41247
51	monte carlo method/	54594
52	monte carlo.ti,ab,kf.	67844
53	Decision Theory/	1886
54	Decision Tree/	25639
55	(decision* adj2 (tree* or analy* or model*)).ti,ab,kf.	59479
56	or/47-55	482247
57	afghanistan/ or africa/ or "africa south of the sahara"/ or albania/ or algeria/ or andorra/ or angola/ or argentina/ or "antigua and barbuda"/ or armenia/ or exp azerbaijan/ or bahamas/ or bahrain/ or bangladesh/ or barbados/ or belarus/ or belize/ or benin/ or bhutan/ or bolivia/ or borneo/ or exp "bosnia and herzegovina"/ or botswana/ or exp brazil/ or brunei darussalam/ or bulgaria/ or burkina faso/ or burundi/ or cambodia/ or cameroon/ or cape verde/ or central africa/ or central african republic/ or chad/ or exp china/ or comoros/ or congo/ or cook islands/ or coted'ivoire/ or croatia/ or cuba/ or cyprus/ or democratic republic congo/ or djibouti/ or dominica/ or dominican republic/ or ecuador/ or el salvador/ or egypt/ or equatorial guinea/ or eritrea/ or eswatini/ or ethiopia/ or exp "federated states of micronesia"/ or fiji/ or gabon/ or gambia/ or exp "georgia (republic)"/ or ghana/ or grenada/ or guatemala/ or guinea/ or guinea-bissau/ or guyana/ or haiti/ or honduras/ or exp india/ or exp indonesia/ or iran/ or exp iraq/ or jamaica/ or jordan/ or kazakhstan/ or kenya/ or kiribati/ or kosovo/ or kuwait/ or kyrgyzstan/ or laos/ or lebanon/ or liechtenstein/ or lesotho/ or liberia/ or libyan arab jamahiriya/ or madagascar/ or malawi/ or exp malaysia/ or maldives/ or mali/ or malta/ or mauritania/ or mauritius/ or melanesia/ or moldova/ or monaco/ or mongolia/ or "montenegro (republic)"/ or morocco/ or mozambique/ or myanmar/ or namibia/ or nauru/ or nepal/ or nicaragua/ or niger/ or nigeria/ or niue/ or north africa/ or oman/ or exp pakistan/ or palau/ or palestine/ or panama/ or papua new guinea/ or paraguay/ or peru/ or philippines/ or polynesia/ or qatar/ or "republic of north	1798332

#	Searches	Results
	macedonia"/ or romania/ or exp russian federation/ or rwanda/ or sahel/ or "saint kitts and nevis"/ or "saint lucia"/ or "saint vincent and the grenadines"/ or saudi arabia/ or senegal/ or exp serbia/ or seychelles/ or sierra leone/ or singapore/ or "sao tome and principe"/ or solomon islands/ or exp somalia/ or south africa/ or south asia/ or south sudan/ or exp southeast asia/ or sri lanka/ or sudan/ or suriname/ or syrian arab republic/ or taiwan/ or tajikistan/ or tanzania/ or thailand/ or timor-leste/ or togo/ or tonga/ or "trinidad andtobago"/ or tunisia/ or turkmenistan/ or tuvalu/ or uganda/ or exp ukraine/ or exp united arab emirates/ or uruguay/ or exp uzbekistan/ or vanuatu/ or venezuela/ or viet nam/ or western sahara/ or yemen/ or zambia/ or zimbabwe/	
58	"organisation for economic co-operation and development"/	3081
59	exp australia/ or "australia and new zealand"/ or austria/ or baltic states/ or exp belgium/ or exp canada/ or chile/ or colombia/ or costa rica/ or czech republic/ or denmark/ or estonia/ or europe/ or exp finland/ or exp france/ or exp germany/ or greece/ or hungary/ or iceland/ or ireland/ or israel/ or exp italy/ or japan/ or korea/ or latvia/ or lithuania/ or luxembourg/ or exp mexico/ or netherlands/ or new zealand/ or north america/ or exp norway/ or poland/ or exp portugal/ or scandinavia/ or sweden/ or slovakia/ or slovenia/ or south korea/ or exp spain/ or switzerland/ or exp united kingdom/ or "turkey (republic)"/ or exp united states/ or western europe/	3919196
60	european union/	32613
61	developed country/	36438
62	or/58-61	3954346
63	57 not 62	1637598
64	56 not 63	450207
65	4 and (46 or 64)	1086

HTA database

compression AND ulcer AND (leg OR ven*)

Trial protocols

ICTRP + Clinical trials.gov

Term	ICTRP	Clinicaltrials.gov
Ulcer AND "compression bandage"	15	46
Ulcer AND "compression wrap"	1	46
Ulcer AND "compression hosiery"	3	2
Ulcer AND compression AND bandag*	45	49
Ulcer AND compression AND wrap*	3	13
Total (deduped)	**106**	

Other sources

MHRA

Compression bandage* OR Compression wrap* OR Compression hosiery OR Venous leg ulcer

Maude

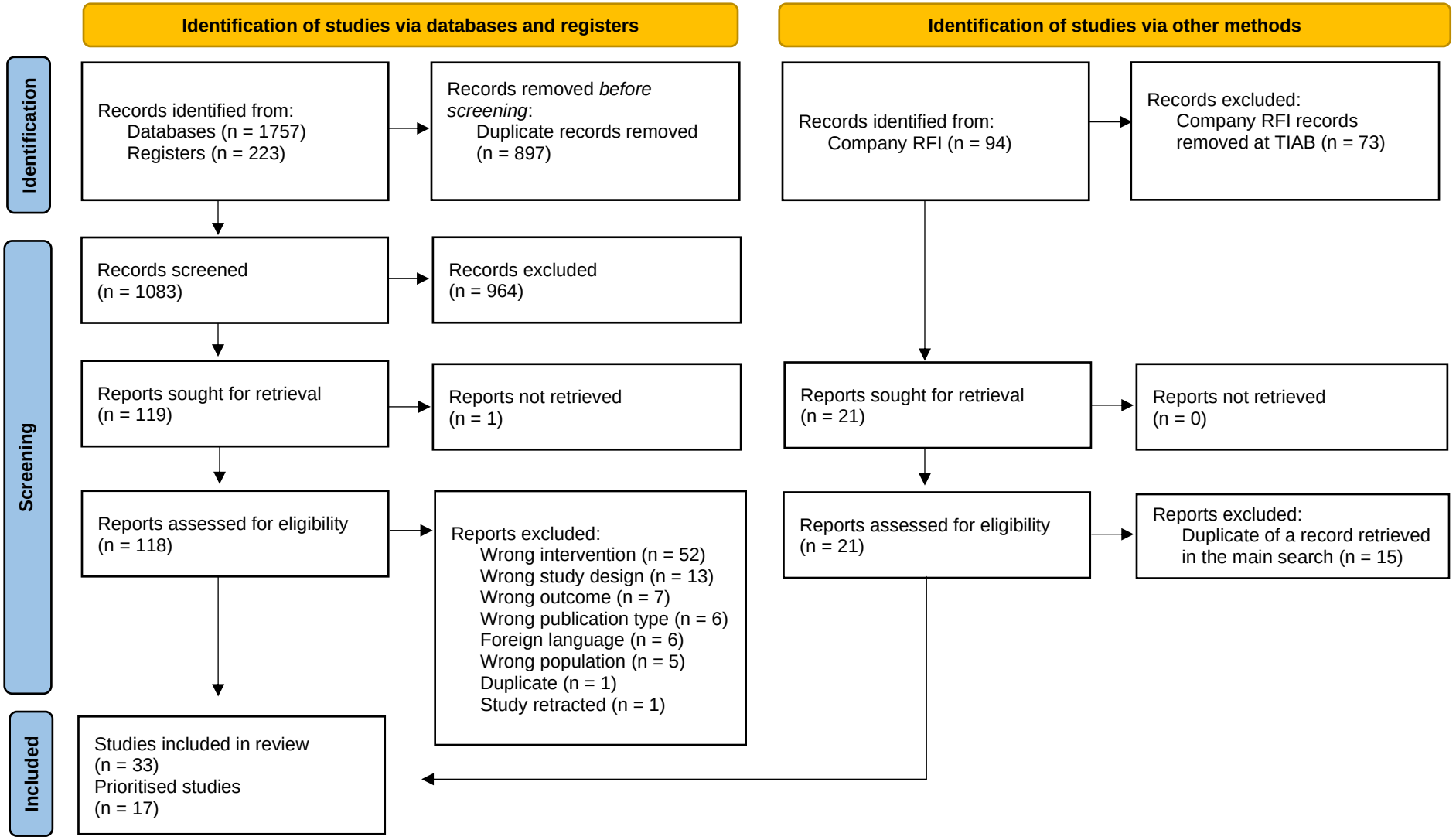
Compression bandage* OR Compression wrap* OR Compression hosiery OR Venous leg ulcer

NICE & SIGN

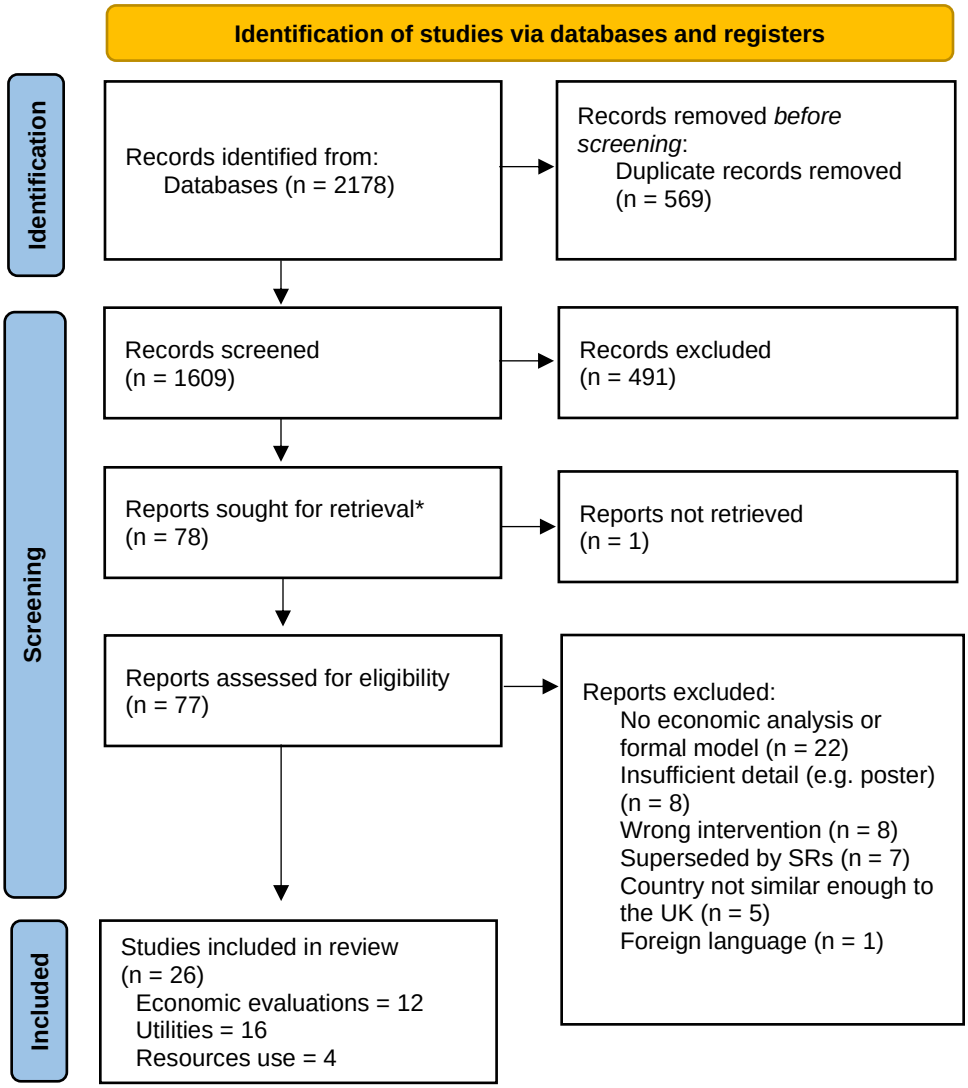
Venous leg ulcer

Appendix B – PRISMA diagrams

PRISMA diagram. Clinical



PRISMA diagram. Economic



Appendix C – Excluded studies

Studies excluded at full text: clinical

Author	Year	Reason for exclusion
Andriessen et al.	2012	Not in English language
Arnold et al.	1994	Wrong intervention. Compression therapy is common to both groups - the difference arises in the different dressings used
Ashby et al.	2015	Not in English language
Baccaglini et al.	1998	Wrong intervention. No comparator that represents 4-layer or NHS SoC
Backhouse et al.	1987	Wrong intervention. Difference between groups is dressings rather than compression therapy
Benigni et al.	2007	Wrong study design. There is no comparator that represents 4-layer bandage or SoC in the NHS
Betts et al.	2005	Wrong outcome. Cost effectiveness study
Bjellerup et al.	1993	Wrong intervention
Bowszyc et al.	1995	Wrong intervention. Compression therapy is common to both arms, they differed only in dressing used
Carr et al.	2015	Wrong intervention. No comparator that represents 4-layer or NHS SoC
Carson et al.	2010	Wrong intervention. No comparator representing 4-layer or NHS SoC
Chan et al.	2023	Wrong intervention. Not a comparison of the 2 compression products
Charles et al.	2002	Wrong intervention. Comparison of dressings rather than compression products
Cherry et al.	1990	Wrong intervention. Details of compression type and strength not provided
Clarke-Moloney et al.	2014	Wrong intervention. Insufficient pressure
Clarke-Moloney et al.	2005	Wrong intervention. Blended comparator
Dabiri et al.	2015	Wrong intervention. No comparator that represents 4-layer or NHS SoC
DePalma et al.	1999	Wrong intervention. Not products used in NHS
Dereure et al.	2005	Wrong intervention. No comparator that represents 4-layer or NHS SoC

Author	Year	Reason for exclusion
Elena et al.	2020	Wrong intervention. No comparator that is 4-layer or represents NHS SoC
Eriksson et al.	1986	Wrong intervention. Not a comparison of 2 compression products
Escaleira et al.	2010	Wrong intervention. No comparator that represents 4-layer or NHS SoC
Forlee et al.	2014	Wrong intervention. Assessing dressing rather than compression therapy
Franks et al.	2007	Wrong intervention. Assessment of dressings rather than compression products
Franks et al.	1995	Wrong intervention. Not strong compression (class 2)
Garavello et al.	2021	Wrong intervention. No comparator that represents NHS SoC
Gibson et al.	2007	Wrong publication type. Commentary
Hankin et al.	2012	Wrong intervention. Not a comparison of compression products
Harley et al.	2004	Wrong intervention. Pneumatic device
Jaiswal et al.	2023	Wrong intervention. Not a comparison between different compression products - no comparator that represents 4-layer or NHS SoC
Jull et al.	2004	Wrong intervention. Not a comparison of different compression products - no comparator arm that represents 4-layer compression or NHS SoC
Junger et al.	2002	Not in English language
Kalodiki et al.	2007	Wrong intervention. Intervention is pneumatic compression with an air pump - given alongside compression stocking, which is common to both arms.
Kapp et al.	2013	Wrong population. Focus on ulcer recurrence
Karanikolic et al.	2020	Wrong publication type
Karimi et al.	2010	Wrong intervention. No mention of pressure, and only comparing antimicrobials not compression itself
Kerstein & Gahtan	2000	Wrong intervention
Lee et al.	2009	Wrong intervention. Single layer products are not within the scope of this appraisal
Lee et al.	2019	Wrong intervention. Analysed by broad class e.g. stockings, bandages - will encompass a range of products and compression strengths

Author	Year	Reason for exclusion
Maggio et al.	2012	Wrong intervention. Not a comparison of two compression products - intervention is a dressing
Mayberry et al.	1991	Wrong intervention. Not comparing different compression products
Meaume et al.	2014	Wrong intervention. Comparing different dressings rather than compression, which was given in the same form to both groups
Melhuish et al.	2000	Wrong population. Healthy volunteer study
Menezes et al.	2019	Wrong intervention. No comparator that is either 4-layer compression or NHS SoC
Meyer et al.	2002	Wrong intervention. Unclear what compression level is for these bandages
Milic et al.	2019	Wrong outcome. Focus on recurrence, not on would healing itself
Milic et al.	2022	Wrong outcome. Focus on recurrence, not on would healing itself
Milic et al.	2015	Wrong outcome. Focus on recurrence, not on would healing itself
Milic et al.	2018	Wrong outcome. Focus on recurrence, not on would healing itself
Milic et al.	2023	Wrong outcome. Focus on recurrence, not on would healing itself
Moffatt et al.	2012	Wrong publication type. Full text PDF unavailable – conference abstract not enough information
Moody[a]	1999	Duplicate. Mean pressure was below 40 mmHg at rest
Moody[b]	1999	Wrong intervention. Wrong pressure
Nair et al.	2022	Wrong intervention. No estimate of pressure
Nelson et al.	2006	Wrong population. Not people with active ulcers
Nelson et al.	2004	Wrong intervention. Not clear the relevant pressures were verified to ensure full/strong compression
Nikolic-Pucar et al.	2017	Wrong intervention. No specific intervention, no account of pressure
O'Brien et al.	2003	Wrong study design. Blended comparator
Ogrin et al.	2007	Wrong outcome. Outcomes apply only to neurovascular changes
Partsch & Horakova	1994	Not in English language
Phillips & Wright	2024	Wrong population. Healthy population

Author	Year	Reason for exclusion
Powell et al.	2015	Wrong study design. Single-arm study
Reich-Schupke et al.	2009	Wrong intervention. Broad classes of compression product across strengths
Rocca et al.	2012	Wrong publication type. Not enough information in this abstract
Santos	2016	Wrong publication type. This is an abstract only, not enough information
Senet et al.	2022	Wrong study design. Single-arm, unclear pressure
Sermsathanasawadi et al.	2017	Wrong study design
Shin et al.	2017	Wrong study design. Case report
Smith et al.	2004	Wrong study design. Single-arm trial
Smith-StrÃ¸m	2006	Not in English language
Stacey et al.	1997	Wrong intervention. Comparison between wound dressings, not compression products
Stansal et al.	2013	Wrong study design. Blended comparator, single-arm trial
Stansal et al.	2024	Wrong study design. Single-arm trial
Stather et al.	2019	Wrong intervention. Suboptimal pressures
Taradaj et al.	2009	Wrong intervention. Pressure not high enough
Taylor et al.	1998	Wrong intervention. Blended comparator
Tiwari et al.	2015	Wrong intervention. Poor quality comparative study, no account of pressure, comparator is unclear and probably not SoC in NHS
Tiwary et al.	2020	Not able to retrieve PDF
Vowden et al.	2001	Wrong study design. Single-arm study
Watson et al.	2011	Wrong intervention. Comparator is ultrasound, SoC same in both arms
Weller et al.	2012	Wrong intervention. Three-layer vs two-layer
Wilkinson et al.	1997	Wrong intervention. Suboptimal pressure
Willenberg et al.	2010	Wrong population. Healthy volunteers
Wong et al.[a]	2012	Wrong publication type. Abstract, so not enough information e.g. about pressures
Wong et al.[b]	2012	Study retracted
Wong et al.	2006	Not in English language

Author	Year	Reason for exclusion
Partsch et al	2001	Wrong intervention. Pressure unclear – strong or reduced compression depended on leg circumference
Stephen-Haynes & Callaghan	2015	Wrong intervention. Not a relevant comparison.
Vowden et al.	2000	Wrong study design. Single-arm study
Wicks	2015	Wrong study design. Single-arm study
Wolff et al.	2011	Wrong study design
Aloweni et al.	2022	Wrong intervention. Broad classes of compression product across different strengths

Studies excluded at full text: economic

Authors	Year	Reason for exclusion
Augustin et al	2017	HRQoL data. No economic analysis.
Augustin et al	2016	Decision analytic model for different intervention.
Barnsbee et al	2019	Wrong country for costs. Other SRs cover QALYs.
Bergemann et al	1999	Older study. Decision analytic model for different intervention.
Betts et al	2018	Poster abstract. Cross-sectional analysis.
Betts et al	2018	Poster abstract. Wrong intervention and wrong population (diabetic foot ulcer).
Bland et al	2015	Validation of HRQoL tool, superceded by SRs of such tools.
Brizzio et al	2010	Poster abstract. RCT that included QoL outcomes. No other economic evaluation.
Carr et al	1999	Older economic evaluation.
Carter et al	2014	Wrong intervention. North American payer perspective.
Charles	2004	HRQoL data only. No economic analysis.
Cheng et al	2018	Poster of 2019 full text paper by same authors.
Cheng et al	2019	Comparison of HRQoL tools. No economic analysis.
De Almeida et al	2022	Focus on venous insufficiency rather than ulcers per se.
De Oliveira et al	2023	Comparison of HRQoL tools. No economic analysis. South American perspective.
Dias et al	2014	HRQoL data only. No economic evaluation. Cross-sectional study.
Engelhardt et al	2014	Validation of HRQoL tool. No economic evaluation.
Finlayson et al	2014	HRQoL data only. No economic analysis.

Authors	Year	Reason for exclusion
Franks et al	2003	SF-36 data for VLUs. No economic comparison. Older study, superseded by systematic reviews.
Franks et al	2001	Comparison of different HRQoL tools. Older study, superseded by systematic reviews.
Gonzalez de la Torre et al	2017	HRQoL data only. No economic analysis.
Guest et al	2024	Decision analytic model on wrong intervention.
Guest et al	2022	Decision analytic model on wrong intervention.
Guest et al	2009	Decision analytic model on wrong intervention.
Guest et al	2018	Decision analytic model on wrong intervention.
Guest et al	2021	Decision analytic model on wrong intervention.
Guest et al	2012	Decision analytic model on wrong intervention.
Hayes et al	2020	HRQoL data only. No economic analysis.
Hopman et al	2013	HRQoL data only. No economic analysis.
Hopman et al	2016	HRQoL data only. No economic analysis.
Iglesias et al	2005	Comparison of HRQoL scales. No economic analysis.
Iglesias et al	2006	Decision analytic model on wrong intervention.
Jaiswal et al	2023	HRQoL data only. No economic analysis.
Jull et al	2018	HRQoL data only. No economic analysis.
Jull et al	2010	Assessment of two HRQoL tools. Superseded by systematic reviews.
Jull et al	2020	HRQoL data only. No economic analysis.
Maunoury et al	2012	Conference abstract.
Massand et al	2021	Non-scoped intervention. Not a decision model – review of papers that assessed cost and efficacy data.
Matejic et al	2016	Conference poster. HRQoL data only. No economic analysis.
Nuijten et al	2012	Conference poster.
O'Brien et al	2003	Cost assessment but no formal economic model.
Ohlsson et al	1994	Cost assessment but no formal economic model.
Palfreyman et al	2008	Paper on HRQoL tool development. No economic evaluation.
Renner et al	2009	Interview-based study.
Sibbald et al	2001	Decision model on wrong intervention. North American perspective.
Sommer et al	2017	Foreign language paper.
Tiwary et al	2021	Unable to obtain full text.
Tuson et al	2024	Decision model on wrong intervention
Walters et al	1999	Comparison of HRQoL tools. Older study/

Authors	Year	Reason for exclusion
Weller et al	2012	Conference poster of study that is also available as full text.
Weller et al	2012	HRQoL data only. No economic analysis.
Wong et al	2012	HRQoL data only. No economic analysis. Asian setting.

Appendix D – prioritised studies

#	Author and date	Decision	Rationale
1.	Adderley 2014	Not prioritised	Not the main report from VenUS-IV.
2.	Ashby 2014 (Lancet)	Not prioritised	The HTA report covers the same VenUS-IV content in more detail.
3.	Ashby 2014 (HTA)	Prioritised study	Large UK pragmatic RCT of 2-layer hosiery vs 4-layer bandage.
4.	Blecken 2005	Prioritised study	Small RCT vs 4-layer bandage – limited evidence on wraps.
5.	Brizzio 2006	Not prioritised	Small, non-randomised study, not from Europe.
6.	Cameron 1996	Not prioritised	Not at RCT.
7.	Coull 2006	Not prioritised	Comparing spiral and figure of 8 bandaging rather than different classes.
8.	Dolibog 2014	Prioritised study	European RCT comparing 5 types of compression, though not all are within scope.
9.	Dolibog 2013	Not prioritised	A more specific population, within scope, but restricted generalisability.
10.	Finlayson 2014	Prioritised study	RCT strong compression hosiery vs 4-layer, but note it's in Australia.
11.	Franks 2004	Prioritised study	UK RCT comparing a generic 4-layer bandage with short-stretch one.
12.	Gillet 2019	Prioritised study	European RCT of innovative 2-layer vs 4-layer.
13.	Guest 2017	Prioritised study	UK retrospective study of two-layer cohesive compression bandage vs two-layer compression system vs 4-layer compression system, note it's a cohort analysis not an RCT.
14.	Guest 2015	Not prioritised	Not prioritised – older publication from the same database as Guest 2017.
15.	Harding 2016	Not prioritised	Not prioritised – adaptive system that includes 4-layer compression but doesn't make one of our prioritised comparisons.
16.	Iglesias 2004	Prioritised study	VenUS-1 – 4-layer vs short stretch, UK RCT.
17.	Junger 2004 (Wounds)	Prioritised study	Stocking vs short stretch bandage, European RCT.
18.	Junger 2004 (Curr Med Res Opin)	Prioritised study	Tubular compression vs short stretch bandage, European RCT.
19.	Karanikolic 2018	Prioritised study	European RCT assessing relationship between pressure strength and healing rate.
20.	Lane 2001	Not prioritised	Subjective outcomes. Non-randomised study.

21.	Lazareth 2012	Prioritised study	2 -layer vs 4-layer bandages, European RCT.
22.	Mariani 2008	Prioritised study	2-stocking system vs short stretch, European RCT.
23.	Meaume 2023	Not prioritised	Non-randomised study that does not offer a unique perspective not already available in the evidence.
24.	Milic 2007	Not prioritised	Narrower population focusing on extensive ulcers, less likely to be generalisable.
25.	Moffatt 2008	Not prioritised	Crossover trial, subject to specific methodological limitations.
26.	Moffatt 2003	Prioritised study	UK RCT of 4-layer vs 2-layer bandages.
27.	Mosti 2020	Prioritised study	Wraps vs inelastic bandages, European RCT.
28.	Polignano 2004	Prioritised study	Stocking vs short stretch, study more directly relevant to UK.
29.	Scriven 1998	Not prioritised	4-layer vs short stretch is a comparison for which we already have multiple prioritised studies.
30.	Stather 2021	Prioritised study	Wrap vs short stretch, UK RCT.
31.	Szewcyk 2010	Not prioritised	Sufficient evidence available for stockings vs multi-layer bandages.
32.	Ukat 2003	Not prioritised	Short stretch vs multilayer is a comparison for which we have sufficient prioritised evidence.
33.	Wong 2012 (JEADV)	Not prioritised	4-layer vs short stretch is a comparison for which we already have multiple prioritised studies.

Appendix E – Quality appraisal checklists of included clinical effectiveness evidence

Study		ROB			
First author	Year	Random sequence generation	Sequence generation justification	Allocation concealment	Allocation concealment justification
Ashby	2014	Low	Stratified by ulcer duration (≤ 6 months or > 6 months) and ulcer area (≤ 5 cm2 and > 5 cm2) using permuted blocks (block sizes four and six)	Low	Prevalidated computer program and remote telephone service
Blecken	2005	Unclear	Not reported	Unclear	Not reported
Dolibog	2014	Low	Computer-generated random numbers sealed in sequentially numbered envelopes	Low	Sequentially numbered sealed envelopes
Finlayson	2014	Low	Centrally generated via a computerised randomisation programme for the total expected sample size.	Low	Sequentially numbered sealed envelopes
Franks	2004	Low	Sealed envelopes opened in sequential order to allocate participants to intervention groups. Randomisation stratified by ulcer size (> or ≤ 10 cm^2). Separate randomisation list used for participants with different ulcer sizes.	Low	Sequentially numbered sealed envelopes
Gillet	2019	Low	Randomisation was computer-generated,	Low	Computer generated list allocated

			balanced per centre and treatment was allocated using a telephone service		using a telephone service
Iglesias	2004	Low	Computer-generated permuted blocks	Low	Person staffing randomisation service would ask the nurse for the patient's name. address and stratification variables (ulcer area etc.) prior to revealing the allocation and study number. Allocation concealed until randomisation
Junger (Wounds).	2004	Low	Centre-stratified randomisation list previously provided by an external randomisation centre	Low	Blindfold randomisation: investigators only received treatment number after patient eligibility was confirmed
Junger (Curr Med Res Opin).	2004	Low	Blocks of four participants used randomisation of these performed at statistical department of a contract research organisation (IMEREM GmbH)	Low	Treatment assigned by a code envelope with available treatment numbers in ascending order
Karanikolic	2018	Low	Computer generated	Unclear	Not reported
Lazareth	2012	Low	Centralised randomisation list previously provided by the statistician	Unclear	Centralised list was previously provided to the clinician, so unclear if there was concealment at the point of allocation

Mariani	2008	Low	Randomisation conducted in two blocks of 10 patients for each of the three centres	Unclear	Not reported
Moffatt	2003	Low	Stratified by centre and ulcer size, using a sequentially numbered list	Unclear	Not reported
Mosti	2020	Low	Using a list randomiser	Unclear	Not reported
Polignano	2004	Unclear	Not reported	Unclear	Not reported
Stather	2021	Low	Randomisation was 1:1 random block stratified by ulcer size using an online system	Low	Use of independent computer system

Study		ROB			
First author	Year	Incomplete outcome data (all outcomes;	Incomplete outcome justification	Blinding outcome assessment	Blinding justification
Ashby	2014	Low	Numbers and reasons given, low number of withdrawals	Low	Both blinded and unblinding outcome assessments available
Blecken	2005	Low	All participants were compliant, all available data were statistically analysed.	Unclear	Not reported
Dolibog	2014	Low	All allocated participants were included in analyses	Unclear	Not clearly reported but it appears that the measurements were not blinded but that statisticains were

Finlayson	2014	Low	Numbers and reasons given, overall number of withdrawals was low, reasonable balance between groups	Low	The nurses assessing the ulcers and providing care were unable to be blinded but acetate ulcer tracings and wound photographs were assessed and area was calculated by an independent research assistant, who was blinded to group allocation
Franks	2004	Low	Number and reasons for withdrawal given, numbers similar across both groups.	Unclear	Not reported
Gillet	2019	Low	Numbers and reasons given, overall number of withdrawals was low	Unclear	Not reported
Iglesias	2004	Low	Numbers and reasons given. Participants who withdrew or switch treatments were included in the analysis of outcomes	Unclear	Appearance of bandage systems were different, so it was not possible to blind the participants.
Junger (Wounds).	2004	Low	Numbers and reasons given, low number of withdrawals	Unclear	Outcome assessors not blinded
Junger (Curr Med Res Opin).	2004	Low	Numbers and reasons given, balanced withdrawals across groups	Low	Assessed by blinded assessors using planimetry to measure ulcer size (primary outcome measured)
Karanikolic	2018	Low	Numbers and reasons given, overall number of withdrawals was low	Unclear	Not reported

Lazareth	2012	Low	Numbers and resons given and appear reasonably balanced across groups	Low	Acetate tracings were measured centrally by two non-participating, blinded clinicians
Mariani	2008	Low	Number and reasons for withdrawal given, numbers similar across both groups.	Unclear	Not reported
Moffatt	2003	Low	Numbers given and most included in analysis	Unclear	Not reported
Mosti	2020	Low	All participants included in analyses	Unclear	Not reported
Polignano	2004	Low	Numbers and reasons given, low number of withdrawals	Unclear	Appearance of bandage systems were different, so it was not possible to blind the participants. No mention of outcome assessor blinding.
Stather	2021				

Study		ROB		
First author	Year	Baseline comparability	Baseline comparability justification	Notes
Ashby	2014	Low	Well balanced and stratified design	None
Blecken	2005	Low	No significant difference in baseline characteristics	None

Dolibog	2014	Low	All baseline characteristics were reasonably balanced across groups	None
Finlayson	2014	Low	All baseline characteristics were reasonably balanced across groups	None
Franks	2004	Low	All baseline characteristics were reasonably balanced across groups. Participants stratified according to ulcer size.	None
Gillet	2019	High	Imbalances between groups in ulcer size, duration, mobility	None
Iglesias	2004	Low	All baseline characteristics were reasonably balanced across groups. Randomisation stratified by ulcer area, duration, episode.	None
Junger (Wounds).	2004	Low	No significant difference in baseline characteristics	None
Junger (Curr Med Res Opin).	2004	Low	All baseline characteristics were reasonably balanced across groups	None
Karanikolic	2018	High	Imbalances between groups in ulcer size, other imbalances in subgroups	Difficult to assess baseline imbalances because data are given for age subgroups rather than overall for treatment groups

Lazareth	2012	Low	All baseline characteristics were reasonably balanced across groups	None
Mariani	2008	Low	All baseline characteristics were reasonably balanced across groups	None
Moffatt	2003	Low	All baseline characteristics were reasonably balanced across groups	Large amount of treatment switching, therefore difficult to interpret the ITT results
Mosti	2020	Low	Group characteristics similar at baseline	None
Polignano	2004	Low	All baseline characteristics were reasonably balanced across groups	None
Stather	2021	Unclear	Some differences but small sample	Note: Feasibility trial, no power calculation, initial plan was to recruit 50 but this was changed to 40 due to poor recruitment

Compression products for treating venous leg ulcers: late-stage assessment [GID-HTE10048]

EAG assessment report cPAS appendix

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Author contributions

Maxwell S. Barnish	Project manager. Clinical effectiveness lead reviewer. Contributed to report writing and editing.
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Alan Lovell	Led the EAG's literature searches and information management. Contributed to clinical and economic reviews. Contributed to report writing and editing.
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1. INTRODUCTION

This confidential appendix reports the results of the economic evaluation and maximum economically justified price calculations using the minimum cost for products from both the publicly available Drug Tariff and confidential NHS Supply Chain catalogue, provided to the EAG by NICE. An additional scenario [redacted] is also presented (Table 2).

The lowest price by product class and size from both sources was selected as the base price for each (Table 1).

Table 1: Unit costs for product type by size (minimum of NHS Supply Chain and Drug Tariff prices)

	4LCB	2LCB	2LCH	CW
Average	[redacted]	[redacted]	[redacted]	[redacted]
Narrow	[redacted]	[redacted]	[redacted]	[redacted]
Wide	[redacted]	[redacted]	[redacted]	[redacted]

Table 2: Unit costs for product type by size (minimum of NHS Supply Chain and Drug Tariff prices [redacted]

	4LCB	2LCB	2LCH	CW
Average	[redacted]	[redacted]	[redacted]	[redacted]
Narrow	[redacted]	[redacted]	[redacted]	[redacted]
Wide	[redacted]	[redacted]	[redacted]	[redacted]

2. RESULTS

Use of the NHS Supply Chain prices does not affect the results of the analysis: CW and 2LCH are of similar cost, with slightly higher QALYs accrued with CW (thus, on average CH is dominated by CW). 4LCB is dominated by CW and CH, and the ICER of 2LCB vs CW is in excess of that normally considered cost-effective (Table 3 & Table 4).

Table 3: Cost-effectiveness analysis results (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Narrow ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Wide ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Medium ankle circumference, non-ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]

Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Narrow ankle circumference, non-ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Wide ankle circumference, non-ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; 2LCH, two-layer compression hosiery; 4LCB, four-layer compression bandage; 2LCB, two-layer compression bandage; CW, compression wrap. *Fully Incremental Analysis

Table 4: Maximum eJP by population sub-group

Analysis	4LCB	2LCB	2LCH	CW
Base case 1 (medium ankle, ambulatory)	[redacted]	[redacted]	[redacted]	[redacted]
Base case 2 (narrow ankle, ambulatory)	[redacted]	[redacted]	[redacted]	[redacted]
Base case 3 (wide ankle, ambulatory)	[redacted]	[redacted]	[redacted]	[redacted]
Base case 4 (medium ankle, non-ambulatory)	[redacted]	[redacted]	[redacted]	[redacted]
Base case 5 (narrow ankle, non-ambulatory)	[redacted]	[redacted]	[redacted]	[redacted]
Base case 6 (wide ankle, non-ambulatory)	[redacted]	[redacted]	[redacted]	[redacted]

Scenario analysis results

The EAG repeated the decision analysis with an assumed lower utility benefit from a healed ulcer. This did not materially affect the results or the eJP analyses (Table 5 and Table 6).

Table 5: Scenario analysis results- lower utility benefit from healed ulcer (expected costs and QALYs from probabilistic analysis)

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Narrow ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Wide ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Medium ankle circumference, non-ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Two-layer compression bandage	[redacted]						
Four-layer compression bandage	[redacted]						
Narrow ankle circumference, non-ambulatory							
Compression wrap	[redacted]						
Two-layer compression hosiery	[redacted]						
Two-layer compression bandage	[redacted]						
Four-layer compression bandage	[redacted]						
Wide ankle circumference, non-ambulatory							
Four-layer compression bandage	[redacted]						
Two-layer compression bandage	[redacted]						
Two-layer compression hosiery	[redacted]						
Compression wrap	[redacted]						

Abbreviations: QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; 2LCH, two-layer compression hosiery; 4LCB, four-layer compression bandage; 2LCB, two-layer compression bandage; CW, compression wrap. *Fully Incremental Analysis

Table 6: Maximum eJP by population sub-group (low utility gain scenario)

Analysis	4LCB	2LCB	2LCH	CW
Base case 1 (medium ankle, ambulatory)	[redacted]			
Base case 2 (narrow ankle, ambulatory)	[redacted]			
Base case 3 (wide ankle, ambulatory)	[redacted]			
Base case 4 (medium ankle, non-ambulatory)	[redacted]			
Base case 5 (narrow ankle, non-ambulatory)	[redacted]			
Base case 6 (wide ankle, non-ambulatory)	[redacted]			

2.1.1. Base Case with [redacted]

Competing option	Expected costs	Expected QALYs	ICER*	NMB20	NHB20	NMB7	NHB7
Medium ankle circumference, ambulatory							
Compression wrap	[redacted]	[redacted]		[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression hosiery	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Two-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Four-layer compression bandage	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Health Tech Programme

GID-HTE10048 Compression products for treating venous leg ulcers: Late-stage assessment

External Assessment Report (EAR)

Collated comments table

Any confidential sections of the information provided should be underlined and highlighted. Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in blue and all that is 'academic in confidence' in yellow

Redacted External Assessment Report – Collated comments table:

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
Factual inaccuracies					
1.	Essity	109	9.2	In summary two-layer compression wraps appear to be the most cost-effective form of compression product – is this a error in wording as throughout the document it states CW not 2 layer wrap	Apologies for the typographical error. Now corrected.
2.	Urgo Ltd	12	Research Recommendations	''It was noted that the VenUS 6 study will address many of the uncertainties in the evidence base once finalised results for all outcomes are published in the peer-reviewed literature''. This is an assumption on evidence that is not publicly available. Peer review may highlight bias or inaccuracies in the protocol or study design that will contradict this statement. Please remove this statement of fact or re-word to show this is an assumption/opinion of EAG.	As part of its work, the EAG conducted a review of the VenUS 6 methods and results. NICE address the process points under 11-19 below.
3.	Urgo Ltd	14	Technologies	'' details of the technologies evaluated in this assessment are provided in the NICE scope''	Refers to comment 3 which is this comment. We have addressed the point about

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				This is incorrect as the definition in the scope is not what is included – see comment 7	definitions of strong compression within the context of an LSA below.
4.	Urgo Ltd	15	Table 2	This is the ***traditional*** approach to compression in the UK This wording is incorrect and should be renamed as HISTORI used in the market today clearly show 4LCB to be a technolog	Clinical advice to the EAG was satisfied with the term 'traditional'.
5.	Urgo Ltd	16	Clinical Context	Standard of care: '' In recent years, there has been increasing acceptance of 2-layer compression products, 2-layer compression hosiery, and compression wraps'' 2LCB 2LCH and CW are dominant in the market both in £ value and volume to 4 layer bandaging (IQVIA data). Therefore, this statement is incorrect.	This statement is based on clinical expert advice.
6.	Urgo Ltd	16	Clinical Context	Standard of care: '' In recent years, there has been increasing acceptance of 2-layer compression products, 2-layer compression hosiery, and compression wraps, provided the wound is small enough'' 2LCB 'increased acceptance' is not related to wound size. Please remove this.	The statement 'provided the wound is small enough' relates to compression wraps, which is clear as it is next to it in the sentence. Clinical expert advice to the EAG was that wound size is important for the use of compression wraps.
7.	Urgo Ltd	45	Table 5	''K Two (now called UrgoKTwo) - 2-layer kit, comprising KTech and KPress bandages''. Please reference that UrgoKTwo contains: Multi-component 2-layer kit, containing K Tech (inelastic bandage) and K Press (elastic) bandages.	Was not a factual inaccuracy but have added for additional detail.
8.	Urgo Ltd	46	Table 5	K-Four is missing from the included technologies. Please include as per submission	Added.
9.	Urgo Ltd	53	5.5.1	''The NMA conceptualised 2-layer compression hosiery (2LCH) and 4-layer compression bandaging (4LCB) as 'evidence-based compression' (EBC), as it saw them as current best practice in the UK. It should be noted that clinical experts consulted by the EAG also saw 2-layer compression bandaging (2LCB) as part of current NHS standard of care as well as best practice. Therefore, there may be limitations in the extent to which this EBC concept generalises to UK clinical practice''	Comments 12, 13 and 14 refer to comments 35, 5 and 6, respectively. The choice of EBC in the NMA was made by the VenUS 6 team not the EAG.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				4LCB is not best practice within the UK. Best practice is delivery of 40mmHg for venous leg ulcers (NWCSP, NICE CKS). Please remove this reference and re calculated any and all synthesis using 4LCB as best practice. In addition, see comments 12,13,14	
10.	Urgo Ltd	110	9.2	''In summary two-layer compression wraps appear to be the most cost-effective form of compression product'' There is no reference anywhere else in the document to 2 layer compression wraps. The terminology throughout has been CW, Wraps, Compression Wraps. Compression wraps are not identified as 2 layer. Can you confirm if this is a spelling error? Can you confirm is CW is meant to be referenced? Can you use consistent terminology throughout so as no errors in interpretation Please amend this section and re-issue with corrections as applicable in reference to comments above	This has been corrected as above.
VenUS 6 data					
11.	Essity			With the amount of retracted information been used in this assessment makes it very hard to accurately feedback on most of the economic information – Without this data its hard to see how we can progress the LSA without this been shared. Would a NDA be possible for members to have full picture of study before published	NICE considers all types of evidence in its evaluations as outlined in section 3 of NICE's health technology evaluation manual. This includes evidence from unpublished data. The results from the VenUS 6 network meta-analysis (NMA) and economic modelling have been made available to NICE for the LSA assessment on an academic-in-confidence basis. This enables us to incorporate the latest relevant research from this topic into the assessment without waiting for the full publication of these results which may take months. NICE does not enter into

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
					NDA agreements during the development of guidance. In relation to the external assessment report and in line with NICE's Health Technology evaluations manual, all information marked as confidential will not be released to stakeholders even though they have signed a confidentiality agreement. Confidential information within published documents is redacted. However, our standard process for dealing with AIC information is that it is presented and discussed in the public part committee meeting.
12.	Essity	62	5.5.1	Evidence from the VenUS 6 NMA suggests that retracted – This feel a very important part of the decision and we are unable to see the outcome	Please see NICE's response to comment 11.
13.	Urgo Ltd	48	5.4 Results	''The EAG did not conduct its own network meta-analysis, due to the availability of the VenUS-IV meta-analysis and the agreement that the appraisal would be paused to await availability of VenUS 6 network meta-analysis results. Therefore, the EAG produced a narrative synthesis.'' The meta-analysis Venus 6is not publicly available, has not been peer reviewed and can therefore not confidently be assumed, that there are no errors, inaccuracies or bias. The LSA should be paused until the published Venus6 and then reinstated using peer reviewed, publicly available information.	Please see NICE's response to comment 11.
14.	Urgo Ltd	52	5.5	Use of non-publicly available data casts doubt on risk of bias, assumptions and overall quality of the LSA. See comment 6 and 34	Comment 6 and 34 refer to comments 20 and 49, respectively. Please see NICE's response to comment 11.
15.	Urgo Ltd	54-60		Re-dacted information due to use of unpublished Venus6 NMA increases risk of bias, incorrect assumptions and lack of transparency.	Comments 6, 34 and 40 refer to comments 20, 49 and 9, respectively. Please see NICE's response to comment 11.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Use of unpublished data doesn't allow for industry, public or health institutions to query the modelling. See also comments 6,34,40	
16.	Urgo Ltd	62	5.6	''Evidence from the VenUS 6 NMA suggests that **********'' Remove reference to the unpublished re-dacted study. See comments 6,34,40, 44	Comments 6, 34, 40 and 44 refer to comments 20, 49, 9 and 22, respectively. Please see NICE's response to comment 11.
17.	Urgo Ltd	66	7.1.1	''In January 2025 following completion of the EAG's analysis, the EAG was provided with an early draft of the decision model based economic evaluation of the VenUS VI study which included a scenario analysis requested by the EAG reflecting the decision question of this appraisal more closely. We compare and contrast the results of that analysis with ours in section 9.3.'' See comments 6,34,40,44,46	Comments 6, 34, 40, 44 and 46 refer to comments 20, 49, 9, 22 and 76, respectively. Please see NICE's response to comment 11.
18.	Urgo Ltd	111	Table 25	Redacted information not publicly available. Risk of inaccuracies and bias that cannot be ascertained. See comments 6, 34, 41, 44, 46, 48,51	Comments 6, 34, 41, 44, 46, 48, 51 refer to comments 20, 49, 27, 22, 76, 63 and 54, respectively. Please see NICE's response to comment 11.
19.	Urgo Ltd	71	7.2.4.1	See comments 6,34,40,44,46,48	Comments 6, 34, 40, 44, 46 and 48 refer to comments 20, 49, 9, 22, 76 and 63, respectively. Please see NICE's response to comment 11.
Decision problem – strong compression, SSBs and outcomes					
20.	Urgo Ltd	13	Decision problem	The scope clearly identified strong compression as delivering 40mmHg – '' 1. Compression products available to the NHS on Part or full compression (defined as 40mmHg or more) fo p.10 LSA Compression final scope 29.8.24	LSA methods require the identification of the most appropriate and relevant evidence for decision-making. This should be aligned as closely as possible with the scope. However, this should be balanced with identifying a sufficient evidence base that addresses all technology categories and combinations of

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				NWCSP state strong compression as 40mmHg ‘’ The NWCSP recommendations state strong compression therapy for suspected venous leg ulcers can be delivered by an elastic system applied to give at least 40mmHg of pressure at the ankle’’ p.3 LSA Compression final scope 29.8.24 It is not acceptable to ‘broaden’’ the definition in the EAG report and subject analyses due to insufficient products not able to be analysed in the LSA due to their RFI showing delivers less than 40mmHg. Please reinstate and analyse all evidence, costs and results as per the published final scope (strong – 40mmHg) Can you confirm how many SSB bandages have from their RFI a strong compression level of 40mmHg and how many have a level of 30 – 4mmHg and therefore not classified as ‘strong’ compression	technologies within the appraisal. This requires pragmatism in prioritisation once the available evidence base has been identified such as not to exclude important evidence that can provide valuable insights to address the question. In this case, there were some studies that provided valuable insight but where the definition of strong compression was 30-40mmHg. These are clearly shown in Table 4 and the inclusion of these was discussed with NICE and clinical experts throughout and confirmed to be appropriate.
21.	Urgo Ltd	16	Clinically relevant outcomes	All of the outcomes are dependent on if they have had an appropriate assessment, the correct level of compression (Strong – 40mmHg) was applied for venous leg ulcer (Gold standard treatment, NWCSP, NICE CKS) Please also see comment 7	Comment 7 refers to comment 3. We agree that outcomes are dependent on appropriate assessment.
22.	Urgo Ltd	61	5.6	‘’which many fitted the scope of this appraisal, i.e. strong compression products’’ Can you confirm that the scope referred to is as per the final scope (strong – 40mmHg) or the ‘broadened scope’ as per EAH report 30 – 40mmHg. If the reference is the ‘broadened’ scope, this statement is incorrect. See comments 7 and 8	Comment 7 and 8 refer to comments 3 and 4, respectively. This has been discussed above.
23.	Urgo Ltd	108	9.2	‘Strong compression’. See comments 71	Comment 84 refers to comment. This has been discussed above.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
Technologies – 2LCB / SSBs and sizes					
24.	Urgo Ltd	23	Included & Excluded studies	'' it was clear that SSB are most frequently used as 2-layer bandages and the best place to categorise them in the clinical review for this appraisal is alongside 2LCB''. Can you confirm that when SSB are most frequently used as 2-layer bandages, this is that both layers are short stretch? Most common practice in UK is the 1st layer is wool, padding or a foam comfort layer that provides NO compression and the 2nd layer is the SSB that provides compression. This is not comparative to a 2 layer multicomponent bandaging system where compression is delivered at both layer 1 and layer 2. 2LCB can be either a 2LCB that consists of layer 1 being a comfort layer that provides no compression, and the top layer provided the compression OR a 2LMCB (2 layer multi component bandage) where both layer 1 and layer 2 provide compression. 2LCB – 1st layer is foam and 2nd layer is compression examples: 3M™ Coban™ 2 Compression System Application/Use | Name | Cat. No. | Size | Rolls/box Below the knee | 3M™ Coban™ 2 Layer Compression System | 2094 | Comfort Layer: 10 cm × 2,7 m Compression Layer: 10 cm × 4,7 m stretched | 2 rolls (1 of each layer) 8 Below the knee (ABPI ≥ 0.5) | 3M™ Coban™ 2 Layer Lite Compression System | 2794E | Comfort Layer: 10 cm × 2,7 m Compression Layer: 10 cm × 4,7 m stretched | 2 rolls (1 of each layer) 8 Above the knee | 3M™ Coban™ 2 Layer Compression System | 20096 | Comfort Layer: 15 cm × 3,5 m Compression Layer: 15 cm × 4,5 m stretched | 2 rolls (1 of each layer) 8	We discussed the different types of short stretch bandaging with clinical experts and our report included relevant commentary on these sub-types. The scope only offers four compression categories: 4LCB, 2LCB, 2LCH and CW, and following discussion with clinical experts, it was agreed that the most appropriate place for these results is as part of 2LCB. Our report includes discussion of the sub-types where it was considered relevant.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Actico®2C Two component leg ulcer kit Size / Kit contains / Product Code / PIP Code / NHS SC Code Actico®2C - 18-25cm kit: Actico®2C Comfort Layer 1 10cm x 3.5m + Actico®2C Compression Layer 2 10cm x 6m: 31770 / 376-5203 / EGJ183 Actico®2C - 25-32cm kit: Actico®2C Comfort Layer 1 10cm x 3.5m + 10cm x 2m + Actico®2C Compression Layer 2 10cm x 9m: 31771 / 376-5211 / EGJ184 Actico®2C Comfort Layer 1: 10cm x 3.5m: 31772 / 378-0699 / ECA246 Actico®2C Compression Layer 2: 10cm x 6m: 31773 / 378-0707 / ECA245 2LMCB – 1st and 2nd layer both provide compression example:  The differences in types of 2LCB (2LCB & 2LMCB as above) need to be shown and referenced throughout and should not be included in the same broad 2LCB category.	
25.	Urgo Ltd	39	Table 4: Prioritised studies	''short stretch bandaging (consists of a comfort and compression layer)'' Please reference all SSB comparators and components included in SSB evidence correctly as has been shown above – see comment 20	Comment 20 refers to comment 38. Discussed above.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
26.	Urgo Ltd	50	5.4.4	‘’three studies was short stretch. Clinical input to the EAG was that this should be classified alongside other 2-layer bandaging systems, and it is also not listed as a separate feature on the NICE scope for this appraisal’’ SSB bandages typically consist of 1 layer (foam, wool) which provides NO compression and a 2nd layer (SSB) that provide the compression. This is not comparative to UrgoKTwo (“LCB) which provide compression in both layer 1 and layer 2. See comment 20	Comment 20 refers to comment 38. Discussed above.
27.	Urgo Ltd	53	5.5.1	‘’Two-layer compression bandage systems (2LCB) - bottom layer with cohesive compression bandage - sub-compression wadding layer and cohesive bandage’’ This is only describing some 2LCB system typically short stretch (SSB). UrgoKTwo is a Two layer multicomponent bandage system (“LCB) – 1st layer K Tech (inelastic bandage), 2nd layer K Press (elastic bandage) Please update this in the document and clearly define the different types of 2LCB	Discussed above.
28.	Urgo Ltd	43	5.2.2 Technologies Evaluated	‘’ Therefore, while availability of different sizes may be a relevant consideration, available information may be incomplete’’ Different sizes are relevant for larger limbs as this will determine the appropriate level of compression.	We agree and this is why we mention in our report that this information may be incomplete in company submissions.
Table 2 in EAR - The anticipated benefits of features of compression products for people with venous leg ulcers					
29.	Essity	15	Table 2: The anticipated benefits of features of compression products for people with venous leg ulcers	People living in settings where they have access to help changing products, or people who are mobile enough to change their own products, and do not have access to staff with sufficient training to apply 4-layer bandaging. More active patients who would benefit from a product that is less restrictive of mobility. Younger people who may not accept bandaging for cosmetic or psychological reasons. – Essity would highlight that all age groups may have a cosmetic or psychological reason for wanting this treatment	This table was checked by clinical experts who considered it to be accurate.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
30.	Essity	15	Table 2: The anticipated benefits of features of compression products for people with venous leg ulcers	People living in settings where they have access to help changing products and do not have access to staff with sufficient training to apply 4-layer bandaging. Essity would point out that this would be appropriate to add CW as a product of choice for people in care homes. The ability to train care workers on how to apply CW/CH would reduce the burden of rebandaging patients in care homes. This would also allow my skin health and hygiene as the care workers could take the CW/CH off and reapply without any clinical resource been impacted	This table was checked by clinical experts who considered it to be accurate
31.	Essity		Table 2: The anticipated benefits of features of compression products for people with venous leg ulcers	General feedback on table the table makes assumption of what product I best for patients needs and also states band of nurse who can apply. This can vary depending on the trust or care settings policy. Can we be shared evidence that supports this assumption	Nurse band was based on clinical expert advice to the EAG. We have added comments to the discussion (Section 9.1) in response to similar comments elsewhere. The EAG has also explored the impact of nurse grade with an additional scenario analysis on the decision model.
32.	Urgo Ltd	15	Table 2	2lCB '' Can be changed by staff with less specialist training, such as nursing associates (Band 4)''. This contradicts assumption made throughout the report which states that band 5 and higher is needed to apply 2LCB or 4LCB. There is no evidence available for any compression product on the Band of nurse that can apply. See comment 2,4. Please update all EAG report and remove all references and costing assumptions on Band of nurses required per compression product.	Refer to comments we've made on the economic analysis, additions to Section 9.1 and the scenario analysis.
33.	Urgo Ltd	15	Table 2	2LCB & kits - Groups of people who may use these – ''People in care homes''. There is no indication on the groups of people who may use these products, and this is merely an opinion. 2LCB & kits are widely used in a variety of community and acute settings including care homes, patients own home, GP practice, wound clinic, outpatients' department, vascular department, dermatology department.	This is based on clinical expert advice.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Please change the wording to show ‘’used in a variety of community and acute settings for treating venous leg ulcers’’.	
34.	Urgo Ltd	15	Table 2	‘’2LCB & kits - Groups of people who may use these – 2. with sufficient training to apply 4-layer bandaging. This section is relating to 2LCB & Kits and there should be no reference to 4-layer kits. NO evidence to show 4-layer is superior or preferred. Please remove the entire sentence relating to 4-layer bandaging.	This is based on clinical expert advice.
35.	Urgo Ltd	15	Table 2	All ‘’groups of people’’ comments include – ‘’access to staff with sufficient training to apply 4-layer bandaging’’. 4-layer is not a preferred or dominant bandaging system. There is evidence to show the 2LCB performs as well of slightly better than 4LCB. 4LCB was the original compression system (historic), however, is the least used compression bandaging system within UK (IQVIA prescription data). Please remove all references or inference that 4 layer is the ideal/best/preferred option	This is based on clinical expert advice.
Clinical evidence – included studies					
	Urgo Ltd	11	Clinical and technological evidence	‘’ Hosiery and wraps (noting there was only one study on wraps for this comparison) were shown to be equivalent to 4-layer bandaging’’. Mosti 2020 (prioritised study) study objective was to ‘’compare the efficacy and comfort of inelastic bandages (IBs) and adjustable Velcro® compression devices (AVCDs) in reducing venous leg edema in the initial treatment phase’’ This is not treatment of venous leg ulcer but managing one of the symptoms of venous insufficiency. The conclusion of the study was: ‘’Re-adjustable AVCDs with a resting pressure of around 40 mmHg are more effective in reducing chronic venous edema than IBs with a resting pressure of around 60 mmHg. AVCDs are effective and well tolerated, not only during maintenance therapy, but also in the	We drew conclusions based on the available evidence, which includes the published studies in our report. NICE respond above regarding the VenUS 6 data.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				initial decongestive treatment phase of patients with venous leg edema''. It does not report on the treatment of venous leg ulcers. Not all compression wraps are indicated for the management of venous leg ulcers and as such should not be included in this LSA as they are out of scope of this assessment. Only compression wraps that are indicated for treating venous leg ulcers (not some of the symptoms or oedema) should be included in the LSA. Examples of wraps that do not meet the inclusion criteria of management of treating venous leg ulcers is below: ReadyWrap Calf : (IFU Below) Assist in management of some symptoms of venous ulcers Assists in helping limit venous ulcer recurrence	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				 EasyWrap: LOWER LIMB INDICATIONS The type of easywrap is printed on the garment's label. Primary Indications:	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Light for mild to moderate lymphoedema or oedema; palliative care Strong for severe and stubborn lymphoedema or oedema; rebound oedema; primary lymphoedema of long duration IFU-EWL-2017-03.pdf Stather 2021 (prioritised study) conclusion states: '' This study has shown the feasibility and necessity of running a multicentre trial to evaluate the use of Velcro wrap devices for venous ulceration''. With minimal evidence available on comparison of CW vs. 4LCB or 2LCB, how has the assumption been made and stated that they were shown to be '' equivalent to 4-layer bandaging''?	
36.	Urgo Ltd	20	5.1	'' EAG included studies in adults with venous leg ulcers that compared a scoped strong compression product''. The final published scope defines strong compression as 40mmHg. The products used in the EAG analysis is not within the published final scope. Please amend and adjust as per comment 7	Comment 7 refers to comment 3. Discussed above. Discussed above.
37.	Urgo Ltd	24	Table 4: Prioritised studies	3. Ashby et al, 2014,1 VenUS IV, RCT, UK Relevant outcomes and key measures do not accurately reflect the study. This study shows: In this study of 227 patients randomised to the hosiery group, 90 patients discontinued treatment 90 discontinued intervention (moved to non-trial treatment) 2 had an increase in ulcer area for 2 consecutive weeks 15 had ulcer deterioration 37 found compression uncomfortable/painful 10 were not compliant with compression treatment for another reason 26 changed treatment for another reason With 39.6% of patients in hosiery arm discontinuing, this deserves additional commentary on suitability	The EAG is satisfied that it has extracted the data for VenUS IV correctly.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				With 6.6^ of patients in hosiery arm experience ulcer deterioration, again this deserves commentary	
38.	Urgo Ltd	26	Table 4: Prioritised studies	Dolibog et al, 2014,25 RCT, Poland Strong compression (40mmHg) is within scope for this assessment and as this evidence has arms not within scope, this evidence should be removed from included evidence.	Discussed above.
39.	Urgo Ltd	26	Table 4: Prioritised studies	Finlayson et al, 2014,24 RCT, Australia The compression hosiery was 30-40 mmHg whilst correctly applied 4 layer provides 40mmHg, therefore the 2 values are not comparable, and this study should not be included as comparative evidence.	Discussed above.
40.	Urgo Ltd	29	Table 4: Prioritised studies	Gillet et al, 2019,27 RCT (non-inferiority), France As neither of the products appear within the UK either of Drug Tariff or NHSSC, what is the relevance of including this study?	LSA methods are about product features and types of compression not specific products. While we focused on products used in the UK wherever possible, we discussed with NICE and clinical experts and it was agreed that we should not exclude studies just because the specific products are not used in the UK if the study provides valuable insight that is not offered by other studies.
41.	Urgo Ltd	30	Table 4: Prioritised studies	Guest et al, 2017,21 retrospective cohort study, UK The study has many limitations including inaccuracies in study design, reported relevant parameters and bias that include: • 75% of Patients lacked a differential diagnosis for either a venous or mixed aetiology leg ulcers. The type of leg ulcer and the compression therapy chosen are not comparable therefore, the results of efficacy for venous leg ulcers, cannot be accurately determined • Significant differences in co-morbidities amongst the 3 groups making head to head comparison of outcomes unreliable and potentially biased • Interventions that may impact the wound healing outcome and time to healing, including wound	LSA methods allow the inclusion of observational studies. We discussed this study thoroughly. It is particularly relevant for decision-making as it is a large study comparing different types of compression conducted in the setting of UK clinical practice. Funding source is not a reason for exclusion and it is common for studies in submissions to NICE to be funded by manufacturers.

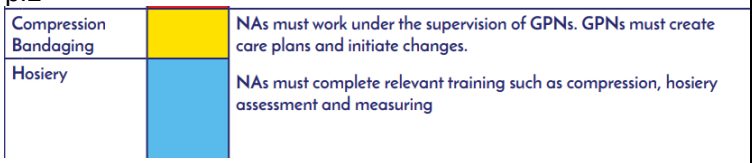
Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				severity and exudate level were not accurately reported Limitations on cost effectiveness. If healthcare resources outside the GP surgery were used/incurred, this is not documented in general practice records and would not have been included in the THIN database • Study was fully funded by the company that owns the product found to be 'most effective' which may increase the likelihood of bias	
42.	Urgo Ltd	40	Table 4: Prioritised studies	''Compression hosiery was 'significantly easier to apply' than short stretch bandaging (p=0.0439)'' Was there a reliance of patients to self-apply short stretch bandaging? This would bias the results	There is an increasing move towards self-application of compression where feasible and this is an area that could be discussed with clinical experts at committee.
43.	Urgo Ltd	41	Table 4: Prioritised studies	Demonstrates that patients can and do remove hosiery so will not benefit from correct therapeutic pressures or form wearing compression product for the correct amount of time. . As part of the user preference, ''users agreed that acceptable levels of performance would be that the patients find the product relatively comfortable and wears the product for the required time'' (user assessment report, p. 13 criterion 1). Therefore, hosiery cannot be considered as fully acceptable with 78% of patients removing the hosiery as shown in this evidence.	The user preference report is not produced by the EAG.
44.	Urgo Ltd	48	5.3 Quality appraisal	''One of the prioritised studies was not an RCT. The risk of bias in this study was not assessed because it cannot be reasonably compared with the prioritised RCTs. Instead, the EAG highlight that this study is, by design, at higher risk of bias than the other prioritised studies, and that this should be considered when interpreting the study result'' Due to risk of bias and interpretation of any guidance on the LSA assessment, this study should be removed from the analysis. If no evidence is available, it should not be included or form part of LSA or guidance.	The LSA methods allow the inclusion of observational evidence.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
45.	Urgo Ltd	50	5.4.7	Bias and incorrect study design and analysis. See comment 25	Comment 25 refers to comment 25.
46.	Urgo Ltd	50	5.4.3	‘’Only one prioritised study compared 4-layer bandaging and compression wraps. This was a small (n=12 per arm) RCT23 conducted in the USA. There was no other evidence available for this comparison’’ With such a low patient inclusion, conducted in non UK and with no other evidence available for the comparisons (4LCB vs CW), this study should not be included as it is not generalisableto demonstrate and superiority or comparison of products in the study.	LSA methods focus on identifying evidence where it is available to address our questions and then evaluating the available studies. It is appropriate therefore to include this study.
Clinical evidence – summary sections (QA, study populations, generalisability)					
47.	Urgo Ltd	43	5.2.1 Study populations	‘’mean population age for each prioritised study was in the 60s or 70s, reflecting a typically older population, in line with clinical input; Older age is associated with reduced mobility, reduced dexterity and increased co-morbidities. Self-application of 2LCH or CW requires a patient to be able to bend at the waist to reach their feet. In addition, for 2LCH, the patient will need to be able to stretch the hosiery to don the hosiery. Is it unreasonable to assume that self-application is suitable for the all patients with a venous leg ulcer based on the physical act of application and removal for 2LCH and CW.	Clinical expert advice to the EAG was that self-application is becoming more common.
48.	Urgo Ltd	50	5.4.2	‘’ non-trial treatment was more common in the compression hosiery group’’. Is this due to patient being able to remove their hosiery and therefore no longer receive correct therapeutic pressure or wear compression garment for recommended length of time? See comment 28	Comment 28 refers to comment 48. It is unknown why this particular finding was observed.
49.	Essity	17	Generalisability of international evidence	Generalisability of international evidence. The EAG was advised that studies in Europe would be broadly applicable, although venous leg ulcer care in other developed countries may be ahead of the UK and compression levels in Europe tend to be higher for hosiery. Therefore, benefits in European studies may overestimate expected benefits in an NHS	This was based on expert advice from UK clinical experts.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				setting. In the UK, only specialist nurses would tend to use compression at levels of >= 40 mmHg. There may also be differences in healthcare system organisation, where for example in New Zealand, the EAG was advised that the standard of care can generally be higher as there are fewer patients per clinic due to population differences. Although other countries do have different health structures and policies the 40mmHg is the evidence level of compression to support healing he evidence of 40mmHg to heal venous leg goes back to Stemmer's theoretical framework in 1980 suggested which suggested that an external pressure of at least 40mmHg at the ankle was required to achieve ulcer healing in patients with chronic venous insufficiency (Stemmer R, Marescaux J, Furderer C. [Compression therapy of the lower extremities particularly with compression stockings]. Hautarzt 1980; 31(7): 355-65.)	
Economic modelling – inputs and assumptions					
50.	Essity	71	7.2.3	The EAG's base case reflected an 'average' / medium sized ankle, with sub-group analyses for smaller and larger ankles. – Essity agrees taking into consideration average with sub groups is effective way of grouping sizes. What would "average" ankle size be and is the referenceable ? When looking at cost unless a made to measure garment the cost would remain the same through DT as size of product does not make a change in cost	This is stated in section 7.2.5.2, "consumables". Medium was defined as an ankle width 18-25cm, based on categorisation in the Drug Tariff. We noted that many products were the same price, irrespective of size, but this was not true for all manufacturers.
51.	Essity			Report Reliable sources for the average number of dressing changes per week for an unhealed venous leg ulcer could not be located	This was based on clinical opinion as stated in 7.2.5.1, "unhealed", paragraph 1.
52.	Urgo Ltd	71	7.2.2.1	''A five-year time horizon was used for the analysis'' Venous leg ulcers with a life span of 5 years is incorrect. Non healing VLU after 12 weeks would be referred to a specialist. Overall healing rate of 84% at 52 weeks for all lower limb wounds (Evaluation report, NWCSP)	The time horizon in the model was set to be long enough to capture healing time for the vast majority of patients. We included scenario analyses exploring shorter modelling time horizons (Table 21).

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
53.	Urgo Ltd	75	7.2.5	Why is a podiatrist referenced? Venous leg ulcers are generally not managed by podiatrists. Please remove all costings associated with podiatry visits as this is not relevant of the resource used in treating venous leg ulcers.	This was based on clinical advice to the EAG (approx. 1 visit every 10 weeks).In the clinical expert meeting, experts said they try to get their patients to see podiatrists on a regular basis.
54.	Urgo Ltd	68	7.1.3	LSA AMD scope was to look at healing of leg ulcers with topical AMD's. However as stated in this LSA EAG ''the EAG understood that all ulcers will carry infection to some degree, but this was only likely to be substantially impactful on either patient quality of life or resource use if develops cellulitis''. This pulls into question, the entirety of the LSA AMD as if resource use or quality of life is only impacted by development of cellulitis, then the cost of a topical AMD is irrelevant is it does not include cellulitis development within the scope.	This was based on clinical advice to the EAG. Comment on other LSAs is out of scope for the EAG.
Economic modelling – resource use					
55.	Urgo Ltd	11	Economic evidence and analysis	''The difference in cost between product types is driven to a large part by the requirement for a band 5 nurse to apply 2LCB and 4LCB, but a band 3 or 4 for CW and CH''. What evidence base is used for is this assumption? There are no regulations or guidance on which band nurse can apply compression. This is determined by the healthcare professionals local trust and policies. In order to choose the correct compression product, the underlying aetiology to confirm venous insufficiency and rule out arterial involvement, is necessary before compression should be applied. For any and all compression products (4LB, 2LB, 2LCH, CW) ALL need to have an exclusion of red flags (Immediate and necessary care, NWCSP) prior to choosing or applying any compression product (NWCSP Leg Ulcer Recommendations, July 2024). Within 14 days a full holistic assessment including ABPI (doppler) needs to be undertaken to determine the underlying aetiology and to provide correct treatment including compression therapy. This	Thank you for this comment. Our base case assumptions are based on clinical advice to the EAG. We have added a paragraph to the discussion (9.1) that a driver of cost is the band of nurse administering the product. We have also conducted an additional scenario analysis assuming a Band 3 nurse is able to apply 4LCB and 2LCB. Exclusion of red flags and ABPI prior to application of compression product is common to all arms, therefore this does not affect the incremental analysis (it would be adding a constant to mean cost for all arms). For convenience such common costs are excluded from economic evaluations.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				needs to be considered for the Markov model, ABPI dopplers are performed at the unhealed stage and not solely performed after healing - as is assumed in the model. If venous disease is suspected, a venous duplex scan is considered a gold standard form of assessment for individuals with lower leg ulcers so should also be part of assessment ((NWCSP Leg Ulcer Recommendations, July 2024). ABPI's either by handheld, automated doppler or venous duplex scans can only, be undertaken by nurses who have received training and are competent in undertaking an ABPI. This training and competencies are not defined by band of nurse but by attendance and completion of training and competencies as per trust policies. Therefore, the band of nurse cannot be generalised to a band 4 minimum. For application of compression products, this is not determined by band of nurse but by training and competencies on application of compression whether this be a 2LCB, 2LCH or CW. Again, the training and skills needed are dictated by trust policy and not Band of nurse. 2LCB & 4LCB can be applied by non-registered health practitioners as per trust policies and protocols, please see evidence/information below: p.45 Appendix 1:4 Protocol and Competency for Compression bandaging for Assistant Practitioner (AP) and Nurse Associate Competency-Skills-and-Qualification-Framework.docx p.4 Compression therapy should only be applied by those HCPs competent to do so, providing the most appropriate treatment which will deliver safe, effective, efficient, equitable and timely person centred care NHSGGC Core Formulary for Compression Bandaging in Venous Ulceration	

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				p.2  Career-Start-NA-General-Practice-Competencies-Sept23.pdf Leg Ulcer assessment competency leg-ulcer-assessment-competencies.doc p.3 The assessment of the patient and diagnosis of the cause of ulceration should be undertaken by a health care professional trained in leg ulcer management LOWER LIMB PREVENTION AND MANAGEMENT GUIDELINES 6.0.docx **Please amend the report and all costs that base 2LCB and 4LCB on Band 5 nurse vs band 3 or 4 for CH or CW as this is incorrect**	
56.	Urgo Ltd	11	Economic evidence and analysis	'' The difference in cost between product types is driven to a large part by the requirement for a band 5 nurse to apply 2LCB and 4LCB, but a band 3 or 4 for CW and CH''. This is merely an assumption. Many unregistered staff apply compression bandaging (4LCB, 2LCB). Please see comment 2 for supporting evidence. Please remove this comment and re-calculate all costs and guidance using same resource for 2LCB, 4LCB as used in 2LCH and CW	Comment 2 refers to comment 36.
57.	Urgo Ltd	16	Resource use	''initial appointments need to be conducted by at least Band 5 staff, while follow-up appointments can be Band 3 or above.'' If a full holistic assessment including ABPI is required then follow up appointments may not be a Band 3 or above, but with healthcare staff who have the skills and competencies to conduct said assessment, This is not defined by band of	Comment 2 refers to comment 36.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				nurse. Please see comment 2 for information on competencies and skills on leg ulcer assessment for evidence.	
58.	Urgo Ltd	74	7.2.5	Four layer and two layer (Band 5) nurse. This is incorrect and needs revising throughout entre report and in all cost analyses. See comments 2,10,13,16	Comments 2,10,13 and 16 refer to comments 36, 33, 5 and 6, respectively.
59.	Urgo Ltd	85	7.3.1	'' Band 5 nurse to dress''. See comments 2,10,13,16 and update accordingly	Comments 2,10,13 and 16 refer to comments 36, 33, 5 and 6, respectively.
60.	Urgo Ltd	103	8.2.5.2	Resource use: Incorrect assumption on resource uses. See comments 2,10,13,16	Comments 2,10,13 and 16 refer to comments 36, 33, 5 and 6, respectively.
Economic modelling – costs					
61.	Urgo Ltd	54	5.5.1	''although the EAG noted that it is possible for the number of layers in SSB to vary in practice'' This will increase the costs associated and should be clearly shown in the document, any guidance and cost modelling.	Costs used in the model were based on the lowest cost complete kits in the Drug Tariff, as described in section 7.2.5.2, "consumables".
62.	Urgo Ltd	70	7.2.2.1	ABPI and full holistic assessment must be undertaken prior to application of strong compression. See comments 11 and 16 Please update model based on evidence re. ABPI and full holistic assessment	See response to comment 55 above.
63.	Urgo Ltd	74	7.2.5.1	''compression wraps, only a single kit would be given to last 6 months''. Patients will use liners underneath the wrap to prevent soiling. The cost of the liners needs to factored into the cost analysis and therefore impact on the cost effectiveness	Costs were based on complete kits as per Drug Tariff. The EAG understands this includes all components.
64.	Urgo Ltd	74	7.2.5.1	''compression wraps, only a single kit would be given to last 6 months''. A compression wrap will also need a foot piece to provide compression on the foot and prevent oedema being pushed into the toes. Has the cost of a foot price been included in the cost analysis and therefore the cost effectiveness?	See response to comment 63
65.	Urgo Ltd	75	7.2.5.1	Dressing used under 2LCH and CW vary from under 2LCB or 4LCB. User assessment report comments included that a bordered dressing may be used. The cost of a bordered	Dressings are assumed included in kits. The numbers reported in the table refer to

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				dressing is significantly higher than non-bordered dressings typically used under 2LCB or 4LCB. Please include bordered dressing with CW and 2LCH and a non bordered for 2LCB and 4LCB and recalculate the cost analysis and therefore cost effectiveness	frequency of changes, so the cost is not calculated separately.
66.	Urgo Ltd	85	Table 16	Please confirm and update if needed, the cost for CW that includes liners and foot piece. See comments 54 and 55	Comment 54 and 55 refer to comments 65 and 66, respectively.
67.	Urgo Ltd	87	Table 17	See comments 54,55 and 60	Comment 54, 55and 60 refer to comments 65, 66 and 68. respectively.
68.	Urgo Ltd	104	8.2.5.2	‘’whilst a dressing is of minimal cost’’. Please see comments 54,56,60	Comment 54, 55and 60 refer to comments 65, 66 and 68. respectively.
69.	Urgo Ltd	109	9.2	‘’assumes that some dressing changes are handled’’……. The effect on overall cost based on the dressing itself is not represented and not included in the cost modelling therefore, inflating to potential cost savings. Please see comment 56,57 and 58	Comment 56, 57 and 58 refer to comments 72, 77 and 60, respectively.
70.	Urgo Ltd	109	9.2	2LCH is available as a ready to wear (standard sizes) or made to measure (MTM). For patients who have abnormal limb shapes or skin folds, MTM is recommended to ensure comfort, correct fitting and to endure the therapeutic compression level is provided by the 2LCH. There is a significant price difference between standard 2LCH and MTM 2LCH. Has the cost of MTM been included in the cost modelling?	Our analyses explored medium, narrow and wide ankle fittings, but excluded made to measure. Comment added to section 9.2.
71.	Urgo Ltd	75	7.2.5.2	See comment 56	Comment 56 refers to comment 72.
Equality issues					
72.	Urgo Ltd	18	Equality issues	People within prisons, remand centres, detention centres are missing from the identified equality areas. There are a high proportion of former/current IV drug users within these environments and this should be included within the equality impact	Added.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
Conclusions					
73.	Urgo Ltd	12	Key points for decision makers	'' Based on this rapid overview economic modelling, 2-layer compression wraps are the most cost-effective option at the lowest priced product available. However, CW and CH may be considered broadly equivalent in terms of cost-effectiveness. Other product types should only be recommended where 2LCH is not appropriate for the person with VLU'' Based on comments above and the assumptions without evidence, this commentary is incorrect. Please amend as per comments 2,4	Comment 2 and 4 refer to comments 36 and 74, respectively.
74.	Urgo Ltd	51	5.4.6	How can a recommendation on the efficacy and cost effectiveness of 2LCH be made without any comparative data to CW?	The relative efficacy data are taken from the VenUS 6 study.
75.	Urgo Ltd	66	7.1.1.	''If equivalence between 2-layer and 4-layer compression bandaging is assumed''. Page 11 states that 'some evidence 2-layer may be better'. If there is some evidence for this, why has an assumption been made that 4L and 2L are equivalent?	This refers to the VenUS-IV study. The EAG's analysis did not make this assumption.
76.	Urgo Ltd	84	7.3.1	See comment 56 and 57 and update all cost effectiveness analyses accordingly	Coment 56 and 57 refer to comments 72 and 77, respectively
77.	Urgo Ltd	90	7.3.3	Please adjust based on comment 71	Comment 71 refers to comment 84.
78.	Urgo Ltd	94 - 95	7.5	''The EAG's analysis found that two-layer compression wraps dominated other compression product types; they were on average less expensive and more effective than all other product types.'' The summary is based on extremely limited clinical evidence, of which evidence for superiority for wraps should be excluded (see comment 36) and incorrect assumptions on resource use (see comments 2,10,13,16). Please update all report and cost analysis and then re-issue summary.	Comments 2,10,13, 16 and 36 refer to comments 36, 33, 5, 6 and 26, respectively.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
79.	Urgo Ltd	106	Discussion	The cost modelling to determine cost effectiveness is flawed with incorrect assumptions on resource use, cost of the products (including lines and foot prices). See comment 54,56	Comment 54 and 56 refer to comments 65 and 72, respectively.
80.	Urgo Ltd	106	Discussion	‘’The point estimate economic analysis results suggest that CW are the most cost-effective product class’’ Please see comments 54,56,67 as this will impact the cost effectiveness	Comment 54, 56 and 67 refer to comments 65, 72 and 81, respectively.
81.	Urgo Ltd	107		‘’The economic results must be interpreted with caution. The analysis reported here was constrained by the resources and time allowed for a late-stage assessment evaluation’’ For such potentially pivotal guidance impacting on the healing of patients with venous leg ulcers, quality of life, resource of NHS and tax-payers funding, if there was not sufficient time to complete a full analysis that provides value for money, informs clinical decision making, improves patients quality of life and is best use of tax payers money, then the LSA should have been passed and completed, only at a time where there was resource and time to complete.	This is out of scope for the EAG to answer as it relates to the methods of an LSA.
82.	Urgo Ltd	108	9.2	‘’It is a rapid overview of the economics of the market for compression products in the NHS and should therefore be considered an approximate guide to the costs and benefits rather than a definitive assessment. ‘’ How can draft guidance and guidance be provided on cost effectiveness, when an identified weakness is approximate guides to costs. There are numerous incorrect assumptions throughout the modelling	Please see response to comment 81. This is out of scope for the EAG to answer as it relates to the methods of an LSA.
Treatment switching					
83.	Urgo Ltd	109	9.2	‘’The model also did not account for treatment switching’’. ‘’The EAG considers this may bias the analysis in favour of compression hosiery or compression wraps, since their higher unit cost means that wastage resulting from switching would have a greater cost impact.’’	The EAG has noted this as a limitation of its analysis.

Comment no.	Stakeholder	Page no.	Section no.	Comment	EAG Response
				Evidence of treatment switching provided in comment 21. The treatment switching is this study was 11.45%. This would significantly impact the cost assumptions and have a greater cost impact.	

NICE National Institute for Health and Care Excellence

HealthTech Programme

Late-stage assessment

Compression products for treating venous leg ulcers: late-stage assessment

User preference report

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1. Introduction

Alongside the assessment of a technology's value based on costs and effectiveness, the late-stage assessment on compression products for treating venous leg ulcers includes an assessment of user preferences that influence decision making when selecting which technology to use (NICE's Interim methods and process statement for late-stage assessment). This report presents the key findings from the user preference assessment that was done to understand:

- the criteria that are important to users when choosing a compression product
- the relative importance of the criteria, and
- how the criteria can be measured.

The user preference report should be read alongside the external assessment group (EAG)'s assessment report.

2. Background

Leg ulcers are ulcers that originate on or above the ankle but below the knee and take more than 2 weeks to heal. Most leg ulcers (60- to 80%) happen because of venous insufficiency. There are an estimated 739,000 leg ulcers in England (National Wound Care Strategy Programme, 2020).

In community and primary care, compression products are supplied using an NHS prescription for technologies listed in part IX of the Drug Tariff or the NHS Supply Chain framework. There are at least 20 companies providing over 200 compression products (including different sizes, products and colours) to the NHS across a range of procurement routes. Interventions included in this evaluation include 1) 4-layer compression bandage systems and kits, 2) 2-layer compression bandage systems and kits (these include 2-layer inelastic systems and 2-layer multi-component systems), 3) 2-layer compression hosiery, and 4) compression wraps.

3. Methods

This user preference assessment was done in line with NICE's Interim methods and process statement for late-stage assessment. The aim of capturing user preferences is to transparently collect and present information to the committee on the criteria that users consider important when deciding which technology to choose. Users are defined as those who will use the technology and are directly involved in the decision to choose one technology over another.

3.1 Participants

For this user preference assessment, users were identified as district nurses, practice nurses, tissue viability nurses, specialist clinic nurses and vascular nurses. This is because they decide which compression product is best suited to meet the needs of a specific patient. In addition to the user preference assessment, a patient survey is being used to capture a broad range of patients' views and preferences about the use of compression products for treating venous leg ulcers. Users were recruited in line with NICE's Interim methods and process statement for late-stage assessment. NICE's policy on declaring and managing interests for NICE advisory committees was considered during the recruitment process. A declarations of interest register will be published alongside the guidance document on NICE's topic page.

3.2 Assessment stages

The user preference assessment has been designed with Multicriteria Decision Analysis (MCDA) principles (ISPOR Task Force Report, 2016). Data on user preference was collated through participation in 2 online workshops and 2 email tasks. The process followed 4 stages:

- Stage 1: identifying and defining criteria (workshop 1)
- Stage 2: ranking criteria in order of importance (email task 1)
- Stage 3: weighting of criteria (email task 2)
- Stage 4: development of performance rules (workshop 2)

Stage 1: identifying and defining criteria

Users were asked to identify key factors that are important when choosing a compression product for treating venous leg ulcers. A list of criteria and definitions were identified and agreed on during an online workshop with users.

Stage 2: ranking criteria in order of importance

Users were then asked to rank the criteria in order of importance to them via email. Ranked lists from all respondents were collated, averaged and ordered from most important to least important, creating a final ranked list of criteria and definitions (using the SMART ranking technique; see appendix C for a detailed definition).

Stage 3: weighting criteria

Users were asked to weight the 7 criteria to show how much more important 1 criterion was compared with the criterion ranked below (using the swing weighted technique, see appendix C for a detailed definition). To weight the criteria, users were asked to give each criterion a score from 0 to 100%. A score of 0% meant that there was no difference in importance between a criterion and the criterion ranked below, and a score of 100% meant that it was considered twice as important. Weighted lists for all respondents were collated, averaged and weights were calculated. As per our methods, criteria with a weight of lower than 5% were not taken forward to stage 4 below.

Stage 4: developing performance rules

During the second online workshop, performance rules were created by consensus for each criterion. To do this, users were asked how they would measure performance of the technology against each criterion. For rules with multiple answers, users were asked what would be considered acceptable or unacceptable levels of performance. In some cases, a level of acceptable performance could not be reached due to variation in opinion and the group

was unable to come to a consensus. Where this was the case, it is highlighted in table 3.

3.3 Patient survey

In addition to this user preference assessment, NICE has also conducted a patient survey to include the views of people with venous leg ulcers. Results are reported in section 4.2.

4. Results

4.1 User preference assessment

In total, 11 users participated in the user preference assessment. Most participants were vascular or tissue viability nurses. A detailed list of participants can be found in Appendix A. Table 1 shows user engagement for all 4 stages of the assessment. Six users participated in stage 1, 10 in stage 2, 8 in stages 3 and 5 in stage 4.

Table 1. User engagement for all stages of the assessment

Stages	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	Total
1	√	X	X	X	√	√	√	√	√	X	X	6
2	√	√	√	√	√	√	√	√	√	√	X	10
3	√	√	X	√	√	√	√	√	X	X	√	8
4	√	X	√	X	X	X	√	√	√	X	X	5
Total	**4**	**2**	**2**	**2**	**3**	**3**	**4**	**4**	**3**	**1**	**1**	

4.1.1 Identifying and defining criteria

During the workshop, users identified and defined criteria that are important when selecting compression products to treat people with venous leg ulcers. However, users noted that choosing a compression product is driven by multiple factors and that these vary based on individual needs. Alongside user preferences, choice is also driven by clinical need for certain features. Therefore, criteria were split into 2 categories: criteria related to clinical presentation and criteria related to product features.

Anonymised individual responses from the ranking exercise can be found in appendix B (table 4).

Criteria related to clinical presentation

Users stated that the clinical factors associated with the situation are very important in the choice of compression product used. At the first workshop users identified and defined 3 criteria related to clinical presentation: wound condition, patient characteristics and for recurrent or non-progressing venous leg ulcers: previous treatment regimen and treatment efficacy (table 2). These criteria are presented separately to the other criteria and were not included in the ranking and weighting stages, and no performance measures were created. This is because what may be important for one person with a specific clinical presentation may not be important for someone else, so ranking them in order of importance is not appropriate.

Users noted that clinical need can have a big impact on which compression product is chosen. For example, they noted that compression product suitability does not only depend on the wound condition including levels of exudate, but also on the leg shapes and sizes. Furthermore, users noted that patient concordance to treatment is important. One user raised that sometimes patients are unable to tolerate the compression product prescribed, so they are unable to stick to the treatment plan. One reason provided for this was that some patients may not initially focus on the wound to heal but their initial concern is to make the pain go away. All the relevant factors discussed during the workshop are captured in each definition in table 2.

During the workshop, it was also stated that some of these criteria related to clinical presentation are closely related to the criteria independent of clinical presentation and that there may be some overlap between them. For example, within the patient characteristics criteria, the patient's lifestyle was raised as being important in considering which compression product to use, which is also covered in the 'bulkiness of the product' criteria in table 3.

Table 2. Criteria and definitions related to clinical presentation

Criteria	Definition
Wound condition	The condition of the wound is characterised by aspects which include: • Tissue type (slough, granulation, necrosis, epithelisalisation) • Wound size and depth of wound • Levels and type of exudate (Exudate volume & type) • Wound malodour • Signs of inflammation or infection • Wound location • Wound status (progressing, deteriorating, static) • Condition of peri-wound
Patient characteristics	Patient characteristics include the physiological and psychological factors that can influence outcomes related to treating venous leg ulcers. These may include: • Age • Medical history and underlying aetiology (including genetic factors) • Full lower limb assessment including ABPI result, presence of foot pulses and doppler sounds • Allergies/sensitivities • Mobility and range of ankle function • Lifestyle including patient's choice of clothing and / or footwear • Pain • Ability to self-care or have support of a carer • Hygiene needs • Fragility of the skin • Lower limb skin condition • Leg shape and size (including presence of skin folds) • Current medications • Suitable wear time of product
For recurrent or non-progressing venous leg ulcers: previous treatment regimen and treatment efficacy	• Duration of wound and other treatments • Patient experience and patient preference • Treatment concordance • Lifelong compression post-healing • Other specialist interventions

Criteria independent of clinical presentation

Criteria independent of clinical presentation are factors related to the product features and characteristics which may also be considered by the user when choosing a compression product. A total of 7 criteria were identified and defined by the users in the first workshop. Some users attended the second

workshop only and raised some factual inaccuracies in the criteria and definitions, which were agreed on by consensus and amended in workshop 2. The final criteria and definitions can be found in table 3.

4.1.2 Ranking criteria in order of importance

Criteria independent of clinical presentation

Ten users returned the ranking exercise. The top 3 criteria to consider when choosing compression products were comfort, use and bulkiness of the products. The most important criterion was comfort of the product. Users were in general agreement on this with 7 users ranking it as the most important criterion, followed by 3 users that ranked it as the second most important. Use of the product by healthcare professional, patient and carer was ranked as second most important, with all users ranking it in the top 3. Bulkiness of the product was ranked third most important, however only half the users ranked this criterion in the top 3, with the other 5 users ranking it in 5th place.

Visibility of the product and impact on sustainability were both ranked as the least important criteria. Even though users felt that sustainability is an important issue for delivering a net zero NHS, and that compression products such as hosiery and wraps can reduce not only the carbon footprint but also product waste (Morton et al. 2022), it was ranked as the least important criteria by 7 users when it comes to choosing a compression product. Regarding the visibility of the product, the rankings were mixed, ranging from relatively important to the least important. Users noted that there were not many options in terms of colours for compression products for treating venous leg ulcers. However, they did note that more colours and patterns were available for maintenance hosiery, possibly because people wear these for longer. So, even though currently only a limited choice of colours is available for treating venous leg ulcers, several users stated that this is an area that could be improved as it can be important to patients.

Table 3. Criteria independent of clinical presentation ranked in order of importance

Order of importance	Criteria	Definition
1	Comfort of the product	Using the right product for the patient. Consideration of product for individual patient's needs: • Conformable • Breathability of fabrics • Range of sizes, made to measure availability
2	Use of product by healthcare professional, patient or carer	• Ease of application • Training and safe application • User friendly application instructions • Ongoing manufacturer support and online training and resources • Time to apply • Compression level indicators • Accessibility to application aids
3	Bulkiness of product	The thickness of the compression product adding light or heavy layers to the ankle and leg, which may impact on the patient's ability to wear own footwear or mobility
4	Cost and associated costs of the compression product	• Product cost • Single or multiple use product • Number and duration of appointments required • Level of healthcare professional training required • Clinical setting responsible for patient care (initial assessment and follow-up) • Associated product costs (e.g. aids, dressings, emollients)
5	Healthcare professional familiarity with compression product	• Listed on local formulary • Healthcare professional expertise and sharing knowledge
6	Visibility of product	Some compression products may come in a range of colours and designs which facilitate patients to increase or reduce the product visibility to the outside world
7	Impact on sustainability	• Product materials • Ethically sourced, biodegradable • Reducing clinical waste disposal • Appropriate product choice for each individual patient • Product durability, reusability • Travel and manufacturing emissions

		• Stock management and storage (expiration dates) • Packaging (recyclable, volume)

4.1.3 Weighting criteria and creating performance rules

Weighting criteria

All 7 criteria independent of clinical presentation were weighted by users and are shown in the performance matrix (table 4). Anonymised raw data of weighting scores can be found in Appendix B (table 5).

Eight users participated in the weighting exercise. There was variation in the weights for all criteria, and for all of them apart from 1, the weights varied from 0 to 100% between users. Just over a third of the total weighting score was given to comfort of the product (34.2%). Users agreed that patient comfort is important but that it is also related to the healthcare professionals choosing the right product for the patient. One user also stated that patient concordance is related to the comfort of the compression product. The top 3 criteria hold nearly three quarters of the weights (70.9%).

Creating performance rules

Performance rules are created for each criterion to help users identify how well compression products perform against the outcomes in the criteria and what levels of performance are acceptable or unacceptable. Performance rules may also be based on the physical features or attributes of compression products. During the second workshop, users were asked to create performance rules for 6 criteria. The impact on sustainability agenda criterion was weighted less than 5% and therefore as per our methods, no performance rules were created for this criterion.

Each criterion has multiple performance rules associated with it because users were able to create performance rules related to different aspects of the criterion. Most of the performance rules can be answered as a simple yes or no answer, whereas others may be measured in terms of time, or have

multiple options. Users were asked to state acceptable and unacceptable levels of performance. This was achieved for 4 out of the 6 criteria. For the criterion use of product for healthcare professional, patient and carer, users were happy to not have any (un)acceptable levels of performance. For visibility of the product, 1 user suggested that perhaps unacceptable levels of performance would be to not have a choice in colour of compression products, but no consensus was reached.

While users created performance rules, it was noted that some criteria were more suitable for some of the compression product types compared with others. However, it was agreed that rather than asking about specific compression products, the performance rules should be generic so that these differences can be picked up in the way the questions are answered.

Criterion 1: comfort of product

Users agreed that this criterion will be measured using patient feedback. In total, 7 main performance rules were developed to measure comfort of the product. These included whether the product is comfortable to wear in general, but also for people with bony protrusions or skin folds, if the fabric or product feels itchy or hot to wear, if they come in appropriate or different sizes and strengths and whether the product contains additional skin preparations or latex free options to aid comfort.

Users agreed that the comfort of the product is extremely important. They noted that none of the patients necessarily want to wear compression products, and therefore the question should be whether they would be happy to continue using the prescribed compression product. They also noted that there will be a range of answers that can be provided to the question ‘is the product comfortable to wear’ because the perception of comfort is dependent on the individual patient. Some aspects of the product, for example fabric, a lighter top band or zips, may be important in providing comfort to some patients but not others. One user noted that specifically for compression bandages, the soft underlayer may cause irritation or itching, which can vary

per person. Another user noted that a cotton layer could potentially help prevent itchiness. Users agreed that acceptable levels of performance would be that the patient finds the product relatively comfortable and wears the product for the required time. They also agreed that it would be considered unacceptable if the products are removed because of pain or other discomfort.

Users noted that patients will let the healthcare professional know if the product makes their leg feel hot, and that most patients talk about the itchiness of the product. Some compression products contain additional skin preparations or latex free options to aid comfort. One user noted that ointments, calamine and zinc induced bandages used as an initial layer, or latex free options can help with itching from a venous eczema point of view. One user noted that a padding layer may add comfort for people with bony protrusions. Users agreed that the products do not make the leg or feet sweaty, so this is not an issue. Users also agreed that it is extremely important that the fit is measured accurately by the healthcare professionals and that the patient fit needs to be right. As each patient can be different, it is important to have appropriate sizes including the right length and width. Users agreed that it would be unacceptable if the products move or slip. If this is the case, then this should be corrected immediately. Users also agreed that it is unacceptable if there is skin damage from inappropriate use of compression products.

Criterion 2: use of product for healthcare professional, patient and carer

Performance rules related to this criterion included who can apply the compression product and the ease of use, the level of training needed by different groups to apply the products, are there user-friendly instructions available, is the manufacturer providing ongoing support, time needed for compression product application and whether compression level indicators or aids are available to assist in applying or removing the product.

For each compression product, consideration needs to be given to whether specific competences or capabilities are needed to apply the product. Users agreed that certain compression bandages can only be done by nurses trained at a band 4 minimum. One user noted that to make a capable workforce, online training resources need to be available. Users agreed that this includes patient or carer education on applying and removing products such as hosiery and wraps. One user raised that these online training resources need to be accessible for everyone, including for people with hearing or reading difficulty and people with limited understanding of English language when no interpretation support is available. In terms of time to apply compression products, users noted that this depends on the skill of the person applying it, the number of layers, level of training, dexterity and aids available. They also noted that it is important to allow the time to do apply the products. One user also noted that some people are moving away from 4-layer compression bandages to 2-layer compression bandages as they are not only quicker to apply but they are also less bulky allowing patients to wear their own footwear. This can lead to improved concordance. It was also noted that compression level indicators would not apply to all compression product types and that application aids are not always needed. The users were all happy to not have any levels of acceptance for these performance rules.

Criterion 3: bulkiness of product

For this criterion, users agreed that the performance rules are related to the patient's lifestyle and acceptability rather than the product features. The thickness of a compression product is fixed but different compression products vary in their bulkiness. However, the acceptability of a specific level of bulkiness depends on patients' daily activities and their desire to wear their own footwear. Users noted that typically compression bandages are bulkier than compression hosiery or wraps. One user also noted that bulkier products reduce the range of ankle movement, and this may increase the patient's risk of falling. The users agreed that the levels of acceptability were difficult to determine, because everyone is different and may find different things

acceptable or unacceptable. They agreed that acceptability may vary between patients and that some patients may be happy to wear prescribed or different footwear or may be happy with the impact of the compression product on their mobility, whereas others may not.

Criterion 4: cost and associated costs of the compression product

Users created multiple performance rules for this criterion, which are mostly related to the cost of the compression product as well as associated product costs and healthcare professional level of training and time. Users agreed that the biggest cost associated with compression products for treating venous leg ulcers is healthcare professional time (including visits) which can be reduced significantly if the products allow patients to self-care. Users agreed that it was unacceptable if wear time is less than 7 days. One user noted this would be for all compression products, whereas another user noted that this would mainly be for compression bandages. This is because nursing resource, especially those with appropriate training is limited, so longer wear time will reduce the burden on the nursing teams, especially in community settings. However, multiple users noted that some patients have leaky wounds with high levels of exudate, which could impact on the wear time, needing more frequent dressing changes. They did note that this should be managed by using superabsorbent dressings, and not the compression product itself. For compression hosiery, products need to be changed more often especially if there are high levels of exudate, and therefore may not be suitable at this stage. One user highlighted that compression products such as bandages, wraps or hosiery should be chosen based on appropriateness rather than time spent applying the compression product. Finally, users also agreed that it is unacceptable to limit the application of compression products to certain settings only. They should include home visits as well as appointments in clinics or elsewhere.

Criterion 5: healthcare professional familiarity with compression product

Users created 3 performance rules for this criterion which included whether compression products were listed on the local formulary or used locally, if healthcare professionals were trained to use products appropriately and safely and if there is access to specialist advice and training available. The availability of formularies across the NHS varies. Users advised that in some areas most of the compression products used were chosen from local formularies. This had the advantage that the same products that were often initially prescribed in hospital, could continue to be used in community care. Both hospital and community staff would be very familiar with the use of these products. In some cases, compression products not listed on the local formulary could also be prescribed if this suited the patients' needs better. Compression bandages are listed on part IX of the NHS Drug Tariff. Compression hosiery is grouped and listed under generic 'elastic hosiery' heading. It does not list all the individual products and there is a set price for these products. Most compression wraps listed on the NHS Drug Tariff have a primary indication for Lymphoedema management which are outside the scope of this assessment. However, there are some compression wraps listed for which the primary indication is treating venous leg ulcers. Users agreed that it is unacceptable if healthcare professionals do not have any training in the compression product used. They noted that it is important that people applying compression products have the skills and that the products are intuitive to use. One user noted that people should use the products they know how to use, and that adding variation will dilute this. However, another user noted that the system allows for new innovations and products and that expert knowledge on the different products is key. Users also agreed that it is unacceptable for manufacturers to not provide training or clinical support. They noted that clinical educators from companies add huge value, because they can provide specialist advice where this may be lacking locally.

Criterion 6: visibility of product

Performance rules included whether compression products were available in different colours and whether the compression products are visible when

people are wearing them. A consensus could not be reached on what would be considered acceptable or unacceptable levels of having different colours available. Users agreed that compression products for treating venous leg ulcers come in limited colours (black or sand) and one user noted that it would be nice if they came in different skin tone colours. One user questioned whether more colours should be available as they know that this is important to patients. Another user questioned this and noted that patients should only use these products for 12 weeks, and that this may be more important for maintenance hosiery. Two users stated that the second performance rules are more important, because if people can cover the compression products either with clothing or by being able to wear their own footwear, then the colour matters less. One of these users noted that discreetness and privacy is key to patients.

Table 4: Performance matrix

Order of importance	Weight (%)	Criteria	Performance rule (how to measure criteria and levels of performance considered acceptable)

1	34.2%	Comfort of the product	The criteria will be measured using patient feedback
			• Is the product comfortable to wear?
			  ○ Is the patient happy to continue with this compression therapy product? (Y/N)
			  ○ Does the compression product move during wear? (Y/N)
			• Does the fabric feel itchy? (Y/N)
			• Does the product feel hot to wear? (Y/N)
			• Does the compression product come in appropriate/different sizes and strength? (Y/N)
			  ○ Is the appropriate size available (length and width)? (Y/N)
			  ○ Does the compression product fit well? Is there any digging? (Y/N)
			  ○ Are made to measure products available? (Y/N)
			• Does the compression product contain additional skin preparations or latex free options to aid comfort? (Y/N)
			• Is the product comfortable for bony protrusions? (Y/N)
			• Is the product comfortable for skin folds? (Y/N)
			
			Levels of performance considered acceptable:
			• Patient finds product relatively comfortable and wears the product for the required time
			Levels of performance considered unacceptable:
			• Products are removed because of pain or other discomfort
			• Products move or slip
			• Skin damage from inappropriate use of compression products (for example incorrectly sized product)

2	21.9%	Use of product for healthcare professional, patient and carer	• Who can apply the compression products (HCP, carer, patient)?
			  ○ Are the products easy to apply?
			  ○ Are specific competencies/capabilities needed to apply the product? (Y/N)
			• What level of training is required by the different groups to apply the products?
			• Are the application instructions user friendly and clear so that a lay person can understand the instructions? (Y/N)
			• Is the manufacturer providing ongoing support?
			  ○ Are online training and resources available for healthcare professionals? (Y/N)
			  ○ Are online patient education resources available and accessible to all patient groups? (Y/N)
			• How long does it take to apply the compression product? (time in minutes)
			• Does the compression product have compression level indicators? (Y/N)
			  ○ Are they required and appropriate for use? (Y/N)
			• Are application aids available to assist application and removal of the compression product? (Y/N)
			  ○ Are online patient education resources available and accessible to all patient groups? (Y/N)

3	14.8%	Bulkiness of product	Patient lifestyle and acceptability • Is the thickness of the compression product acceptable? (Y/N) • Are patients able to wear their own footwear? (Y/N) • Are patients able to carry out daily activities? (Y/N) • Does the bulkiness of compression product increase risk of falls? (Y/N) Levels of acceptability may vary between patients

			• Some patients may be happy to wear prescribed or different footwear • Some patients may be happy with the impact of product on mobility

4	10.5%	Cost and associated costs of the compression product	• What is the cost of the compression product? (in pounds)
			  ○ Does this compression product facilitate self-care?
			• Can the product be reused? (Y/N)
			  ○ How often does the product need to be replaced?
			  ○ Does the product need cleaning?
			• What is the frequency and duration of nurse healthcare professional visits required? (weekly; minutes)
			• What is the healthcare professional level needed for visits? What is the cost of training healthcare professionals?
			• Where does the initial assessment and follow up take place?
			• What is the cost of associated products? (in pounds) Are these included in the cost of the product?
			
			Levels of performance considered unacceptable:
			• Wear-time less than 7 days
			• Compression product must not be limited to application in certain settings only

5	8.6%	Healthcare professional familiarity with compression product	• Are the compression products listed on the local formulary/used locally? (Y/N) • Have healthcare professionals been trained to use products appropriately and safely? • Is there access to specialist advice and training about the product and provision of clinical support? Levels of performance considered unacceptable:

			• Healthcare professional has no training in the compression product • Manufacturers not providing training or clinical support

6	5.9%	Visibility of product	• Does the compression product come in different colours? (Y/N)
			• Are compression products visible when wearing them? (Y/N)
			  ○ Can they be hidden by clothing? (Y/N/partially)
			  ○ Can the patient wear their own footwear? (Y/N)
			
			Unable to reach consensus on acceptable levels of having different colours available

4.1.4 Additional considerations

During the user preference workshops, users highlighted some criteria that could be important but that are external to compression product features. These mainly related to availability of and access to types of compression products, which can differ between geographical areas. One user noted that there may be some geographical overlap where they can prescribe a compression product which is then not available through the patient's GP. There was some discussion around the need for users to familiarise themselves and be up to date with the products that are available with a user noting that some people have a preference for certain compression products. It was also raised whether it should be up to the specialist to raise awareness of which products are available to use, as in some places the products may be there but not everyone may be aware of this. It was noted that sharing of knowledge is important.

4.2 Patient survey

Patient characteristics

In total, 18 people who used compression products for treating venous leg ulcers completed the survey, of which 1 only partially completed the survey. Most participants were female (89%), aged 50 or above (82%), and white British/English/Welsh/Scottish/Northern Irish/ Irish (72%). Six people had venous leg ulcers once, while the other 11 people had recurrent venous leg ulcers, recurring at least twice. Activity levels varied between the participants from sedentary (12%), low active (47%), and active (35%) to very advice (6%). People with venous leg ulcers reported that it can have a big impact on their lives including feeling stigma and shame especially when the wound is leaking or has malodour, Other factors which impacted their lives include: the pain associated with the wound, unable to wear own shoes, reduced mobility, emotional distress about having a long-term wound including feeling anxious or depressed, and feeling socially isolated.

“Stigma and shame of going out when [having] leaking wounds and smell of legs. This isolates [a] person from doing other activities, for example social events etc. Painful and open wounds which limit activity and the skin tears very easily which slows healing”

“Very painful and very wet. Couldn’t wear nice clothes. Couldn’t go swimming. Had to keep taking time off work for clinic appointments. Had lots of different staff looking after me but no continuity of care. All had different ideas.”

“Having to wear bandages and have dressings changed had a massive effect on how I could dress and what I could wear on my feet. I am very active and until I bought several pairs of shoes I was unable to be active for fear of falling in badly fitting shoes or I couldn’t fit shoes on. I couldn’t wear anything other than leggings and it affected my confidence. […]*”*

Knowledge and use of different types of compression products

Almost all participants have heard of 2-layer compression hosiery (89%), followed by 2-layer compression bandages (78%), compression wraps (72%) and 4-layer compression bandages (61%). In terms of compression products used, most people had used 2 or more compression products, only 3 people had only used 1 compression product. Of the15 participants (83%) who had used 2 or more compression products the majority (n=9) had used 2 compression product types; 4 used all 4 compression types and 2 people used 3 compression product types. One person had also used 3-layer hosiery, with each layer consisting of 10mmHg. The compression product type ranking according to preference is shown in Table 5. Compression wraps were preferred where used because of their ease of use, comfort and facilitation for self-care. The 2-layer compression bandages were reported to be comfortable but affected use of own footwear. Some people preferred the 2-layer hosiery because they allow self-care and use of own footwear. The 4-layer compression bandages were reported to be bulky.

Table 5. Mean ranking of compression product types (n=17 participants)

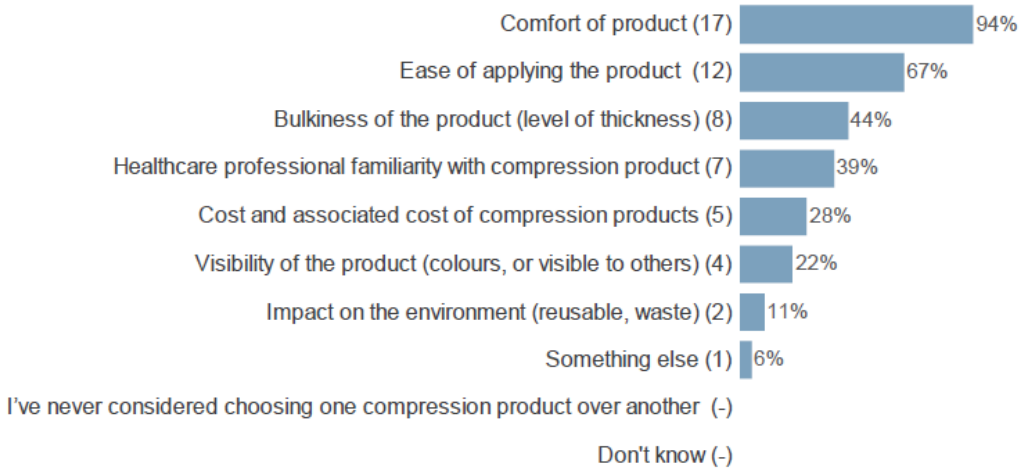
	Mean	Standard deviation	No. participants
4-layer compression bandages	4	1.49	12
2-layer compression bandages	2	1.35	12
2-layer compression hosiery	3	1.01	14
Compression wraps	1	0.95	13

Participants were also asked who applied their compression products when last using them. Eight of them only ticked 1 option, either a carer, for example a family member, or a nurse. The others had ticked multiple options, ranging from doing it themselves, to a carer, district nurse, a specialist nurse or a paid carer. Out of the 18 participants, 10 ticked only 1 option when asked whether they were involved in the decision-making process when deciding which compression product to use. The other 8 ticked 2 or more options. The most ticked options were 'I was given a choice between products' (39%, n=7), and 'I was involved in the discussion about the type of product, but the choice was made for me' (39%, n=7). This was followed by 'I was asked about my previous experience with products' (33%, n=6), and 'I was not involved in the discussion and the choice was made for me' (33%, n=6). Some people were asked which product they wanted but didn't feel comfortable making the decision (17%, n=3), while other people asked for and received the type of product they wanted (11%, n=2). Only 1 participant noted that they asked for a particular product but were not given it (6%, n=1).

Identifying and ranking criteria in order of importance

Participants were asked which product factors would make them choose one compression product over another, using the criteria identified during the user preference assessment. They also got the opportunity to add any other criteria they felt would impact on their choice. Some participants only ticked 1 criterion that would influence their choice (n=4), others ticked 2 criteria (n=4), whereas most participants ticked more than 2 criteria (n=10). Comfort of the product was by far the most important criterion, followed by ease of applying the product and bulkiness of the product.

Figure 1. Product factors that would influence choosing one compression product over another



Participants were also asked to rank the criteria. The average ranking of the criteria is presented in table 5 and is exactly the same as those ranked by healthcare professionals during the user preference assessment. There was some variation in rankings between participants, as shown by the standard deviation in table 5. The highest variation was seen for impact on sustainability, bulkiness of the product and costs and associated costs of the compression product, with some participants ranking those higher than others.

Table 5. Criteria independent of clinical presentation ranked by patients

Order of importance (patients)	Criteria	SD
1	Comfort of the product	0.71
2	Use of product by healthcare professional, patient or carer	1.39
3	Bulkiness of product	1.85
4	Cost and associated costs of the compression product	1.78

5	Healthcare professional familiarity with compression product	1.53
6	Visibility of product	1.48
7	Impact on sustainability	1.93

Eleven participants added additional contextual responses regarding their rankings, however no new criteria were identified. Most participants emphasised the importance of comfort of the product and ease of application. Out of these, 6 participants explicitly noted that they moved from bandages to hosiery once the wound reduced in size, the swelling reduced, or the wound stopped leaking.

4. Discussion

Eleven participants took part in this user preference assessment to identify what is important to users when choosing a compression product for treating venous leg ulcers. A total of 7 criteria independent of clinical presentation were identified, defined, ranked in order of importance and weighted. For criteria weighted higher than 5% performance rules were created to show how performance for each criterion could be measured (n=6). The top 3 criteria included comfort of product, use of product by healthcare professional, patient or carer and bulkiness of the product which had a combined weighting of 70.9%. In addition, 3 criteria related to clinical presentation were identified. However, these were not ranked, weighted or had performance rules developed because what may be important for one person with a specific clinical presentation may not be important for someone else. Both sets of criteria are closely related and thus there may be some overlap between them.

While consensus on the defined and ranked criteria was reasonably good, there was some variation in the ranking and weighting of the criteria. The impact on sustainability agenda criterion was ranked last and weighted less

than 5%, with some user variation, and therefore no performance rules were created for this criterion. This does not mean that users did not think this criterion was important, but that it would not weigh heavily in the decision-making process when choosing which compression product to use. However, the NHS is aiming to reduce its carbon footprint to net zero by 2040 and wound care uses a lot of products and require considerable travel as most care is delivered in the community (Morton et al. 2022). Users agreed that using reusable compression products or products that allow for supported self-care may improve sustainability and may also reduce waste and carbon footprint.

Eighteen people completed the patient survey. The survey highlighted that venous leg ulcers have a big impact on people's lives including physical and emotional effects. It also highlighted that comfort and ease of use and bulkiness of the products were the most important criteria when choosing a compression product. The criteria ranking from the patient survey were in the same order as the ranking from the healthcare professionals. However, the variation in the ranking differed slightly between the two groups. For the patient survey, the highest variation in individual ranking was found for impact on sustainability, bulkiness of the product and cost and associated costs of the compression product. For healthcare professionals, this was bulkiness of product, visibility of the product and healthcare professional familiarity with compression product.

Engagement in the assessment was mixed (see table 1). In total, 11 participants took part in the user preference assessment. Three participants engaged with all four stages in the assessment, and 4 participants attended both workshop 1 and workshop 2. Regarding the email tasks, 10 participants returned their rankings (task 1), and 8 participants returned their weighted criteria (task 2). Initially, attendance for the second workshop was very low. It was therefore decided to move the workshop to a date where more people could attend. Some participants attended workshop 2 without having attended

workshop 1 and identified some factual inaccuracies in the definitions, which were corrected in workshop 2 through group consensus.

A limitation of the user preference assessment and patient survey is volunteer bias. Users and patients volunteered to take part in the relevant activities, and it is likely that the sample of participants is not fully representative of the wider populations. For the user preference assessment, participants included all experts and all specialist committee members (SCMs), apart from 1 for this topic, plus 2 additional experts. Most participants were vascular nurse practitioners or tissue viability nurses. No district or practice nurses participated in the user preference assessment, which is a limitation. Even though there were no district or practice nurses included, participants that worked in the community were included.

In conclusion, this assessment provides insights into the user preferences and considerations when choosing compression products for treating venous leg ulcers, from both a healthcare profession and patient perspective. It highlights the importance of clinical presentation such as wound condition, patient characteristics and for people with recurrent or non-progressing venous leg ulcers, previous treatment regimen and treatment efficacy, which can vary greatly between patients. It also highlights that individual patient needs need to be considered and that product comfort, use of the product by different groups and the bulkiness of the product are the most important features in deciding which products to use.

Appendix A. Participants

Leanne Atkin, Vascular nurse consultant and senior research fellow, Mid Yorks NHS Trust/University of Huddersfield

Priti Bhatt, Tissue viability lead, community services, Guys and St Thomas' NHS Foundation Trust

Hannah Blake, Tissue Viability Clinical Nurse Specialist, Livewell Southwest

Debera Drew, Tissue Viability Specialist Nurse & Senior Community Research Nurse, Northumbria Healthcare Foundation Trust

Stacey Evans-Charles, Tissue Viability Nurse Lead, NHS Highland

Rachael Lee, Acting Programme Manager, National Wound Care Strategy Programme

Nicky Morton, Supply and Distribution Workstream Lead, National Wound Care Strategy Programme

Maria Poole, Tissue viability nurse and project consultant, The Lindsay Leg Club Foundation

Julie Thackray, Vascular Nurse Specialist, Leeds Teaching Hospitals NHS Trust

Jane Todhunter, Vascular nurse practitioner, North Cumbria Integrated Care NHS Foundation Trust

Beverley Wright, Operational lead, tissue viability, Northumbria Healthcare Foundation Trust

Appendix B. Raw data from ranking and weighting stages

Table 4. Raw data from ranking exercise

Criteria	User 1	User 2	User 3	User 4	User 5	User 6	User 7	User 8	User 9	User 10	Mean	SD	Final rank
Comfort of product	1	2	2	1	1	1	2	1	1	1	1.3	0.48	1
Use of product for healthcare professional, patient and carer	2	1	1	3	2	2	3	3	2	2	2.1	0.74	2
Bulkiness of product	3	5	3	2	5	5	1	2	5	5	3.6	1.58	3
Cost and associated costs of the compression product	5	3	5	4	4	4	6	4	6	4	4.5	0.97	4
Healthcare professional familiarity with compression product	6	6	6	5	3	3	4	6	4	3	4.6	1.35	5
Visibility of product	4	7	4	6	7	6	5	5	3	7	5.4	1.43	6
Impact on sustainability agenda	7	4	7	7	6	7	7	7	7	6	6.5	0.97	7

Table 5. Raw data from weighting exercise

Rank	Criteria	User 1	User 2	User 4	User 5	User 6	User 7	User 8	User 11	Mean importance	SD	Overall weight*
1	Comfort of product	90	10	50	100	100	0	50	50	56.25	38.52	34.2%
2	Use of product for healthcare professional, patient and carer	80	50	0	100	100	0	25	25	47.50	41.58	21.9%
3	Bulkiness of product	80	25	50	25	25	100	0	25	41.25	33.35	14.8%
4	Cost and associated costs of the compression product	75	30	0	25	25	0	0	25	22.50	24.93	10.5%
5	Healthcare professional familiarity with compression product	60	10	25	100	100	25	50	0	46.25	38.43	8.6%
6	Visibility of product	70	0	50	30	30	25	100	0	38.13	34.22	5.9%
7	Impact on sustainability agenda											4.2%

*points are attributed to the criterion based on the mean importance relative to the criterion below. These are used to calculate the final weight

Appendix C. Glossary

Term	Definition
SMART ranking technique	A multi-criteria decision-making technique that allows criteria to be ordered by importance. Individual responses from each member of a group are collated and averaged, ensuring equal say among the group (Von Winterfeldt D, Edwards W. (1993) Decision analysis and behavioral research. Cambridge: Cambridge University Press).
Swing weighting technique	A technique used for calculating and reporting the relative importance (weight) of each criterion from a ranked list. Each member of a group provides individual responses deciding how important each criterion is over the criterion below it (on a scale of 0-100%). Individual responses from each member of the sample are collated, averaged and weights are calculated (Von Winterfeldt D, Edwards W. (1993) Decision analysis and behavioral research. Cambridge: Cambridge University Press).
Performance rule	A rule which describes how the users measure performance of the technology in question against the criteria.
Performance matrix	A list of the most important criteria to users, and the performance rules associated with these criteria.

Health Tech Programme

GID-HTE10048 Compression products for treating venous leg ulcers: Late-stage assessment

User Preference Report

Collated comments table

Any confidential sections of the information provided should be underlined and highlighted. Please underline all confidential information, and separately highlight information that is 'commercial in confidence' in blue and all that is 'academic in confidence' in yellow

User preference report – Collated comments table:

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE's Response
1	Essity	14	Criterion 2	Training band 4 to deliver compression would be to work independently. Currently band 3 and below can work with a band 5 and above in clinics and still apply compression.	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to change or add details retrospectively. No change was made to the report.
2	Essity	16	Criterion 5	Compression wraps are currently not listed on the NHS Drug Tariff for treating venous leg ulcers – This is incorrect. Essity JOBST FarrowWrap 4000 is indicated for leg ulcer management as its primary indication. This is listed on Drug Tarrif and IFU states this. Other wraps on market have 2nd indication for venous with a primary indication of lymphoedema management. This would need to be updated to reflect that products are available in wraps for Venous treatment	Thank you for your comment. We have amended this statement in the report to reflect that the NHS Drug Tariff lists compression wraps for treating venous leg ulcers.
3	Essity	13	Criterion 1	They also agreed that it would be considered unacceptable if the products are removed because of pain or other discomfort. – Essity agree with patient comfort been the key	Thank you for your comment. This user preference report details the discussions and

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE's Response
				factor in concordance with compression. The pain element of compression if correct size and type of garment may be down to the wound itself creating pain when compressed. As part of the pathway recommendation Essity would like to understand if part of the discussion would be appropriate pain management used to help support patients pain levels and comfort during healing of wounds	opinions of the participants. It is not possible to change or add details retrospectively. No change was made to the report.
4	Essity	12	Criterion 1:	kits should be excluded here. None are relevant for Boney prom or skin folds	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to change or add details retrospectively. The user preference report presents the key findings from the user preference assessment which identified criteria that are important to users when choosing a compression product, their relative importance and how they can be measured. The assessment did not consider specific products but looked across 4 types of compression products specified in the decision problem. Criterion 1 talks about the compression products in general and highlights the importance of whether compression products are comfortable to wear, specifically for people with bony protrusions or skin folds. On page 13 it also states, 'One user noted that a padding layer may add comfort for people with bony protrusions.' Section 4.1.1 'criteria related to clinical presentation' states that 'users noted that clinical need can have a big impact on which compression product is chosen. For example, they noted that compression

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					product suitability does not only depend on the wound condition including levels of exudate, but also on the leg shapes and sizes. It was also stated that some of these criteria related to clinical presentation are closely related to the criteria independent of clinical presentation and that there may be some overlap between them.'
5	Essity	16	Criterion 5	Based on market knowledge its is very rare for compression therapy to be started in the acute setting due to short stays in beds. In vascular and podiatry services products may be used and patients discharged in our experience the district nurses are best placed to deliver compression therapy and Essity would be interested to understand the number of DNs involved in the uses assessment panel	Thank you for your comment. The list of users that participated in the user preference assessment is detailed in Appendix A. No district nurses participated in the user preference assessment, which has been noted as a limitation in the discussion.
6	Urgo Ltd	6	4.1	With circa 15,500 registered nurses (NHS Workforce Statistics Nov 2023, Primary care Workforce England December 2024), the respondent survey rate of 11 is extremely low and represents < 0.00071% of both registered district nurses and primary care nurses. The views expressed within the user assessment report cannot be considered representative.	Thank you for your comment. NICE acknowledged that a limitation of the user preference assessment and patient survey is volunteer bias. Users and patients volunteered to take part in the relevant activities, and it is likely that the sample of participants is not fully representative of the wider populations. NICE publicly advertises its specialist committee member roles and encouraged companies, professional organisations and patient organisations to nominate or share this opportunity. In addition to this stakeholder comment period, NICE holds public consultation on the draft recommendations and associated documents. So, other users (healthcare professionals) and patients can provide additional comments. The user preference assessment is not intended to supersede the outcome from the clinical and economical evaluation. It is intended to compliment it

Comment no.	Stakeholder	Page no.	Section no.	Comment	NICE's Response
					and provide a transparent insight into the preferences identified by the users involved in the assessment.
7	Urgo Ltd	12	Criterion 1	Comfort of product: The question ''is the product comfortable to wear in general'' is too broad and comfort can mean different things to different people. There is a high risk that the responses you receive will be that compression is not comfortable. Compression therapy, can have some discomfort ''Compression can be a little uncomfortable when you first start treatment but should not cause you any pain. Any discomfort should reduce as the swelling goes down'' What is Compression Therapy? Compression Bandages, Socks & Tights, Legs Matter UK Can you consider re-wording the questions to be specific on what is meant by comfort and what you are trying to determine and discover in relation to 'comfort'	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to change or add details retrospectively. No change was made to the report.
8	Urgo Ltd	13	Criterion 1	''users agreed that acceptable levels of performance would be that the patients find the product relatively comfortable and wears the product for the required time''. In some compression products (2LCH, CW), patients and or their carers are able to easily remove the top stocking (2LCH) or loosen the CW to provide comfort without the heath care professional knowing. This removal or loosening needs to be captured in the questions as provides information on the true comfort level of the 2LCH & CW.	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to change or add details retrospectively. No change was made to the report.
9	Urgo Ltd	13	Criterion 1	''unacceptable if the products are removed because of pain or other discomfort''. There many be other factors that contribute to pain or discomfort and therefore removal of the compression product, such as a change in the wound (e.g. infection). Wound infection can increase pain and/or discomfort a patient experiences, but this is not in direct relation to the compression product. 2LCH and CW can be removed in entirety by the patient and/or carer and then re-applied without a health care	Thank you for your comment. This user preference report details the discussions and opinions of the participants. It is not possible to change or add details retrospectively. No change was made to the report.

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				professional being aware. This specific question needs to be factored in. Can this question be broken into 2 elements: Is the product removed due to pain or discomfort of the compression products that is unrelated to change a wound status? Is the product removed due to discomfort or pain and then re-applied?	

10	Urgo Ltd	13	Criterion 1	''unacceptable if there is skin damage from inappropriate use of compression products''.
				Can you elaborate on what is deemed as inappropriate?
				For example, if a compression system is applied to a limb without padding bony prominences and skin damage occurs, this is incorrect use of the compression products by a healthcare professional and not as a result of the product itself.
				Additionally, if a compression product for an ankle size 25 – 32cm is applied to a limb that has an ankle circumference of 18 – 25cm, the compression product will deliver a higher level of compression. This again is incorrect/inappropriate application by the healthcare professional and not the product itself.
				Can you clearly define what ''inappropriate use is''
					Thank you for your comment. This relates to 'Users also agreed that it is extremely important that the fit is measured accurately by the healthcare professionals and that the patient fit needs to be right. As each patient can be different, it is important to have appropriate sizes including the right length and width.' In many cases, 'inappropriate use' occurs when the clinician does not choose the correct product for the individual patient, for example an incorrectly sized product.
					
					Within table 4, this level of performance relates to the following performance rules:
					• Does the compression product come in appropriate/different sizes and strength? (Y/N)
					  ○ Is the appropriate size available (length and width)? (Y/N)
					  ○ Does the compression product fit well? Is there any digging? (Y/N)
					  ○ Are made to measure products available? (Y/N)

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					An example has been added to table 4 to explain what is meant by 'inappropriate use'.
11	Urgo Ltd	14	Criterion 2	'' For each compression product, consideration needs to be given to whether specific competences or capabilities are needed to apply the product. Users agreed that certain compression bandages can only be done by nurses trained at a band 4 minimum''. Can you confirm that specific competencies/capabilities on diagnosing the aetiology of venous leg ulcers (ABPI & full holistic assessment) have been considered, as the application of bandaging and specific competencies are different for diagnosis and application. In order to choose the correct compression product, the underlying aetiology to confirm venous insufficiency and rule out arterial involvement, is necessary before compression should be applied. For any and all compression products (4LB, 2LB, 2LCH, CW) ALL need to have an exclusion of red flags (immediate and necessary care, NWCSP) prior to choosing or applying any compression product (NWCSP Leg Ulcer Recommendations, July 2024). Within 14 days a full holistic assessment including ABPI needs to be undertaken to determine the underlying aetiology and to provide correct treatment including compression therapy. If venous disease is suspected, a venous duplex scan is considered a gold standard form of assessment for individuals with lower leg ulcers so should also be part of assessment ((NWCSP Leg Ulcer Recommendations, July 2024). ABPI's either by handheld or automated doppler or venous duplex scans can only, be undertaken by nurses who have received training and are competent in undertaking an ABPI. This training and competencies are not defined by band of nurse but by attendance and completion of training and	Thank you for your comment. As per the scope, the focus of this LSA is on compression products for treating venous leg ulcers. Full lower limb assessment and ABPI result, presence of foot pulses and doppler sounds have been captured in table 2 which outlines the criteria and definitions related to clinical presentation. This specific point has been considered under patient characteristics. The criteria related to clinical presentation were presented separately to the other criteria and were not included in the ranking and weighting stages, and no performance rules were created. This is because what may be important for one person with a specific clinical presentation may not be important for someone else, so ranking them in order of importance is not appropriate. The focus of the user preference report is on the criteria independent of clinical presentation. These criteria relate to the product characteristics deemed important when a decision is being made by users to select a product for a person with a venous leg ulcer which need to be treated with strong compression.

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				competencies as per trust policies. Therefore, the band of nurse cannot be generalised to a band 4 minimum.	
12	Urgo Ltd	15	Criterion 5	''Compression wraps are currently not listed on the NHS Drug Tariff for treating venous leg ulcers.'' Not all compression wraps are indicated for the management of venous leg ulcers and as such should not be included in this LSA as they are out of scope of this assessment (''The evaluation will assess the clinical and economic benefits of compression products for treating venous leg ulcers, as well as evaluating how product features impact outcomes and user preference''. Introduction, GID-HTE10048 Final Scope). Only compression wraps that are indicated for treating venous leg ulcers (not some of the symptoms or oedema) should be included in the LSA. Examples of wraps where they do not meet the inclusion criteria of management of venous leg ulcers as per published final scope: ReadyWrap Calf : (IFU Below) Assist in management of some symptoms of venous ulcers Assists in helping limit venous ulcer recurrence	Thank you for your comment. This LSA is only including compression wraps that are indicated for treating venous leg ulcers. Thank you for providing examples of wraps that do not meet the inclusion criteria of management of venous leg ulcers as described in the published scope.

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				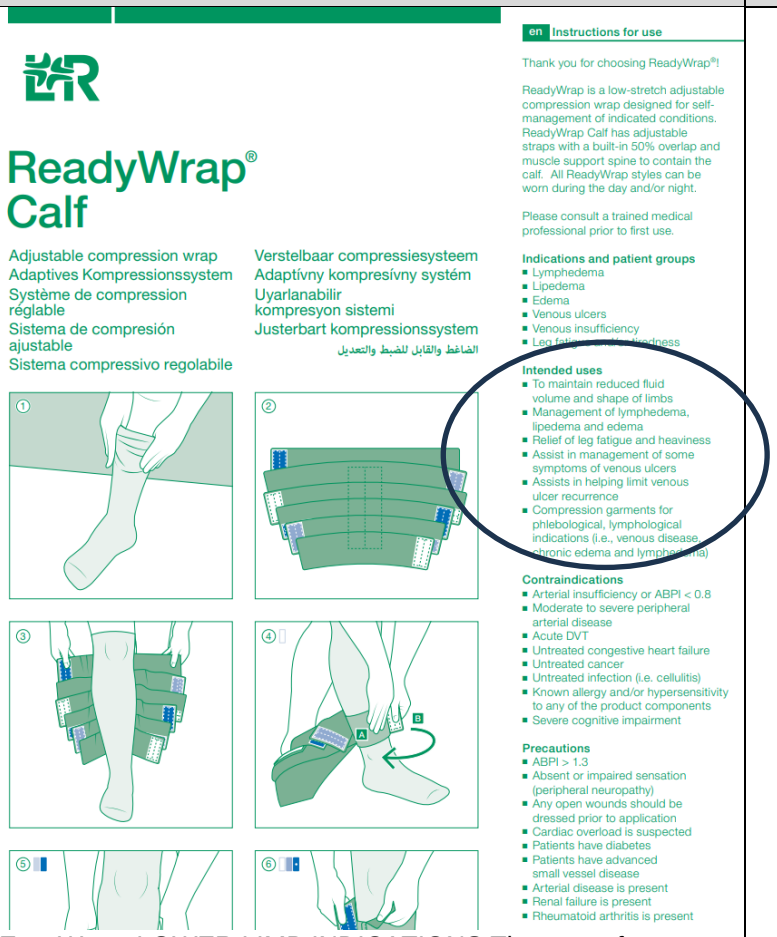 EasyWrap: LOWER LIMB INDICATIONS The type of easywrap is printed on the garment's label. Primary Indications: Light for mild to moderate lymphoedema or oedema; palliative care	

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				Strong for severe and stubborn lymphoedema or oedema; rebound oedema; primary lymphoedema of long duration IFU-EWL-2017-03.pdf	
13	Urgo Ltd	18	Table 4: Comfort of the product	See comment 3	This corresponds to comment number 8 in this table. Please see NICE's response to comment 8.
14	Urgo Ltd	19	Table 4: Use of product for healthcare professional, patient and carer	See comment 6	This corresponds to comment number 11 in this table. Please see NICE's response to comment 11.
15	Urgo Ltd	22 - 28	4.2	'' 18 people who used compression products for treating venous leg ulcers completed the survey'' Based on an estimated 739,000 leg ulcers in England (GID-HTE10048 Final Scope), this respondent amount equates to only 0.002% of the estimated population and should not be considered as representative of the population within the scope of this LSA	Thank you for your comment. Please see NICE's response to comment 6.
16	Urgo Ltd	28	5.	'' Most participants were vascular nurse practitioners or tissue viability nurses. Even though there were no district or practice nurses included participants that worked in the community were included''. One of the main drivers of cost saving potential is resource costs (time) with much of the cost modelling being nursing time (Bd 3, 4 or 5 nurse). However, these band nurses were not, a participant of the user preference. This is a severe limitation of the user preference report and should be included/commented as such.	Thank you for your comment. We have added a sentence to the limitations paragraph in the discussion stating: *'No district or practice nurses participated in the user preference assessment, which is a limitation.'*