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REVIEW ARTICLE

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A meta-review of the impact of compression therapy on venous leg ulcer healing

Declan Patton[1,2,3,4,5] | **Pinar Avsar**[1,2] | **Aicha Sayeh**[1] | **Aglecia Budri**[1,2] | **Tom O'Connor**[1,2,3,4,6] | **Simone Walsh**[1] | **Linda Nugent**[1,2,3] | **Denis Harkin**[7] | **Niall O'Brien**[8] | **Jonathan Cayce**[9] | **Michael Corcoran**[10] | **Mario Gaztambide**[10] | **Zena Moore**[1,2,3,4,6,11,12,13,14]

[1]Skin Wounds and Trauma Research Centre, The Royal College of Surgeons in Ireland (RCSI), University of Medicine and Health Sciences, Dublin, Ireland

[2]School of Nursing and Midwifery, The Royal College of Surgeons in Ireland (RCSI), University of Medicine and Health Sciences, Dublin, Ireland

[3]Fakeeh College of Medical Sciences, Jeddah, Saudi Arabia

[4]School of Nursing and Midwifery, Griffith University, Southport, Queensland, Australia

[5]Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, New South Wales, Australia

[6]Lida Institute, Shanghai, China

[7]The Royal College of Surgeons in Ireland (RCSI), University of Medicine and Health Sciences, Faculty of Medicine and Health Sciences, Dublin, Ireland

[8]The Royal College of Surgeons in Ireland (RCSI), University of Medicine and Health Sciences, Dublin, Ireland

[9]DeRoyal Industries, Knoxville, Tennessee, USA

[10]DeRoyal International, Dublin, Ireland

[11]Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia

[12]Department of Public Health, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

[13]University of Wales, Cardiff, UK

Abstract

This meta-review aimed to appraise and synthesise findings from existing systematic reviews that measured the impact of compression therapy on venous leg ulcers healing. We searched five databases to identify potential papers; three authors extracted data, and a fourth author adjudicated the findings. The AMSTAR-2 tool was used for quality appraisal and the certainty of the evidence was appraised using GRADEpro. Data analysis was undertaken using RevMan. We identified 12 systematic reviews published between 1997 and 2021. AMSTAR-2 assessment identified three as high quality, five as moderate quality, and four as low quality. Seven comparisons were reported, with a meta-analysis undertaken for five of these comparisons: compression vs no compression (risk ratio [RR]: 1.55; 95% confidence interval [CI] 1.34-1.78; $P < .00001$; moderate-certainty evidence); elastic compression vs inelastic compression (RR: 1.02; 95% CI: 0.96-1.08; $P < .61$ moderate-certainty evidence); four layer vs <four-layer bandage systems (RR: 1.07; 95% CI: 0.82-1.40; $P < .63$; moderate-certainty evidence); comparison between different four-layer bandage systems (RR: 1.08; 95% CI: 0.93-1.25; $P = .34$; moderate-certainty evidence); compression bandage vs compression stocking (RR 0.95; 95% CI 0.87-1.03; $P = .18$; moderate-certainty evidence). The main conclusion from this review is that there is a statistically significant difference in healing rates when compression is used compared with no compression, with moderate-certainty evidence. Otherwise, there is no statistically different difference in healing rates using elastic compression vs inelastic compression, four layer vs <four-layer bandage systems, different four-layer bandage systems, or compression bandages vs compression stockings.

[14]National Health and Medical Research Council Centre of Research Excellence in Wiser Wound Care, Menzies Health Institute Queensland, Southport, Queensland, Australia

Correspondence
Pinar Avsar, PhD, MSc, BSc, RGN, Lecturer RCSI University of Medicine and Health Sciences, School of Nursing and Midwifery, Dublin, Ireland.
Email: pinaravsar@rcsi.com

KEYWORDS
compression bandages, compression therapy, healing, meta-review, venous leg ulcers

Key Messages

- compression therapy (CT) represents the gold standard for venous leg ulcers management
- there is a statistically significant difference in healing rates when compression is used compared with no compression, with moderate-certainty evidence
- a clinician might also consider concerns about patient compliance with CT to maximise the probability of wound healing
- further meta-reviews, which focus on challenges faced by health care professionals and patients when using CT, need to be undertaken

1 | INTRODUCTION

Venous leg ulcers (VLUs) are chronic wounds that occur within the lower region of the leg between the knee and ankle as a consequence of venous insufficiency.[1] Venous valve dysfunction, deep vein occlusion, and the failure of the calf muscle represent the mechanisms that cause venous insufficiency and associated venous hypertension.[2,3] Venous leg ulcers distress patients, cause pain, increase the risk of infection, can exude odour, and severely impact patients' mobility and quality of life.[4,5]

The incidence of venous leg ulceration ranges between 1% and 3% in adults.[6] While the risk of VLU increases with age, 22% of individuals develop their first VLUs by 40 years of age and 13% before 30 years of age, negatively affecting their ability to work and participate in social activities.[7] The healing of VLU represents a notoriously slow process, 93% of VLUs will heal in 12 months and 7% remain unhealed after 5 years, while the recurrence rate within 3 months of healing is around 70%.[8]

Compression therapy (CT) represents the standard of care for conservative treatment of VLU.[9] CT works by generating external pressure on the superficial veins and tissues, thereby assisting venous return. Improved venous return helps to reduce peripheral oedema and promotes lower limb wound healing.[10] Published healing rates of VLU managed with CT vary widely from 40% to 95%.[11] Clinicians can provide CT by three different techniques: bandage systems, stockings/hosiery, or active intermittent compression devices.[7] This meta-review of existing systematic reviews considers the impact of CT on VLU healing.

2 | RESEARCH QUESTION

The research questions explored in this meta-review were as follows:

1. *What is the effect of compression therapy on venous leg ulcer healing?*
2. *What is the effect of venous leg ulcer compression therapy on adverse events?*

2.1 | Aim

The aim of this meta-review was to appraise and synthesise the evidence from existing systematic reviews that measured the impact of CT on VLU healing.

3 | METHODS

We conducted a meta-review of systematic reviews. Meta-reviews aggregate the summarised results of systematic reviews and help to inform policy and practice decision-making.[12] Similar to systematic reviews, meta-reviews include selecting systematic reviews, quality appraisal of the reviews, providing results, giving an overview of results for practice, and research-related implications.[13] Using the PICO framework[14] as a guide, this meta-review appraised existing systematic reviews that measured CT's impact on venous leg ulcer healing.

The components of the PICO were:

- Population: Patients with a venous leg ulcer
- Intervention: CT, however, specified by the review author(s).
- Comparison: Other intervention or none
- Outcome: Primary—healing (time and rate). Secondary—adverse events

The author team followed the standard approach advocated for systematic reviews and used the Preferred Reporting Items for Systematic Reviews and Meta-

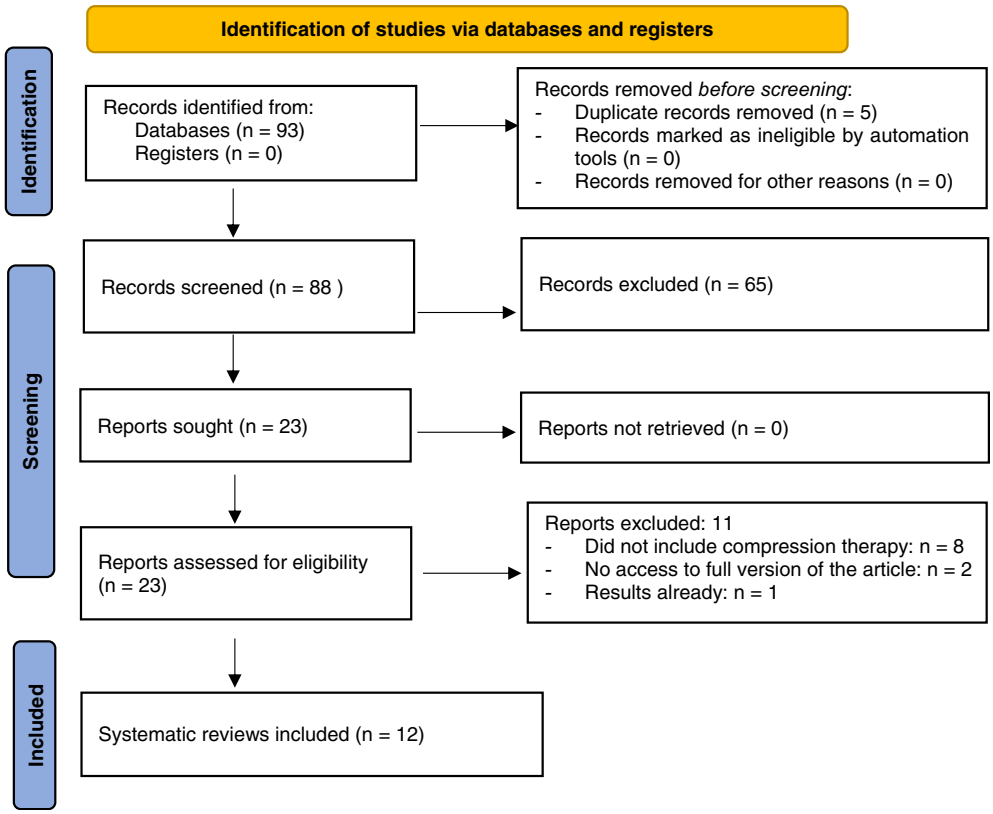

FIGURE 1 PRISMA 2020 flow diagram for study selection[31]

Analyses (PRISMA) guidelines[15] to guide the conduct and reporting of the meta-review. The PRISMA refers to present records identified through all databases searched and is presented in Figure 1. The study protocol was pre-registered with the International Prospective Register of Systematic Reviews (CRD 42021233417).

3.1 | Search strategy

The following inclusion criteria were used,

- Published systematic reviews, with no geographic restriction for study sites.
- Reviews are written in English.
- Healing as a primary or secondary outcome.
- Reviews only consider studies in adults (aged over 16 years).
- Clinical setting of any type.
- CT, however defined in the review.

The exclusion criteria were as follows,

- An identified review included results from paediatric patients.
- Non-English reviews.

TABLE 1 Search terms used

#1 Chronic Venous leg Ulcer OR Venous Leg Ulcer, OR Ulcers, leg ulcers
#2 Healing OR heal OR wound healing OR VLU healing
#3 Time to healing OR Time to heal
#4 Compression Therapy OR Compression therapies OR dressing, bandage OR Dressings, Bandages
#5 Venous Leg ulcer recurrence OR ulcer recurrence
#6: #1 OR #2 OR #3 OR#4 OR #5
#7 effectiveness
#8: #6 AND #7
#9 Wound care
#10: #8 AND #9

A Health Sciences Librarian advised on the literature search in July 2021. The primary search included five databases (MEDLINE (Ovid), EMBASE (Ovid), EBM Reviews, and Cochrane Library (Ovid), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science). Search terms are in Table 1. To identify further published systematic reviews, secondary searches were included.

- Reference lists of all included reviews
- Grey literature using OpenGrey (www.opengrey.eu);
- Conference proceedings, research reports.

3.2 | Screening

Four team members independently assessed the article titles and abstracts of existing systematic reviews. The same team then reviewed the full-text versions of potentially relevant reviews against the inclusion/exclusion. To include a review, the four team members reached a consensus through discussion. A fifth team member adjudicated when the four reviewing team members could not agree on inclusion or exclusion of a specific review.

3.3 | Data extraction

For included reviews, three authors extracted data independently using a purpose-built and piloted data extraction table. The data extracted related to the review type, types of papers reviewed, sample, setting and population, intervention, control, and the results. A fourth author adjudicated on disagreements or discrepancies.

3.4 | Quality assessment

For quality assessment, we used the 16-item AMSTAR-2 tool as it enables a reliable and swift quality appraisal of systematic reviews.[16] The 16 questions included relating to the review question, methods, search strategy, data extraction, data analysis, and risk of bias. Two authors completed the AMSTAR-2 tool, with a third intervening where disagreements or discrepancies occurred. While not giving an overall score, the AMSTAR-2 tool allowed the group to determine an overall quality rating for each included review. In addition, the certainty of the evidence related to each of the main outcomes was evaluated by using GRADE (Grades of Recommendation, Assessment, Development, and Evaluation). This certainty of the evidence was assessed against five principle domains: (a) limitations in design and implementation; (b) indirectness of evidence or generalisability of findings; (c) inconsistency of results, for example, unexplained heterogeneity and inconsistent findings; (d) imprecision of results where confidence intervals (CIs) are wide; and (e) publication bias.[17]

TABLE 2 Excluded studies

Author	Reason for exclusion
Norman, Westby[32]	Relates to dressings rather than compression bandages
Palfreyman, Nelson[33]	Relates to dressings rather than compression bandages
Palfreyman, Nelson[34]	Relates to dressings rather than compression bandages
Bouza, Muñoz[35]	Relates to dressings rather than compression bandages
Turner-Boutle, Fletcher[36]	Could not access the full version of the article
de Carvalho[37]	Could not access the full version of the article
Jull, Slark[38]	Not directly focused on compression therapy and healing
Health Quality Ontario[39]	Focused on prevention rather than treatment
Nelson and Bell-Syer[40]	Focused on prevention rather than treatment
Valle, Maruthur[41]	Relates to dressings rather than compression bandages
Nelson[42]	Repeating results of already included systematic review

3.5 | Synthesis

After removing duplicate data from studies included in multiple reviews, where appropriate meta-analysis statistical synthesis was undertaken using RevMan.[18] Relative risks (RR) and 95% CIs were calculated for dichotomous outcomes, and mean differences and 95% CI were calculated for continuous outcomes. Results of comparable trials were pooled using a fixed-effect model and 95% CI. Heterogeneity was investigated by calculating the I^2 statistic.[17]

4 | RESULTS

4.1 | Overview of all included studies

Figure 1 outlines the flow of articles through the screening process that led to the inclusion of 12 systematic reviews.[19-30] Table 2 identifies the nine excluded studies and the reason for exclusion from the final screening step.

4.2 | Review characteristics

Table 3 provides a summary of the included reviews' characteristics. Twelve systematic reviews met

TABLE 3 Characteristics of included reviews

Author	Types of studies in the SR	Sample, setting and population
De Carvalho, Peixoto[21]	4LB vs SSBs	Seven RCTs undertaken in Europe, one in Asia, and one in North America. One thousand four hundred and thirty-five patients: 657 (45.78%) male and 778 (54.48%) female, average age 70 (range 23-97) years, with venous disease and had an ABI >0.9 mm Hg treated using 4LB and 726 using SSB.
Fletcher, Cullum[22]	Compression for healing of venous leg ulcers	Twenty-four RCTs with six unpublished studies: 1. Compression vs no compression (six trials). 2. Elastic multi-layer high compression bandages vs inelastic compression (six trials). 3. Multilayer high compression systems vs single layer systems (four trials). 4. Comparisons between different medium and high 5. Compression systems (four trials) 6. Compression hosiery vs compression bandaging (two trials) 7. Intermittent pneumatic compression treatment (two trials)
Goka, Poku[23]	Multicomponent compression systems	Three multicentre RCTs Belgium, Canada, Germany, Italy, the Netherlands, United Kingdom, and United States, the United Kingdom. One thousand five hundred nine patients, Aged between 62.5 years to 76.9 years. Ulcer duration and measurements (5.8 months to 48.8 months and 7 cm^2 to 11.8 cm^2).
Mauck, Asi[24]	Compression stockings vs compression bandages,	Thirty-eight eligible studies: 36 unique studies in 34 published articles: 1. Twelve RCTs: compression stockings vs compression bandages 2. Six RCTs: 4LB compression vs compression with less than four layers 3. Eighteen RCTs (2 of them unpublished abstracts): SSB compression vs LBB compression 4. Two Cochrane Systematic reviews
O'Meara, Cullum[19]	Compression bandage or compression stockings compared with no compression or an alternative type of compression	Forty-eight RCTs reporting 59 comparisons (4321 participants in total).
Cullum, Nelson[28]	Compression bandaging or stocking	Twenty-three RCTs 1. Three trials compared the use of compression with the use of dressings alone 2. Three studies compared different forms of compression bandage 3. Three studies compared elastic high compression three-layer bandaging with low compression 4. Two trials compared four-layer bandaging with single layer compression bandaging 5. Two studies compared four-layer or three-layer and self-adhesive single layer bandages 6. Six studies compared multi-layer high compression with inelastic compression 7. The original "Charing Cross" 4LB compared both with a 4LB 8. One study compared the 4LB with a combination of three bandages plus class 2 compression stockings. 9. One trial compared Unna's boot with moderate compression provided by a single bandage 10. One study compared combination of two compression stockings with a short-stretch bandage 11. One study compared compression stockings with Unna's boot
O'Meara	Two types of compression for the treatment of VLU	Six trials (797 patients): Four trials conducted in the United Kingdom and two in mainland Europe. All trials were individually randomised and recruited participants with VLU 1. Five trials compared the 4LB with a short-stretch bandage. 2. One compared two types of primary dressing as well as the two bandage systems.

TABLE 3 (Continued)

Author	Types of studies in the SR	Sample, setting and population
Amsler, Willenberg[19]	Stocking based compression vs bandages	Eight trials. All studies were prospective and open-label. Randomization was in two parallel groups except for one study which had a cross-over design. Studies included a total of 692 patients, 277 men, and 359 women. The overall mean patient age was 60.7 years with a range per study between 56 and 65 years. 1. 24 mm Hg stockings (Futuro, Style 50, 3M) vs Unna's boots. 2. The stocking group: hosiery designed for the prophylaxis of deep venous thrombosis donned over the dressing and a second stocking over a bandage group: a single short-stretch bandage. 3. Hydrocolloid dressings combined with a stocking vs a not specified dressing combined with an Unna's boot. 4. Stocking kit vs a bandage. 5. Tubular compression device vs a single short-stretch bandage 6. Two-stocking system vs a single short-stretch bandage 7. Tubular compression system vs an elastic multi-layer bandage 8. Double-stocking system vs a multi-layer short-stretch bandage.
Stather, Petty[26]	Velcro-based wrap devices	Sixteen studies: 1. One trial comparing both bandaging and JuxtaCures in patients with bilateral ulcers with each limb randomised, 2. One audit 3. Fourteen case series ranging from 1 to 35 patients, with 192 patients reported in total. 4. Thirteen studies used the JuxtaCures (or the JuxtaLite or JuxtaFit) + 1 study used the JOBST FarrowWrap Strong and Lite + 1 study used ReadyWrap + 1 study used multiple devices.
Welsh[27]	Both elastic and inelastic components (mixed-component systems MCSs).	Eight publications: Four of the papers used ulcer healing as an outcome for the proposed efficacy
Palfreyman, Lochiel[25]	Compression therapies.	Eight trials involving 750 participants within the United States and United Kingdom.
Shi, Dumville[29]	Compression bandages or stockings vs no compression	Of the 14 included studies (all RCTs), 13 had a parallel-group design, and one applied a cross-over design. The median follow-up duration was 12 weeks (range: 1 day to 12 months). Included a total of 1391 participants with venous leg ulcers (median study sample size: 51 participants; range: 11-321). Across the eight studies that specified participant sex, 526 (50.1%) participants were male and 524 (49.9%) were female. The average participant age was specified in 11 studies, with a median of 70.1 years (range: 58.0-76.5 years)

Abbreviations: ABI, ankle brachial index; 4LB, four-layer bandage; LBB, long stretch bandage; MCS, mixed-component systems; RCT, randomized controlled trial; SR, systematic review; SSBs, short-stretch bandages; VLU, venous leg ulcers.

the inclusion criteria, 83% (N = 10) of which included meta-analyses.[19-25,28-30] Publication dates ranged between 1997 and 2021. Review authors represented several countries, but most authors originated from the United Kingdom (N = 9, 75%).[20,22,23,25-30]

Nine reviews[19-23,25,28-30] included only randomized controlled trials (RCTs), one review included RCTs and Cochrane reviews,[24] one review included RCTs, audit, and case series,[26] and one review included RCTs, cohort studies, case series, and qualitative studies.[27] The mean sample size across nine reviews was 93 (±92) and ranged from 15 232 patients[26] to 3785[20] patients across the reviews (see Table 3).

4.3 | Type of CT

The type of CT varied between the reviews (see Supplementary document).

4.4 | Primary outcome: Wound healing

4.4.1 | Comparison 1: Compression vs no compression (10 trials; 768 participants)

Outcome: Wounds healed

Figure 2 presents the results for the meta-analysis of studies comparing compression with no compression.

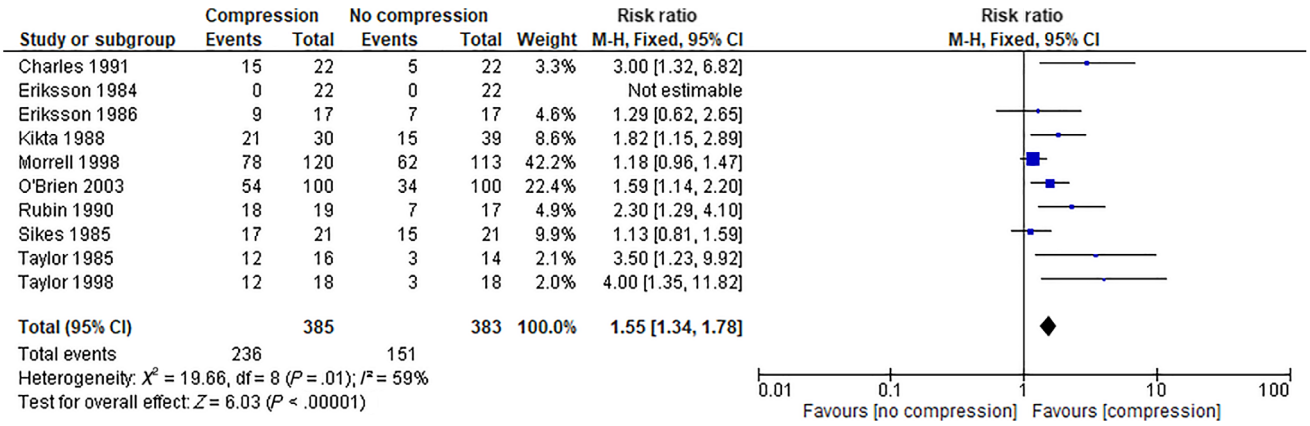

FIGURE 2 Forest plot: Compression vs no compression, outcome: Wound healed. CI, confidence interval

TABLE 4 Included studies: Compression vs no compression

Author	Comparison	Total participants	Number achieving healing	
			Compression	No compression
Charles[43]	Short-stretch bandage vs usual treatment	44	15/22	5/22
Eriksson[44]	Two-layer bandage vs procine or aluminium foil dressing	44	0/22	0/22
Eriksson[45]	Compression vs no compression	34	9/17	7/17
Kikta, Schuler[46]	Unna's boot vs Duoderm hydrocolloid dressing	69	21/30	15/39
Morrell, King[47]	Compression vs usual treatment	233	78/120	62/113
O'Brien, Grace[48]	Four-layer bandage vs no compression	200	54/100	34/100
Rubin, Alexander[49]	Unna's boot vs polyurethane foam dressing	36	18/19	7/17
Sikes[50]	Unna's boot vs dressings	42	17/21	15/21
Taylor[51]	Four-layer bandage vs usual treatment	30	12/16	3/14
Taylor, Taylor[52]	Compression vs usual treatment	36	12/18	3/18
Total		768	236/385	151/383

The I^2 is 59%, indicating moderate heterogeneity among the studies; therefore, a fixed-effects model was used for the meta-analysis. A total of 61% (n = 236/385) of participants in the compression group healed, compared with 39% (n = 151/383) of participants in the no compression group (RR: 1.55; 95% CI 1.34-1.78; $P < .00001$; moderate-certainty evidence, downgraded twice for high risk of performance and detection bias) (Table 4).

4.4.2 | Comparison 2: Elastic compression vs inelastic compression (33 trials; 3346 participants)

Outcome: Wounds healed

Figure 3 presents the results for the meta-analysis of the studies comparing elastic compression with inelastic compression. The I^2 is 61%, indicating moderate heterogeneity among the studies; therefore, a fixed-effects model was used for the meta-analysis. A total of 54.3% (n = 959/1764) of participants in the compression group healed, compared with 54.9% (n = 870/1582) of participants in the no compression group (RR: 1.02; 95% CI: 0.96-1.08; $P < .61$ moderate-certainty evidence, downgraded twice for high risk of performance and detection bias). This indicates no statistically significant difference in healing rates between the two study groups, with moderate certainty (Table 5).

4.4.3 | Comparison 3: Comparison four layers vs <4 layers bandage systems (eight trials; 971 participants)

Outcome: Wound healed

Figure 4 presents the results for the meta-analysis of studies comparing four layers with <4 layer bandage systems. The I^2 is 74%, therefore a fixed-effects model was

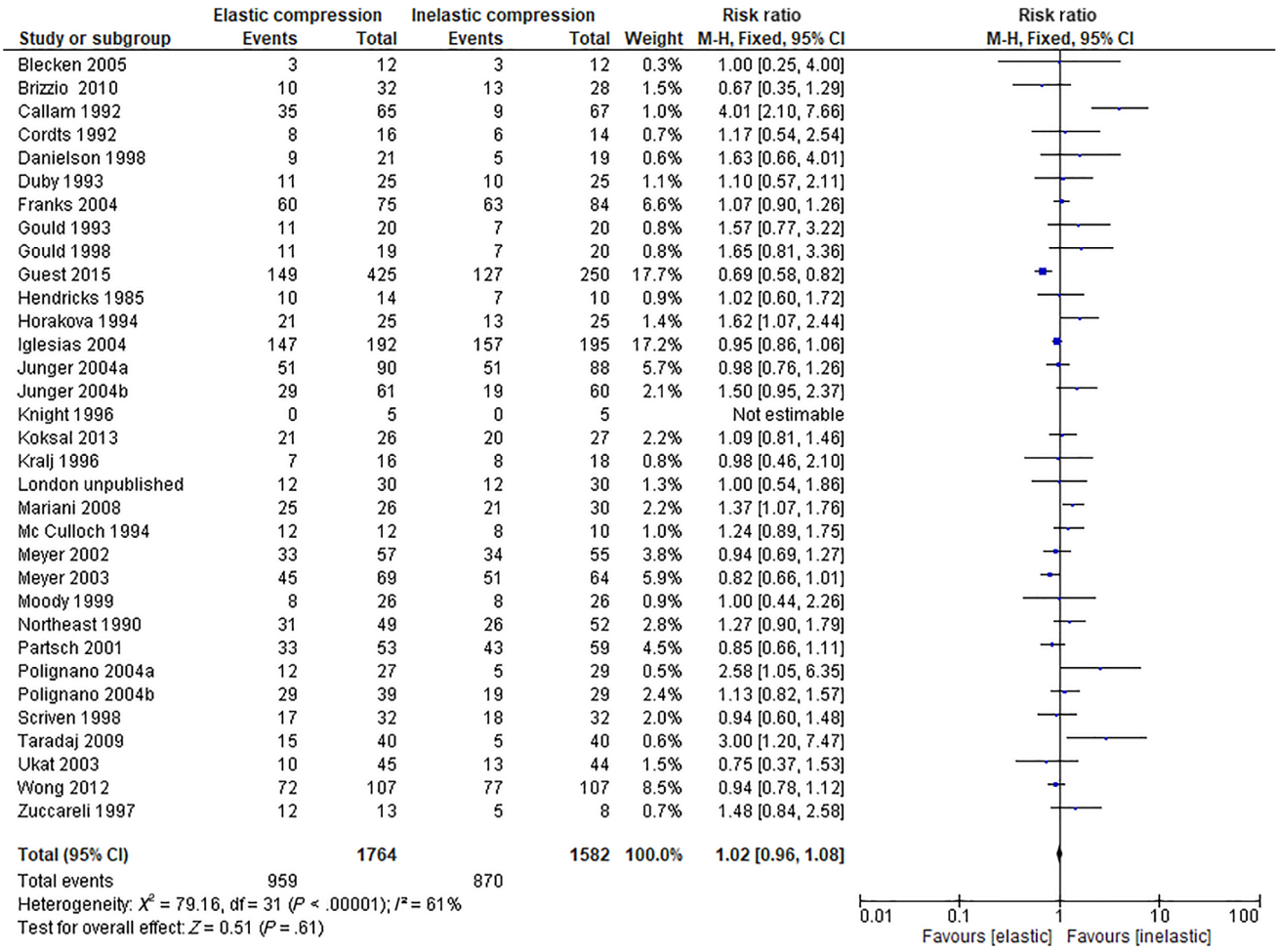

FIGURE 3 Forest plot: Elastic compression vs inelastic compression, outcome: Wound healed. CI, confidence interval

used for the meta-analysis. A total of 50% (n = 244/486) of participants in the four-layer group healed, compared with 49% (n = 236/485) of participants in <4 layer group (RR: 1.07; 95% CI: 0.82-1.40; $P < .63$; moderate-certainty evidence, downgraded twice for high risk of performance and detection bias). This indicates no statistically significant difference in healing rates between the two study groups, with moderate certainty (Table 6a).

4.4.4 | Comparison 4: Comparison between different four-layer bandage systems (two trials; 267 participants)

Outcome: Wound healed

Figure 5 presents the results for the meta-analysis of studies comparing different four-layer bandage systems. The I^2 is 8%, indicating there might not be important heterogeneity among the studies, therefore a fixed-effects model was used for the meta-analysis. A total of 74% (n = 99/134) of participants in system 1 healed, compared with 68% (n = 91/133) of participants in system 2 (RR: 1.08; 95% CI: 0.93-1.25; $P = .34$; moderate-certainty evidence, downgraded twice for high risk of performance and detection bias). This indicates no statistically significant difference in healing rates between the two study groups, with moderate certainty (Table 6b).

4.4.5 | Comparison 5: Comparison between different elastic compression bandage systems (two trials; 176 participants)

Outcome: Wound healed

Two trials[95,96] were not included in a meta-analysis as they reported too dissimilar elastic compression bandages systems (see Tables 6c and 7). Milic, Zivic[95] compared a multilayer bandaging system with a heelless open-toed elastic compression device knitted in tubular form and elastic bandages vs a multilayer bandaging system with elastic bandages only. The healing rate was 71% (n = 53/75) in the multilayer bandaging system and 33%

TABLE 5 Studies comparing elastic compression with inelastic compression

Author	Comparison	Total participants	Number achieving healing	
			Elastic	Inelastic
Blecken, Villavicencio[53]	Four-layer bandage vs compression boots	24	3/12	3/12
Brizzio, Amsler[54]	Compression stocking vs inelastic compression	60	10/32	13/28
Callam, Harper[55]	Three-layer elastic compression vs three-layer inelastic compression	132	35/65	9/67
Cordts, Hanrahan[56]	Duoderm plus compression vs inelastic compression	30	8/16	6/14
Danielsen, Madsen[57]	Four-layer high compression vs inelastic compression	40	9/21	5/19
Duby[58]	Four-layer high compression vs inelastic compression	50	11/25	10/25
Franks, Moody[59]	Four-layer high compression vs inelastic compression	159	60/75	63/84
Gould[60]	Three-layer elastic compression vs three-layer inelastic compression	40	11/20	7/20
Gould, Campbell[61]	Three-layer elastic compression vs three-layer inelastic compression	39	11/19	7/20
Guest, Ayoub[62]	Four-layer and two-layer compression vs inelastic compression	675	149/425	127/250
Hendricks and Swallow[63]	Elastic support stocking vs inelastic compression	24	10/14	7/10
Horakova[64]	Elastic support stocking vs inelastic compression	50	21/25	13/25
Iglesias, Nelson[65]	Four-layer compression vs inelastic compression	387	147/192	157/195
Jünger, Wollina[66]	Compression vs inelastic compression	178	51/90	51/88
Junger[67]	Compression stockings vs inelastic compression	121	29/61	19/60
Knight[68]	Elastic compression vs inelastic compression	10	0/5	0/5
Koksal and Bozkurt[69]	Hydrocolloid and compression vs inelastic compression	51	21/26	20/27
Kralj[70]	Multilayer compression vs inelastic compression	34	7/16	8/18
London et al Unpublished	Multilayer compression vs inelastic compression	60	12/30	12/30
Mariani[71]	Two-stocking system vs inelastic compression	56	25/26	21/30
McCulloch, Marler[72]	Intermittent pneumatic compression vs inelastic compression	22	12/12	8/10
Meyer, Burnand[73]	Three-layer elastic compression vs three-layer inelastic compression	112	33/57	34/55
Meyer, McGuinness[74]	Four-layer high compression vs inelastic compression	133	45/69	51/64
Moody[75]	Two-layer elastic compression vs two-layer inelastic compression	52	8/26	8/26
Northeast[76]	Multilayer elastic compression vs inelastic compression	101	31/49	26/52
Partsch, Damstra[77]	Multilayer elastic compression vs inelastic compression	112	33/53	43/59
Polignano, Bonadeo[78]	Compression stocking vs inelastic compression	56	12/27	5/29
Polignano, Guarnera[79]	Four-layer high compression vs inelastic compression	68	29/39	19/29
Scriven, Taylor[80]	Multilayer elastic compression vs inelastic compression	64	17/32	18/32
Taradaj[81]	Compression stockings vs inelastic compression	80	15/40	5/40
Ukat, Konig[82]	Four-layer high compression vs inelastic compression	89	10/45	13/44
Wong, Andriessen[83]	Four-layer high compression vs inelastic compression	214	72/107	77/107
Zuccarelli[84]	Elastic compression vs inelastic compression	21	12/13	5/8
Total		3346	959	870

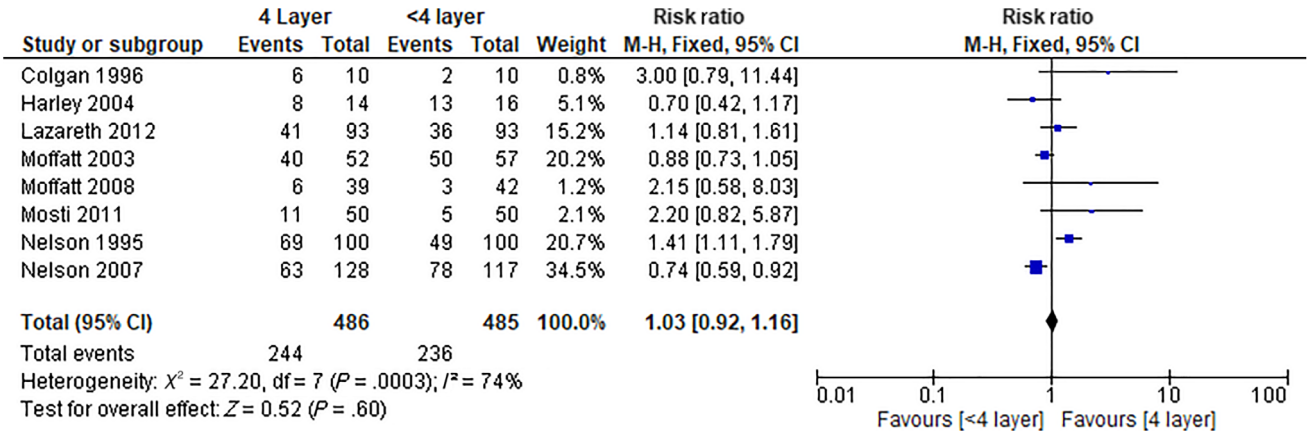

FIGURE 4 Forest plot: Comparison between four layers vs <4 layer bandage systems, outcome: Wounds healed. CI, confidence interval

TABLE 6a Studies comparing four layers vs <four layers bandage systems

Author	Comparison	Total participants	Number achieving healing	
			Intervention	Control
Colgan[85]	Four-layer bandage vs single bandage	20	6/10	2/10
Harley[86]	Four-layer bandage vs two layer	30	13/16	8/14
Lazareth, Moffatt[87]	Four-layer bandage vs less than four-layer bandage	186	41/93	36/93
Moffatt, McCullagh[88]	Four-layer bandage vs two layer	109	50/57	40/52
Moffatt, Edwards[89]	Four-layer bandage vs two layer	81	3/42	6/39
Mosti, Crespi[90]	Four-layer bandage vs two layer	100	5/50	11/50
Nelson[91]	Four-layer bandage vs single bandage	200	69/100	49/100
Nelson, Prescott[92]	Four-layer bandage vs single layer	245	78/117	63/128
Total		971	486	485

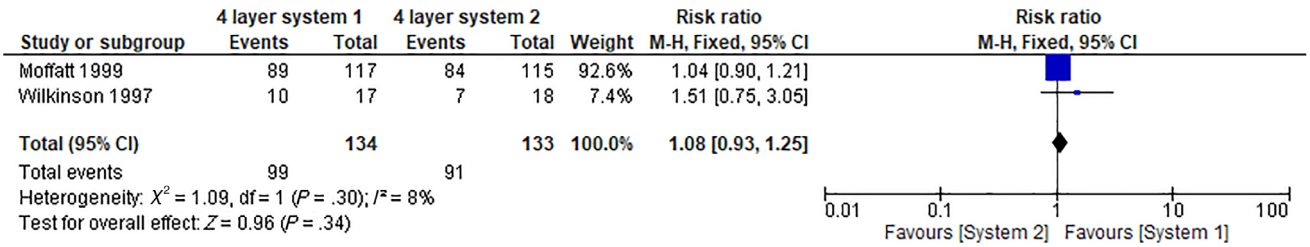

FIGURE 5 Forest plot: Comparison between different four-layer bandage systems, outcome: Wounds healed. CI, confidence interval

TABLE 6b Studies comparing between different four-layer bandage systems

Author	Comparison	Total participants	Number achieving healing	
			Intervention	Control
Moffatt[93]	Four-layer bandage vs Charing Cross four-layer system	232	89/117	84/115
Wilkinson, Buttfield[94]	Four-layer bandage vs other four layers	35	10/17	7/18
Total		267	99	91

TABLE 6c Studies comparing between different elastic compression bandage systems

Author	Comparison	Total Participants	Number Achieving Healing	
			Intervention	Control
Milic, Zivic[95]	Multilayer bandaging system with the Tubulcus (a heelless open-toed elastic compression device knitted in tubular form) and elastic bandages vs control group (patients treated with a multilayer bandaging system with elastic bandages only)	150	53/75	25/75
Travers[96]	Three-layer elastic high compression vs single bandage	26	0/13	0/13

TABLE 7 Studies comparing compression bandage with compression stocking

Author	Comparison	Total participants	Numbers achieving healing	
			Bandage	Stocking
Ashby, Gabe[97]	Four-layer bandage vs stocking	453	157/223	163/230
Brizzio[98]	Compression bandage vs stocking	35	8/14	19/21
Brizzio, Amsler[54]	Short-stretch bandage vs stocking	60	13/28	10/32
Dolibog, Franek[99]	Four-layer bandage vs stocking	48	2/25	5/23
Finlayson, Courtney[100]	Four-layer bandage vs stocking	103	41/53	33/50
Hendricks and Swallow[63]	Unna's boot vs stocking	24	7/10	10/14
Horakova[64]	Compression bandage vs stocking	50	13/25	21/25
Jünger, Wollina[66]	Compression bandage vs stocking	178	51/88	51/90
Jünger 2004c	Short-stretch bandage vs stocking	121	19/60	29/61
Koksal and Bozkurt[69]	Unna's boot vs stocking	51	20/27	21/26
Milic, Zivic[11]	Bandage & stocking vs stocking alone	131	63/89	13/42
Polignano, Bonadeo[78]	Unna's boot vs stocking	56	5/29	12/27
Szewczyk, Jawień[101]	Two-layer bandage vs stocking	31	10/16	8/15
Szewczk (2010b)	Four-layer bandage vs stocking	46	19/31	8/15
Taradaj[81]	Short-stretch bandage vs stocking	80	5/40	15/40
Total		1575	467	464

(n = 25/75) in the multilayer bandaging system with elastic bandages only. Travers[96] compared three layers of elastic high compression vs a single bandage. None of the participants in either group healed.

4.4.6 | Comparison 6: Comparison: compression bandage vs compression stocking (15 trials; 1575 participants)

Outcome: Wounds healed

Figure 5 presents the results for the meta-analysis of studies exploring compression bandage vs compression stocking. The I^2 is 67%, indicating moderate heterogeneity among the studies; therefore, a fixed-effects model was used for the meta-analysis. A total of 57% (n = 467/813) of participants in the compression bandage group healed, compared with 61% (n = 464/762) of participants in the compression stocking (RR 0.95; 95% CI 0.87-1.03; $P = .18$; moderate-certainty evidence, downgraded twice for high risk of performance and detection bias). This indicates no statistically significant difference in healing rates between the two study groups, with moderate certainty (Figure 6).

4.4.7 | Comparison 7: Comparison between different types of inelastic compression systems (1 trial; 38 participants)

Outcome: Wound healed

One study compared different types of inelastic compression systems. In DePalma (1999), adjustable compression boots were compared with paste bandages. A total of 89%

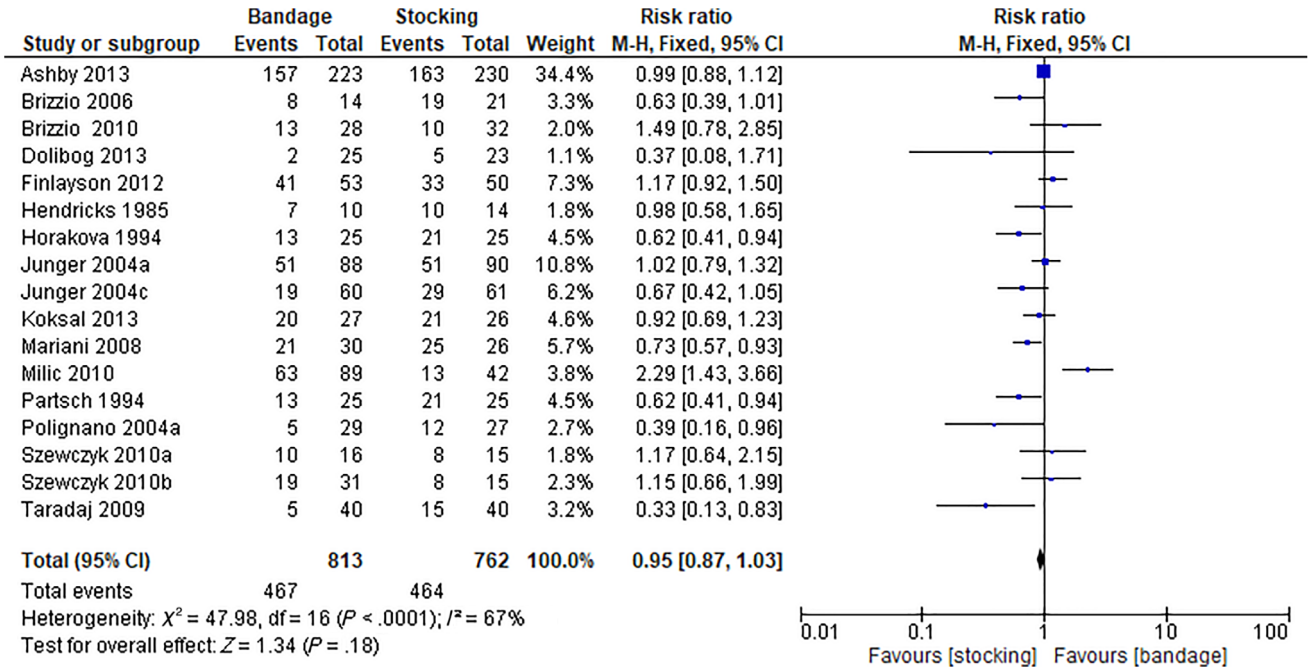

FIGURE 6 Comparison: Compression bandage vs compression stocking, outcome: Wound healed. CI, confidence interval

(n = 17/19) of participants in the Thera-Boot group healed, compared with 58% (n = 11/19) of participants in the Unna boot group.

4.5 | Secondary outcome: Adverse events

Device-related adverse events reported mainly included pain and maceration with a low incidence rate. Data from two RCTs (Moffatt 2008, Vanscheidt 2012) showed no significant differences in the occurrence of one or more adverse events between two layers bandages and four layers bandages or two layers (Two layers vs four layers: 50% vs 50%; RR = 1.0; P = .903).

4.6 | Quality appraisal

Table 8 shows the results of the quality appraisal. Three reviews were assessed as high quality,[20,24,29] five as moderate quality,[21,23,25,28,30] and four as low quality.[19,22,26,27]

Of the 16 AMSTAR-2 items, all included reviews expressed the research question in PICO format (Q1 = 100%), and identified the selection of the study designs for inclusion (Q3 = 100%). Only three studies[20,25,28] provided a list of excluded studies, justified the exclusions, and three reviews[20,24,28,29] reported on the sources of funding for the studies included in their review.

5 | DISCUSSION

The aim of this meta-review was to appraise and synthesise the evidence from existing systematic reviews to understand the impact that CT has on VLU healing. Twelve published systematic reviews were included, and the type of CT varied between the reviews. A number of comparisons are made in this meta-review: Compression system vs no compression; elastic compression vs inelastic compression, four layers vs <four layers bandage systems; comparison between different four-layer bandage systems; comparison between different elastic compression bandage systems; compression bandage vs compression stocking; and comparison between different types of inelastic compression systems. CT represents the gold standard for VLU management. The goal of any system is to deliver therapeutic compression during mobility and rest.[102] The key finding to emerge from the review is that there is moderate-certainty evidence of the effect of compression bandages on the healing of VLU when compared with no compression. However, the identified reviews do not conclude which compression systems represent the most effective for healing VLU. In CT, the main indicators for elasticity/inelasticity are characterised by pressure and stiffness.[2,3] The fact that these parameters are almost never reported in the studies' results is our lack of complete knowledge of the elasticity/inelasticity of the compression bandages and its appropriate application. Correctly applied CT is essential in both the preventive and therapeutic care of VLUs.[9,24]

TABLE 8 Quality assessment of the included reviews using the AMSTAR-2 tool (n = 12)

	AMSTAR items																
Authors	**Q1**	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**	**Q7**	**Q8**	**Q9**	**Q10**	**Q11**	**Q12**	**Q13**	**Q14**	**Q15**	**Q16**	**Rating**
Amsler, Willenberg[19]	Y	Y	Y	PY	Y	Y	N	Y	N	N	Y	Y	Y	Y	N	Y	**Low quality**
Cullum, Nelson[28]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	**Moderate quality**
De Carvalho, Peixoto[21]	Y	N	Y	PY	N	Y	PY	Y	Y	N	Y	Y	Y	Y	N	Y	**Moderate quality**
Goka, Poku[23]	Y	N	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	N	N	Y	**Moderate quality**
Mauck, Asi[24]	Y	N	Y	PY	Y	Y	PY	Y	Y	Y	Y	Y	Y	Y	Y	Y	**High quality**
O'Meara, Cullum[20]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	**High quality**
O'meara, Tierney[30]	Y	Y	Y	Y	Y	N	PY	Y	Y	N	Y	Y	Y	Y	Y	Y	**Moderate quality**
Palfreyman, Lochiel[25]	Y	N	Y	PY	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	N	**Moderate quality**
Stather, Petty[26]	Y	N	Y	PY	Y	Y	PY	Y	N	N	NMC	NMC	N	N	N	N	**Low quality**
Welsh[27]	Y	N	Y	PY	N	N	N	Y	Y	N	NMC	NMC	N	N	N	Y	**Low quality**
Fletcher, Cullum[22]	Y	N	Y	Y	Y	Y	N	Y	N	N	Y	N	Y	Y	N	Y	**Low quality**
Shi, Dumville[29]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NMC	NMC	Y	Y	Y	Y	**High quality**
Percentage of reviews completely meeting each criterion	**100**	**42**	**100**	**50**	**83**	**79**	**33**	**100**	**75**	**33**	**75**	**67**	**83**	**75**	**33**	**83**	

Note: Bold items are AMSTAR-2 critical domains.

Abbreviations: N, no; NMC, no meta-analysis conducted; PY, partial yes; Y, yes.

Therefore, healthcare providers' knowledge of bandage materials and their practical ability have an important role in applying adequate pressure successfully. It is not clear in the included studies whether CT was applied by specific expert healthcare providers. It can therefore be assumed that all the studies that do not report pressure and stiffness have poor value. In this study, the only conclusion that can be made from the studies we have is that compression is better than no compression in achieving ulcer healing. No conclusion can be made regarding the superiority of elastic or inelastic material in increasing healing rate because of methodological flaws of the published studies. Rather than advocate one system, it seems more sensible to promote the correct use of any properly applied high CT device. Furthermore, it is essential to consider patient compliance. To facilitate effective CT, the clinician might select the ideal bandage, and obtain the necessary skills for correct application. A clinician might also consider concerns about patient compliance with CT to maximise the probability of wound healing.

In this meta-review, the certainty of the body of evidence was assessed as per the GRADE approach. This approach helps define the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest.[103] Appropriate use of GRADE is important because reliable recommendations require reliable assessments of the certainty of the evidence and therefore require that all steps be carried out in a systematic and transparent manner.[104] The more serious the limitations within the individual studies, the more likely it is that the certainty of the evidence will be downgraded. In all cases, if a reason is found to downgrade the evidence, it should be classified as "serious" (downgrade by one level) or "very serious" (downgrade by two levels). Evidence from the primary outcome of this meta-review was downgraded twice for the high risk of bias because of performance and detection bias. Because of poorly reporting of allocation concealment, blinding (both participants and personnel), and blinding of outcome assessment, evidence quality was downgraded. Lack of blinding can introduce bias, particularly when outcomes are subjective, and may lead to potential overestimation of the effect of the intervention, resulting in a bias in favour of the intervention.[105] However, blinding of participants and caregivers is difficult to achieve in wound care; nonetheless, blinding of outcome assessors is possible. For our primary outcome, this meta-review showed that there was moderate-certainty evidence of the effect of CT. The quality of evidence indicates moderate confidence in the effect estimate. This means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it may be substantially different.[106]

In terms of the AMSTAR-2, the quality assessment varied across the systematic reviews. Most of the systematic reviews (N = 5, 42%) were of moderate quality and four reviews were of low quality. It is interesting to see that some of these systematic reviews were published in earlier years, meaning that a possible explanation for these results is that reviews were published before the AMSTAR-2 quality assessment tool was conceived. Therefore, researchers did not have this quality guide available to them when writing their reviews. Another possible explanation is that systematic review methodology has advanced greatly in the past two decades, so it is not surprising that some of the older reviews did not score as highly as well as more recent ones. Furthermore, it is not unexpected that most of the high-quality systematic reviews were Cochrane reviews. This is because Cochrane reviews are commonly suggested to be of a higher methodological quality. In the literature, it is suggested that for a critical assessment of the quality of non-Cochrane reviews, users should first look at the database of abstracts of reviews of effectiveness.[107,108] Cochrane systematic reviews are recognised as high-quality systematic reviews. Cochrane systematic reviews take a comprehensive, critical approach to the evidence for policy, practice, and research purposes, while at the same time, the rigour of its methods is widely acknowledged and updated periodically in the light of new evidence.[109] What is clear is that researchers need to consider all quality assessment criteria when they are conducting a systematic review.

6 | CONCLUSION

This meta-review sets out to determine the impact of CT on VLU healing by synthesising the data from existing systematic reviews. Twelve systematic reviews met the inclusion criteria. The type of CT varied between the reviews. We made seven comparisons and found that there is moderate-certainty evidence that VLU probably heals when CT is used regardless of the type of compression system, providing it can achieve sustained graduated compression. Further meta-reviews, which focus on challenges faced by health care professionals and patients when using CT, need to be undertaken.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as this study is a meta review.

ORCID

Pinar Avsar https://orcid.org/0000-0002-7637-1700
Aglecia Budri https://orcid.org/0000-0002-0741-9926
Tom O'Connor https://orcid.org/0000-0001-5948-0975
Zena Moore https://orcid.org/0000-0002-4692-9718

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