National Institute for Health and Care Excellence

Early and locally advanced breast cancer: diagnosis and management

[P] Evidence reviews for the non-pharmacological management of lymphoedema in people who have, or have had, breast cancer.

NICE guideline NG101

Evidence reviews underpinning recommendations 2.1.1 to 2.1.6 and research recommendations in the NICE guideline

September 2024

Draft for consultation

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1 Non-pharmacological management of lymphoedema

1.1 Review question

In people who have, or have had, breast cancer and have lymphoedema, what non-pharmacological strategies are effective and cost-effective, for managing it:

1. Complete Decongestive Therapy (CDT)
2. Exercise and Movement
3. Skincare
4. Lymphoedema Education
5. Pneumatic Compression Devices
6. Complementary therapy
7. Psychological interventions
8. Kinesiotaping
9. Wired vs non-wired bras, foam inserts, spaghetti foam
10. Surgical interventions

1.1.1 Introduction

The NICE surveillance review (June 2023) identified some studies that showed that various interventions such as early intervention, exercise and vascularised lymph node transfer may manage lymphoedema, by reducing and controlling swelling in people with breast cancer. The current recommendations in NG101 and CG81 focus on managing lymphoedema in people with advanced breast cancer and do not include people with early breast cancer. As such, there is a need to expand the evidence reviews to cover all people with breast cancer, as well as review any new evidence on the management and treatment of lymphoedema in people with breast cancer.

1.1.2 Summary of the protocol

Table 1: PICOS inclusion criteria

Population	All adults (aged 18 or over) who have, or have had, breast cancer and have lymphoedema of the upper limb (including axilla, hands and fingers), chest wall or breast. Exclusion: None identified
Interventions	Any conservative non-pharmacological interventions/strategies: 1. Complete Decongestive Therapy (CDT) (for example, manual lymphatic drainage (MLD), compression, skin care and exercise, deep oscillation therapy) 2. Exercise and Movement (for example, Pilates, yoga, Tai Chi, range of motion exercises and breathing intervention) 3. Skincare (for example, keeping skin clean and use of moisturisers) 4. Lymphoedema Education (for example, self-management advice, simple lymphatic drainage (SLD), weight management advice, information on lymphoedema complications like cellulitis and sepsis)

	5. Pneumatic Compression Devices (for example, intermittent pneumatic compression (IPC)) 6. Complementary therapy (for example, acupuncture, reflexology) 7. Psychological interventions (for example, acceptance and commitment therapy (ACT), cognitive behavioural therapy (CBT)) 8. Kinesiotaping (for example, K-Tape, elastic therapeutic tape) 9. Wired vs non-wired bras, foam inserts, spaghetti foam 10. Surgical intervention a. Vascularised Lymph Node Transfer (VLNT) b. Lymphovenous Bypass c. Reconstructive Lymphatic Microsurgery d. Lymphaticovenous Anastomosis (LVA) Liposuction for lymphoedema was excluded as there is existing NICE guidance covering its use (IPG723: liposuction for chronic lymphoedema)
Comparator	• No intervention/education only • Each other • Contralateral arm or breast
Outcomes	At all reported timepoints in 6-monthly intervals where applicable (e.g. 0-6 months, 7-12 months) **Primary outcomes:** • Severity of lymphoedema (for example, change from baseline in limb or breast volume/swelling using ultrasound/tissue dielectric constant, arm mobility (including DASH scores), bioimpedance) • Adverse events (for example, infection, surgical complications) **Secondary outcomes:** • Quality of life (for example, LYMQOL, FACT B+4, EQ-5D and EORTC-QoL-C30) • Patient reported outcomes (for example pain, psychological distress) • Changes in tissues and skin condition (for example, softening, hardening, tension) • Reduction in acute inflammatory episodes or cellulitis • Cosmetic impact and body image
Study types	• SRs of RCTs • SRs of cohort studies • RCTs • Prospective cohort studies. The best evidence will be included for each intervention and evidence from lower categories in the hierarchy of evidence will be excluded.

For the full protocol see appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Each of the 10 subsections (families of interventions) of the review protocol was treated as a separate evidence synthesis to allow for tailored approaches to the evidence for each of the subsections, and they are presented sequentially in this evidence review (sections 2 to 11). Evidence synthesis for each subsection was done taking a stepped approach:

1. For subsections where a recent systematic review was found that covered all interventions identified by the committee. That systematic review was used as the primary source of evidence. The outcomes and results from the systematic review were reported in the relevant sections. Primary studies used in the systematic reviews were not checked for additional outcomes not reported by the systematic review. If NICE searches found RCTs not included in the SR (because they were more recent), or that covered interventions in the subsection not covered by the SR then these were reported separately. Due to the heterogenous nature of the existing systematic reviews, it was not appropriate to update meta-analyses with the new studies.

2. For areas where several SRs were found covering all or part of the subsection, these were reported alongside a table of inclusions for each review that shows the overlap and differences. Where relevant, for example because an intervention is not covered in the SRs, or because newer RCTs are available, RCTs will be reported as above.

3. Where no SRs are available, the NICE team have presented data in GRADE from relevant RCTs but were unable to perform meta-analyses due to the data being too heterogenous.

Study selection for systematic reviews:

1. Systematic reviews of randomised controlled trials were only included if they:

    a. Matched the review protocol for the question (including the relevant interventions, comparators, and outcomes).

    b. Used a validated critical tool (for example, Cochrane Risk of Bias tool)

    c. Included a quantitative analysis of the studies (i.e. a meta-analysis, with appropriate statistics).

    d. Where more than one systematic review with the same criteria for the same intervention category was found, the more recent systematic review was selected for inclusion.

    e. Where more than one systematic review was found for each subset of interventions, each systematic review for each subset of interventions was included.

2. Systematic reviews of non-randomised trials were only included if no systematic reviews of randomised trials were included and they:

    a. Matched the review protocol for the question (including the relevant interventions, comparators and outcomes).

    b. Used a validated critical tool (for example, Cochrane Risk of Bias tool)

    c. Included a quantitative analysis of the studies (i.e. a meta-analysis with appropriate statistics).

d. Where more than one systematic review with the same criteria for the same intervention was found, the more recent systematic review was selected for inclusion.

e. Where more than one systematic review was found for each subset of interventions, each systematic review was included.

Study selection for randomised controlled trials and observational studies:

1. Randomised controlled trials (RCTs) were only included if:
    a. They matched the review protocol of the question.
    b. They were not included as primary studies in any of the systematic reviews selected for inclusion.
2. Observational studies were only included if:
    a. Less than 3 RCTs were found for each subset of interventions.
    b. The studies matched the review question protocol (including relevant interventions, comparators, and outcomes).
3. If <3 RCTs were found for each subset of interventions, and no observational studies were found, the RCTs were included.

Defining clinical decision thresholds

Clinical decision thresholds for minimally important differences (MIDs) were used to interpret the evidence. Where there were known published MIDs for an outcome, these were used as the clinical decision thresholds.

- For continuous outcomes, where there were no published MIDs:
    - Where a mean difference (MD) was reported, the NICE default clinical decision threshold of 0.5 of the standard deviation (SD) of the control group for each outcome was used. Where the SD was not reported, the line of no effect was used was used as a clinical decision threshold and a sample size of n <400 was used to provide the second domain to downgrade for imprecision.
    - Where a standardised mean difference (SMD) was reported, the NICE default of +-0.5 was used for the clinical decision thresholds.
- For dichotomous outcomes, where there were no published MIDs the NICE default clinical decision thresholds of 0.8 and 1.25 were used..

1.1.3.1 Search methods

The searches for the effectiveness evidence were run on 19 February 2024. The following databases were searched: Allied and Complementary Medicine (AMED) (Ovid); Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley); Cochrane Database of Systematic Reviews (CDSR) (CRD); Database of Abstracts of Reviews of Effectiveness (DARE) (CRD); Embase (Ovid); Emcare (Ovid); Epistemonikos; Health Technology Assessment (HTA) (CRD); International Health Technology Assessment Database (INAHTA); Medline ALL (Ovid). Full search strategies for each database are provided in appendix B

The searches for the cost effectiveness evidence were run on 22 February 2024. The following databases were searched: EconLit (Ovid); Embase (Ovid); International Health Technology Assessment Database (INAHTA); Medline ALL (Ovid); NHS EED (CRD). Full search strategies for each database are provided in appendix B.

A NICE information specialist conducted the searches. The MEDLINE strategy was quality assured by a trained NICE information specialist and all translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2015 PRESS Guideline Statement.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

A systematic search carried out to identify potentially relevant studies found 2912 references (see appendix B for the literature search strategy).

These 2912 references were screened at title and abstract level against the review protocol, with 2691 excluded at this level. 10% of references were screened separately by two reviewers with 100% agreement. Discrepancies were resolved by discussion.

For this review question, the full texts of 87 systematic reviews (SR) and 133 randomised controlled trials (RCT) were ordered for closer inspection. 9 SRs and 33 RCTs met the criteria specified in the review protocol (appendix A). The following comparators were found in the included studies:

- Complete decongestive therapy
    - 1 SR: Conservative non-drug decongestive therapy vs placebo/no treatment (Jeffs et al., 2018)
    - 1 SR: Manual lymphatic drainage vs no manual lymphatic drainage (Lin et al., 2022)
    - 1 SR: Manual lymphatic drainage vs compression bandaging/usual care (Qiao et al., 2023)
    - 1 RCT: Self lymphatic drainage + compression vs compression (Bahtiyarca et al., 2019)
    - 1 RCT: Compression garment vs no compression garment (Blom et al., 2022)
    - 1 RCT: Fluoroscopy guided manual lymphatic drainage/traditional manual lymphatic drainage vs placebo manual lymphatic drainage (De Vrieze et al., 202)
    - 1 RCT: Mobiderm® bandages vs conventional bandages (Dhar et al., 2023)
    - 1 RCT: Low pressure bandage vs high pressure bandage (Duygu-Yildiz et al., 2023)
    - 1 RCT: Complete decongestive therapy/compression vs control (Karafa et al., 2018)
    - 1 RCT: Negative pressure massage vs manual lymphatic drainage (Lampinen et al., 2021)

- 1 RCT: Combined decongestive therapy vs manual lymphatic drainage/compression (Liu et al., 2023)
- 1 RCT: Night-time compression vs standard care (McNeeley et al., 2022)
- 1 RCT: Mobiderm® compression vs elastic hosiery (Mestre et al., 2017)
- 1 RCT: Adjustable compression garments vs bandaging (Ochalek et al., 2023)
- 1 RCT: Resistance exercise/complete decongestive therapy vs low intensity resistance training (Omar et al., 2020)
- 1 RCT: Manual lymphatic drainage + adjustable compression vs manual lymphatic drainage + multilayered compression (Pujol-Blaya et al. 2019)
- 1 RCT: Complete decongestive therapy vs standard therapy (Sen et al., 2021)

- Exercise & movement
  - 1 SR: Complex decongestive therapy including resistance or aerobic exercises vs standard care (Lytvyn et al., 2020)
  - 1 SR: Complex physical therapy vs multimodal conservative approaches (Rangon et al., 2022)
  - 1 SR: Aqua-therapy/exercise vs Land-based therapy (Yeung & Semicuw, 2018)
  - 1 RCT: Aqua therapy-resistance exercise vs Exercise (Ali et al., 2021)
  - 1 RCT: Complete decongestive therapy + continuous passive motion vs complete decongestive therapy (Kizil et al., 2018)
  - 1 RCT: Exercise vs no exercise (Kilbreath et al., 2020)
  - 1 RCT: Complex decongestive physical therapy + progressive resistance exercise vs Complex decongestive physical therapy (Park et al., 2023)
  - 1 RCT: Pilates vs control (Sener et al., 2017)
  - 1 RCT: Aerobic exercise vs resistance exercise (Singh et al., 2016)
- Lymphoedema education
  - 1 RCT: Self-administered complete decongestive therapy vs usual care (Ligabue et al., 2019)
  - 1 RCT: Group-based/social network-based vs no education (Omidi et al., 2020)
  - 1 RCT: Web-based education vs education pamphlet (Ridner et al., 2020)
- Pneumatic compression devices
  - 1 RCT: Novel pneumatic compression device vs advanced pneumatic compression device (Rockson et al., 2022)
  - 1 RCT: Intermittent pneumatic compression device + compression bandage + exercise vs manual lymphatic drainage + compression bandage + exercise (Sanal-Toprak et al., 2019)

- 1 RCT: Intermittent pneumatic compression device vs usual care (Uzkeser et al., 2013)

- Complementary therapy
  - 1 SR: Acupuncture/moxibustion vs usual care (Gao et al., 2021)
- Kinesiotaping
  - 1 SR: Kinesiotaping vs usual care (Kasawara et al., 2018)
  - 1 RCT: Kinesiotaping + exercise vs complete decongestive therapy (Basoglu et al., 2021)
  - 1 RCT: Kinesiotaping + complete decongestive therapy vs complete decongestive therapy (Ergin et al., 2019)
  - 2 RCT: Kinesiotaping vs compression garments (Ozsoy-Unbol et al., 2019; Tantawy 2019)
  - 1 RCT: Kinesiotaping vs manual lymphatic drainage (Selcuk-Yilmaz et al., 2023)
  - 1 RCT: Bandaging vs complete decongestive therapy (Torres-Lacomba 2020)

- Surgical interventions
  - 1 SR: Lymphaticovenous anastomosis/Vascularised lymph node transfer vs usual care (Winters et al., 2021)
  - 1 RCT: Lymphaticovenous anastomosis vs usual conservative care (Jonis et al. 2024)

For a summary of each of included studies see summary tables in sections 2 to 11 in the evidence review.

The clinical evidence study selection is presented as a PRISMA diagram in appendix C.

See section 1.1.14 References – included studies for the full references of the included studies.

1.1.4.2 Excluded studies

Details of studies excluded at full text, along with reasons for exclusion are given in appendix J.

2 Complete Decongestive Therapy (CDT)

Complete decongestive therapy (CDT) is a lymphoedema treatment program that includes manual lymph drainage (MLD), compression techniques, exercise, and self-care training. It is comprised of an initial reductive (intensive) phase (phase I) followed by an ongoing, individualised maintenance phase (phase II).

2.1 Summary of studies included in the evidence

Table 2 Summary of studies included in the evidence

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Systematic review					
Jeffs et al. (2018) 7 RCTs	Women with unilateral BCRL of the arm who received lymphoedema treatment within 12 months of developing arm swelling.	Any conservative non-drug treatment where the goal was to decongest the arm	Another form of lymphoedema treatment, placebo or no treatment	• Changes in oedema (limb volume/circumference) • Swelling/pain • ROM • QoL • Bioimpedance • Adverse events (acupuncture and moxibustion related)	Low
Lin et al. (2022) 10 RCTs	Women prevented and/or treated for	Manual lymphatic drainage	Control (no manual lymphatic drainage)	• Lymphoedema (volume change)	Low

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	BCRL for whom MLD was performed.			• Quality of life • Patient-reported outcomes (pain)	
Qiao et al. (2023) 8 RCTs	Patients aged 18 or over with BCRL	Manual lymphatic drainage	Compression bandaging or other standard treatment	• Lymphoedema (volume change or arm circumference change) • Quality of life • Patient-reported outcomes (pain, anxiety, mobility)	Moderate
Randomised controlled trials					
Bahtiyarca et al. (2019) n=40 Location: Turkey	People with stage I-II unilateral BCRL, aged over 18 years and more than 3 months after breast cancer treatment.	Self lymphatic drainage (SLD) + compression therapy Participants were given an information leaflet and a clinician instructed them for 10-15 minutes each day prior to SLD. SLD applied to neck, non-affected axilla, anterior chest wall, affected inguinal region, lateral trunk, affected shoulder, affected upper arm, affected forearm, affected hand and fingers. Movements repeated 10 times in various positions.	Compression therapy All patients were given information about lymphoedema, skin care, and physical exercises. Short stretch bandages were kept on for 23 h and replaced the next day. Duration: until no changes were observed in the weekly limb circumference	• Lymphoedema (circumference and limb volume) • Arm function (Quick C-DASH scores) • Patient-reported outcomes (anxiety and depression) • Quality of life	High

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
		All patients were given information about lymphoedema , skin care, and physical exercises. Short stretch bandages were kept on for 23 h and replaced the next day. Duration: until no changes were observed in the weekly limb circumference measurements obtained.	measurements obtained.		
Blom et al. (2022) n=75 Location: Sweden	People with mild breast cancer-related arm lymphoedema, defined as increased skin and subcutis thickness compared to the non-affected arm in addition to either a threshold Tissue Dielectric Constant (TDC) ratio ≥1.45 in the upper arm, and/or ≥1.3 in the forearm), and/or LRV ≥5–≤8%.	Compression garment Participants received circular knitted compression sleeves or if needed, individually adjusted compression sleeves for daily wearing for six months, and counselling in self-care about exercise, weight control, skin care and instructions in self-massage. If the self-massage was perceived as effective, participants were	No compression garment Participants received instructions in self-care only (unclear whether self-care is at same intensity and with same content as intervention group)	• Lymphoedema (progression, arm volume, relative volume)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
		encouraged to continue, otherwise to stop.			
De Vrieze et al. (2022a, 2022b) N=194 Location: Belgium	Unilateral arm and/or hand lymphoedema after breast cancer treatment Chronic lymphoedema stage I to IIb for >3 months ≥5% excess volume between arms and/or hands	Intervention 1: Fluoroscopy-guided MLD group (n=65): MLD tailored based on baseline lymphofluoroscopy Intervention 2: Traditional MLD group (n=64): MLD based on normal lymphatic anatomy	Placebo MLD group (n=65)	• Percentage excess lymphoedema volume at the level of the arm/hand • Lymph-ICF-UL - Lymphoedema Functioning, Disability and Health Questionnaire for Upper Limb Lymphoedema McGill-QoL- McGill-Quality of life questionnaire • Arm and trunk tissue thickness and elasticity	Low
Dhar et al. (2023) n=49 Location: India	Women aged from 18 to 60 years, with established secondary upper limb lymphoedema after breast cancer surgery, considered suitable for intensive phase decongestive lymphoedema therapy	Mobilisation using Mobiderm Multi-layer bandage composed of an inner layer of cotton band (Bande Coton; THUASNE); an intermediate layer (Mobiderm band; THUASNE); and an external layer of elastic short-stretch bandage (Biflexideal®; THUASNE).	Conventional multilayered bandages Multilayered bandages with the intermediate layer comprised of an ortho cotton wool soft pad, whereas the internal and external layers were the same as used in the Mobiderm group.	• Lymphoedema (volume reduction using the volume displacement method) • Patient-reported outcomes (Pain/heaviness using VAS)	High

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Duygu-Yildiz et al. (2023) n=21 Location: Turkey	People with stage 2 unilateral breast cancer-related lymphoedema according to International Society of Lymphology, involving whole extremity.	Low bandage pressure Compression bandage applied at 20–30 mmHg pressure. Four to five short stretch bandages were used until the desired pressure was achieved. The compression bandage stayed on the individual's arm for approximately 23 h.	High bandage pressure As for low pressure group, but compression bandage was applied at 45–55 mmHg pressure.	• Lymphoedema (extremity volume) • Change in tissue/skin condition	High
Karafa et al. (2018) N=96 Location: Poland	Women aged 35-74 years with unilateral breast cancer-related lymphoedema (stage II according to ISL criteria) after modified radical mastectomy	Intervention 1: Complete Decongestive Therapy Compression at 31-40 mmHg Intervention 2: Compression at 41-60 mmHg	Control group (n=32) Compression at 20-30 mmHg	• Patient-reported outcomes • Quality of life • Function • Lymphoedema volume variation (volume excess variation	Moderate
Lampinen et al. (2021) n=28 Location: US	Women aged over 18 years, completed active treatment for breast cancer, diagnosed with unilateral arm lymphoedema for more than 1 year, were not receiving lymphoedema care, and had stable (no	Negative pressure massage treatment device LymphaTouch device used to administer negative pressure between 80-250 mmHg. All women were scheduled for 12 60-minute sessions provided at 2-3 times per week for 4-6 weeks.	Manual lymphatic drainage Given in twelve 60-minute sessions.	• Lymphoedema (interlimb volume difference, L-Dex scores) • Function (DASH scores)	High

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	change in the last 3mo) lymphoedema.				
Liu et al. (2023) n=60 Location: China	Breast cancer survivors with a history of mastectomy who complained of swelling or heaviness in the affected side and diagnosed as lymphoedema stage 2.	Combined decongestive therapy Including both MLD and CB	Intervention 1: Manual lymph drainage 4 basic techniques (stationary circle, rotary technique, pump technique, scoop technique) initiated from the unaffected trunk quadrants (neck and chest), followed by the affected areas of the trunk. Manual lymph drainage was applied to the oedematous limb starting proximally at the shoulder, moving in segments progressively down the limb. Finally, the trunk was cleared, including the affected chest and back. Intervention 2: Compression therapy	• Lymphoedema (volume change, tissue dielectric constant value)	High

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
			Given to patients by certified doctors with short stretch bandages. Bandages were worn soon after MLD and was kept day and night. MLD and bandaging were performed once a day, five times a week for 2 weeks.		
McNeeley et al. (2022) N=120 Location: Canada	Women with BCRL of ipsilateral arm ≥200 mL or 10% increase in arm volume vs unaffected arm ≥1 month post-completion of primary and adjuvant cancer treatments In Lymphoedema maintenance phase Has own properly fitted compression sleeve for daytime use (≥12 hrs/day) Not using nighttime compression pre-study	Intervention 1: SC + nighttime compression bandaging (CB) group (n=44) Intervention 2: SC + nighttime compression system garment (NCSG) group (n=37)	Standard care (SC) group (n=39)	• Percentage Reduction in excess Lymphoedema • Lymph-ICF-UL Lymphoedema Functioning, Disability and Health Questionnaire for Upper Limb Lymphoedema	Low

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Mestre et al. (2017) n=40 Location: France	Women aged 18 years or over, with unilateral secondary upper limb lymphoedema of stage II or III according to the ISL classification. Patients had to have undergone an intensive phase treatment with a decrease of lymphoedema volume at least of 10% prior to study entry.	MOBIDERM® autofit compression People in the night-use group were fitted with MOBIDERM® Autofit device in addition to daytime elastic hosiery for 90 days.	Elastic hosiery People in the no night-use group were fitted with the daytime elastic hosiery for the first 30 days. From Day 31 to Day 90 they were fitted with the Autofit device for night-use.	• Lymphoedema (volume excess variation) • Patient-reported outcomes (arm function al symptoms like heaviness or pain)	Moderate
Ochalek et al. (2023) N=36 Location: Poland	Women with Stage II lymphoedema (per ISL criteria) ≥20% excess limb volume Positive pitting sign No signs of active cancer, venous thrombosis, or previous compression.	Intervention 1: ACW group (n=18): Adjustable compression garments (circaid juxtafit essentials arm sleeve and glove) worn 24 hrs/day for 2 weeks Pressure 20-30 mmHg limb exercises 15 min/day	Multi-layer short-stretch bandaging worn 24 hrs/day for 2 weeks. Pressure 20-30 mmHg Education in self-bandaging during 1st week	• Change in affected limb volume (by circumference measurements) • Percentage reduction in excess volume	High

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Omar et al. (2020) N= 60 Location: Egypt	Women ≥18 years old Unilateral BCRL ≥5% inter-limb volume or circumference differences.	Intervention 1: Rex-Comp group (n=30): Intervention 2: Exercise and Movement + Complete Decongestive Therapy Low-intensity resistance training 3x/week for 8 weeks Instructed to wear compression garment during exercise	Rex group (n=30): Low-intensity resistance training 3x/week for 8 weeks Both groups: 10-12 reps at 50-60% 1RM, 2 sets of 7 upper body exercises	• Reduction excess limb volume (%) • Self-reported Lymphoedema symptoms • Pain • Arm function (DASH scores)	Moderate
Pujol-Blaya et al. (2019) N= 42 Location: Spain	Older than 18 years Female Upper limb lymphoedema after axillary lymph node dissection for breast cancer Lymphoedema affecting at least arm or forearm Lymphoedema volume excess ≥10% Lymphoedema not previously treated or	Manual lymphatic drainage followed by precast adjustable compression system	Manual lymphatic drainage followed by multilayered compression bandages	• Excess limb volume	Low

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	without treatment for last 12 months				
Sen et al. (2021) n=54 Location: Turkey	People with unilateral BCRL with 3-8 cm circumference difference between healthy and affected extremity at any reference point. Completed chemotherapy and/or radiotherapy in the previous 6 months. No previous surgery involving other major node-bearing areas that may affect lymphatic flow.	Complex decongestive therapy (CDT): 15 sessions (every weekday for 3 weeks) of manual lymphatic drainage, compressive multilayer bandaging and exercise training. Both groups received an educational program on lymphoedema .	Standard therapy: 15 sessions (every weekday for 3 weeks) of compressive multilayer bandaging and exercise training. Both groups received an educational program on lymphoedema .	• Lymphoedema (arm volume, excess arm volume) • Patient reported outcomes (arm swelling, discomfort, heaviness) • Function (Quick-DASH score) • Quality of life (Lymph-ICF)	Low

Abbreviation: DASH: Disabilities of Arm, Shoulder and Hand questionnaire; MLD: Manual lymphatic drainage; QoL; Quality of life; ROM: Range of motion; VAS: Visual Analogue Scale.

Table 3: Included studies in systematic reviews

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Jeffs et al. 2018				
Dayes et al. 2013 RCT	MLD and short stretch compression bandaging	Compression therapy	1 year	• Manual circumference measurement • Disabilities of the Arm Shoulder and Hand (DASH) questionnaire

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
N= 56				
Gradalski et al. 2015 RCT N=25	Multi-layer compression bandaging and Vodder II method MLD, exercise and deep diaphragmatic breath.	Compression bandaging 5per week for 2 weeks (10 sessions), followed by 6 months maintenance phase of daily self-care.	6 months	• Manual circumference measurement • VAS scores for pain discomfort • Patient desire to continue treatment
Kim et al.2010 RCT N= 40	Intensive phase: MLD, compression bandage, exercises and breathing exercises, plus Active Resistive Exercise (ARE) program using 0.5 kg dumbbell.	Complex decongestive physiotherapy (CDPT)	After treatment	• Short Form Health Survey (SF-36)
McNeely et al. 2004 RCT N=18	Short stretch bandages plus 45 minutes daily Vodder method MLD. Education re arm care and skin care.	Compression bandaging (CB)	After treatment	• Water displacement & manual • Circumference measurement
Lin et al. 2022				
Sen et al. 2020 Location: Turkey	MLD + Bandaging + Physical Exercise + Skin Care	Bandaging + Physical Exercise + Skin Care	3 weeks	• Oedema • QoL • Shoulder Function
Gol et al. 2020	MLD	Observation	4 weeks	• Oedema

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
N=60				• Pain • Shoulder Function
Tambour et al. 2018 N= 73	MLD + Bandaging + Physical Exercise + Skin Care	Bandaging + Physical Exercise + Skin Care	4 weeks	• Oedema • Pain • QoL
Devoogdt et al. 2018 N= 72	MLD + Physical Exercise	Physical Exercise	20 weeks	• Oedema • QoL • Shoulder Function
Ha et al. 2017. N=35	MLD + Proprioceptive Neuromuscular Facilitation	Proprioceptive Neuromuscular Facilitation	16 weeks	• Oedema • Pain • Shoulder Function • Depression
Zhang et al. 2016 RCT N= 1000	MLD + Physical Exercise	Physical Exercise	1 year	• Oedema • Shoulder Function
Cho et al. 2016 N=41	MLD + Physical Exercise	Physical Exercise	4 weeks	• Oedema • Pain • QoL • Shoulder Function
Gradalski et al. 2015 N= 60	MLD + Bandaging + Physical Exercise + Skin Care	Bandaging + Physical Exercise + Skin Care	2 weeks	• Oedema • QoL
Devoogdt et al. 2011 N= 72	MLD + Physical Exercise	Physical Exercise	20 weeks	• Oedema • QoL

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
McNeely et al. 2004 N=45	MLD + Bandaging	Bandaging	4 weeks	• Oedema
Andersen et al. 2000 N= 41	MLD + Bandaging	Bandaging	12 weeks	• Oedema
Qiao et al. 2023				
Johansson et al. 1999 N= 38	CB + MLD (n=20)	CB (n=18)	Immediately	• Lymphoedema reduction
Andersen et al. 2000 N=44	ST + MLD (n=23)	ST (n=21)	12 months	• Lymphoedema reduction
Sitzia et al. 2002 N= 28	MLD (n=15)	SLD (n=13	>1 month	• Lymphoedema reduction
Williams et al. 2002 N= 60	MLD (n=29)	SLD (n=31)	>3 months	• Lymphoedema reduction
McNeely et al. 2004 N=50	CB + MLD (n=25)	CB (n=25)	>1 month	• Lymphoedema reduction

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Dayes et al. 2013 RCT	CB + MLD (n=57)	CB (n=46)	>6 months	• Lymphoedema reduction
Bergmann et al. 2014 N=57	ST + MLD (n=28)	ST (n=29)	1 month	• Lymphoedema reduction

Abbreviation: CB: Compression bandaging; DASH: Disabilities of Arm, Shoulder and Hand questionnaire; MLD: Manual lymphatic drainage; QoL; Quality of life; ROM: Range of motion; SLD: simple lymphatic drainage; ST: standard treatment; VAS: Visual Analogue Scale.

See appendix D for full evidence tables

2.2 Summary of the effectiveness evidence

Table 4 Manual lymphatic drainage vs control

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Arm volume (ml) +- MID -0.5 to 0.5 follow-up: range 1 months to 3 months	SMD **0 SD** (0.2 lower to 0.21 higher)	370 (Lin 2022)	Moderate	Could not differentiate
Patient-reported outcomes (pain) (lower scores are better)				
Pain (visual analogue scale) +- MID -0.5 to 0.5 follow-up: 1 months	SMD **0.72 SD lower** (1.34 lower to 0.09 lower)	173 (Lin 2022)	Low	Favours manual lymphatic drainage
Quality of life (higher scores are better)				
Quality of life (range of QoL tools used) +- MID -0.5 to 0.5 follow-up: range 1 months to 3 months	SMD **0.26 SD higher** (0.01 lower to 0.52 higher)	223 (Lin 2022)	Low	Could not differentiate

Table 5 Manual lymphatic drainage vs control

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (higher scores are better)				
Upper limb volume change (reduction) by number of manual lymphatic drainage (<20 sessions) +-MID 0.5 follow-up: range 24 days to 7 months	SMD **0.82 SD higher** (0.17 lower to 1.82 higher)	244 (Qiao 2023)	Low	Could not differentiate
Upper limb volume change (reduction) by number of manual lymphatic drainage (>20 sessions) +-MID 0.5 follow-up: range 24 days to 7 months	SMD **0.31 SD higher** (0.03 higher to 0.58 higher)	213 (Qiao 2023)	Low	Favours >20 sessions MLD
Upper limb volume change (reduction) by number of manual lymphatic drainage (<2 weeks treatment) +-MID 0.5 follow-up: range 24 days to 7 months	SMD **2.03 SD higher** (0.39 lower to 4.44 higher)	110 (Qiao 2023)	Low	Could not differentiate
Upper limb volume change (reduction) by number of manual lymphatic drainage (>2 weeks treatment) +-MID 0.5 follow-up: range 24 days to 7 months	SMD **0.23 SD higher** (0.02 higher to 0.44 higher)	347 (Qiao 2023)	Moderate	Favours >20 sessions MLD
Patient-reported outcomes (pain) (lower scores are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Pain (visual analogue scale) +- MID -0.5 to 0.5 follow-up: range 24 days to 7 months	SMD **0.09 SD lower** (0.43 lower to 0.25 higher)	133 (Qiao 2023)	Moderate	Could not differentiate

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Table 6 Manual lymphatic drainage vs compression bandaging

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (volume, local tissue water) (lower scores are better for tissue dielectric constant value; higher scores are better for arm volume change)				
Tissue dielectric constant value in forearm +- MID - 2.02 to 2.02 follow-up: 2 weeks	MD **4.61 lower** (6.48 lower to 2.74 lower)	40 (Liu 2023)	Very low	Favours manual lymphatic drainage
Arm volume change (cm^3) +-MID - 39 to 39 follow-up: 2 weeks	MD **2 lower** (40.18 lower to 36.18 higher)	40 (Liu 2023)	Very low	Could not differentiate

Table 7 MLD + bandaging + exercise vs standard (bandaging + exercise)

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (arm volume) (lower values are better)				
Arm volume (ml) +- MID -192.62 to 192.62 follow-up: 4 weeks	MD **121 lower** (423.84 lower to 181.84 higher)	50 (Sen 2021)	Low	Could not differentiate

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Excess arm volume change (%) +-MID - 7.17 to 7.17 follow-up: 4 weeks	MD **1.9 lower** (10.06 lower to 6.26 higher)	50 (Sen 2021)	Low	Could not differentiate
Patient reported outcomes				
Arm swelling (Visual analogue scale) +- MID -1.22 to 1.22 follow-up: 4 weeks	MD **1.1 lower** (2.33 lower to 0.13 higher)	50 (Sen 2021)	Low	Could not differentiate
Discomfort (Visual analogue scale) +-MID -1.32 to 1.32 follow-up: 4 weeks	MD **1.8 lower** (3.18 lower to 0.42 lower)	50 (Sen 2021)	Low	Favours MLD, bandaging and exercise
Arm heaviness (Visual analogue scale) +- MID - 1.18 to 1.18 follow-up: 4 weeks	MD **1.6 lower** (2.93 lower to 0.27 lower)	50 (Sen 2021)	Low	Favours MLD, bandaging and exercise
Lymphoedema (arm function) (lower scores are better)				
Arm function (Quick-DASH) +- MID -8 to 8 follow-up: 4 weeks	MD **1.9 lower** (6.61 lower to 2.81 higher)	50 (Sen 2021)	Moderate	Could not differentiate
Quality of life (lower scores are better)				
Quality of life-physical (Lymph-ICF) +- MID -10.67 to 10.67 follow-up: 4 weeks	MD **30.9 lower** (41.49 lower to 20.31 lower)	50 (Sen 2021)	Moderate	Favours MLD, bandaging and exercise

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life-mental (Lymph-ICF) +- MID -12.35 to 12.35 follow-up: 4 weeks	MD **12.5 lower** (26.35 lower to 1.35 higher)	50 (Sen 2021)	Low	Could not differentiate
Quality of life-household activities (Lymph-ICF) +- MID -11.33 to 11.33 follow-up: 4 weeks	MD **2.8 higher** (9.9 lower to 15.5 higher)	50 (Sen 2021)	Low	Could not differentiate
Quality of life-mobility (Lymph-ICF) +- MID - 8.2 to 8.2 follow-up: 4 weeks	MD **0.8 higher** (7.04 lower to 8.64 higher)	50 (Sen 2021)	Low	Could not differentiate
Quality of life-life and social activities (Lymph-ICF) +- MID -12.14 to 12.14 follow-up: 4 weeks	MD **5.9 lower** (18.81 lower to 7.01 higher)	50 (Sen 2021)	Low	Could not differentiate

Table 8 Fluoroscopy guided MLD vs MLD

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Excess arm volume change (%) +- MID -7.66 to 7.66 follow-up: 6 months	MD **1.6 lower** (6.84 lower to 3.64 higher)	129 (De Vrieze 2022)	Moderate	Could not differentiate

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (lower scores are better)				
Quality of life-overall (Lymph-ICF) +- MID -9.83 to 9.83 follow-up: 6 months	MD **3.3 lower** (10.12 lower to 3.52 higher)	129 (De Vrieze 2022)	Low	Could not differentiate
Quality of life (McGill) +- MID -0.93 to 0.93 follow-up: 6 months	MD **0.46 higher** (0.18 lower to 1.1 higher)	129 (De Vrieze 2022)	Low	Could not differentiate
Skin changes (higher values better for elasticity; lower values better for thickness)				
Trunk skin elasticity (interlimb ratios) +- MID -0.21 to 0.21 follow-up: 6 months	MD **0.06 higher** (0.09 lower to 0.21 higher)	129 (De Vrieze 2022)	Low	Could not differentiate
Trunk skin thickness (interlimb ratios) +- MID -0.14 to 0.14 follow-up: 6 months	MD **0.01 lower** (0.11 lower to 0.09 higher)	129 (De Vrieze 2022)	Moderate	Could not differentiate
Arm skin elasticity (induration force interlimb ratios) +- MID -0.16 to 0.16 follow-up: 6 months	MD **0.01 higher** (0.1 lower to 0.12 higher)	129 (De Vrieze 2022)	Moderate	Could not differentiate
Arm skin thickness (interlimb ratios) +- MID -0.20 to 0.20 follow-up: 6 months	MD **0.13 lower** (0.26 lower to 0)	129 (De Vrieze 2022)	Low	Could not differentiate

Table 9 SLD + compression therapy vs compression therapy

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Arm volume change (ml) +- MID -52.87 to 52.87 follow-up: 6 weeks	MD **12.9 lower** (80.19 lower to 54.39 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Arm volume change (ml) +- MID -51.6 to 51.6 follow-up: 6 months	MD **11.5 lower** (78.97 lower to 55.97 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Lymphoedema (arm function) (lower scores are better)				
Arm function (QuickC-DASH) +- MID -8 to 8 follow-up: 6 weeks	MD **2.2 lower** (16.2 lower to 11.8 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Arm function (Quick-DASH) +- MID -8 to 8 follow-up: 6 months	MD **0.4 lower** (13.07 lower to 12.27 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Quality of life (higher scores are better)				
Quality of life-physical (SF-36) +- MID -5.41 to 5.41 follow-up: 6 weeks	MD **0.7 lower** (9.23 lower to 7.83 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Quality of life-physical (SF-36) +- MID -6.59 to 6.59 follow-up: 6 months	MD **11.9 higher** (0.12 higher to 23.68 higher)	24 (Bahtiyarca 2019)	Very low	Favours SLD + compression bandaging
Quality of life-mental (SF-36) +- MID -6.22 to 6.22 follow-up: 6 weeks	MD **10.6 lower** (19.66 lower to 1.54 lower)	24 (Bahtiyarca 2019)	Very low	Favours compression therapy

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life-mental (SF-36) +- MID -5.78 to 5.78 follow-up: 6 months	MD **1.1 lower** (11.36 lower to 9.16 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Patient-reported outcomes (lower scores are better)				
Anxiety (HADS-A) +- MID -2.06 to 2.06 follow-up: 6 weeks	MD **0.8 higher** (2.28 lower to 3.88 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Anxiety (HADS-A) +- MID -2.04 to 2.04 follow-up: 6 months	MD **0.1 lower** (2.95 lower to 2.75 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Depression (HADS-D) +- MID -1.55 to 1.55 follow-up: 6 weeks	MD **0.3 higher** (3.04 lower to 3.64 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate
Depression (HADS-D) +- MID -1.52 to 1.52 follow-up: 6 months	MD **0.7 lower** (3.68 lower to 2.28 higher)	24 (Bahtiyarca 2019)	Very low	Could not differentiate

Table 10 Pressure garments vs no pressure

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (progression, limb volume) (RR of less than one represents lower progression rates; lower limb volume measures are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Progression of lymphoedema relative volume ≥2% +- MID 0.8 to 1.25 follow-up: 6 months	**RR 0.27** (0.10 to 0.73)	69 (Blom 2022)	Low	Favours compression garment
Progression of lymphoedema relative volume ≥10% +- MID 0.8 to 1.25 follow-up: 6 months	**RR 0.29** (0.03 to 2.46)	64 (Blom 2022)	Very low	Could not differentiate
Lymphoedema relative volume change (%) +- MID -1.41 to 1.41 follow-up: 6 months	MD **3.9 lower** (5.58 lower to 2.22 lower)	52 (Blom 2022)	Low	Favours compression garment

Table 11 Mobiderm vs conventional multilayered bandages

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Arm volume reduction (ml) +- MID -272.77 to 272.77 follow-up: 15 days	MD **285 lower** (591.89 lower to 21.89 higher)	49 (Dhar 2023)	Very low	Could not differentiate
Patient-reported outcomes (lower scores are better)				
Pain (Visual analogue scale) +- MID -1.3 to 1.3 follow-up: 15 days	MD **1.01 lower** (2.26 lower to 0.24 higher)	49 (Dhar 2023)	Very low	Could not differentiate

Table 12 Compression garment (night and day for 90 days) vs compression garment (daytime)

Outcomes	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Arm lymphoedema volume variation (ml) +- MID -98.39 to 98.39 follow-up: 30 days	MD **46.2 lower** (142.74 lower to 50.34 higher)	40 (Mestre 2017)	Very low	Could not differentiate
Patient-reported outcomes (RR of less than 1 represents fewer symptoms)				
Arm functional symptoms (heaviness and/or pain) +- MID 0.8 to 1.25 follow-up: 30 days	**RR 0.25** (0.08 to 0.75)	40 (Mestre 2017)	Low	Favours compression garment (night time + day time)

Table 13 Negative pressure massage vs MLD

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
L-dex score (bioelectrical impedance ratio of unaffected to affected limb) +- MID -2.25 to 2.25 follow-up: 5 weeks	MD **7.28 lower** (11.85 lower to 2.71 lower)	28 (Lampinen 2021)	Very low	Favours Negative Pressure Massage Treatment
Interlimb volume difference (ml) +- MID -37.05 to 37.05 follow-up: 5 weeks	MD **78.53 lower** (147.09 lower to 9.97 lower)	28 (Lampinen 2021)	Very low	Favours Negative Pressure Massage Treatment

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (arm function) (lower scores are better)				
DASH score change +-MID -7 to 7 follow-up: 5 weeks	MD **2.63 lower** (9.62 lower to 4.36 higher)	28 (Lampinen 2021)	Very low	Could not differentiate

Table 14 CDT vs MLD

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (volume, local tissue water) (lower scores are better)				
Arm volume change (cm^3) +- MID -19.4 to 19.4 follow-up: 2 weeks	MD **0.5 higher** (23.03 lower to 24.03 higher)	40 (Liu 2023)	Very low	Could not differentiate
Tissue dielectric constant value in upper arm +- MID -0.31 to 0.31 follow-up: 2 weeks	MD **1.57 higher** (0.8 higher to 2.34 higher)	40 (Liu 2023)	Very low	Favours MLD
Tissue dielectric constant value in forearm +- MID -0.67 to 0.67 follow-up: 2 weeks	MD **1.37 higher** (0.39 higher to 2.35 higher)	40 (Liu 2023)	Very low	Favours MLD

Table 15 CDT vs compression bandaging

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (volume, local tissue water) (lower scores are better)				
Arm volume change (cm^3) +- MID -39 to 39 follow-up: 2 weeks	MD **1.5 lower** (39.35 lower to 36.35 higher)	40 (Liu 2023)	Very low	Could not differentiate
Tissue dielectric constant value in upper arm +- MID -2.37 to 2.37 follow-up: 2 weeks	MD **3.23 lower** (5.43 lower to 1.03 lower)	40 (Liu 2023)	Very low	Favours CDT
Tissue dielectric constant value in forearm +- MID -2.02 to 2.02 follow-up: 2 weeks	MD **3.24 lower** (5.17 lower to 1.31 lower)	40 (Liu 2023)	Very low	Favours CDT

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2.3 Narrative summary of the effectiveness evidence

For some of the evidence, it was not possible to complete GRADE because the data reporting was incomplete. Specifically, the original studies or reports did not provide standard deviations or other measures of variability for their outcomes. Therefore, assessing the precision of effect estimates was not possible. and as such evidence statements were produced to summarise the evidence narratively.

Decongestive Lymphoedema Treatment

Lymphoedema (volume)

One systematic review of 7 studies (5 RCTs, 2 uncontrolled studies; Jeffs et al. 2018), at low to high risk of bias, found data from:

- 5 studies at moderate to high risk of bias (n=152) that found that CDT significantly reduced excess arm volume post-intervention, with percentage reductions ranging from 28% to 47% ($p<0.05$)
- There were no statistically significant differences in excess arm volume reduction between CDT and compression therapy alone in two studies at moderate risk of bias (Dayes 2013, McNeely 2004).
- One study (Gradalski 2015) reported reduced excess arm volume at 6 months post-intervention for the CDT group.

Quality of life

3 RCTs at moderate to high risk of bias (n=119) assessed health-related quality of life. They found that:

- There were no significant improvements in SF-36 scores in the CDT group compared to compression therapy alone (Dayes 2013).
- There were statistically significant improvements in SF-36 scores in both the CDT and CDT plus exercise groups, with greater improvement in the CDT plus exercise group (Kim 2010).
- One study (Gradalski 2015) reported a statistically significant improvement of 1.69 points (on a 10-point scale) in lymphoedema-specific quality of life scores in the CDT group post-intervention.

Arm Function

- 1 RCT (Dayes 2013) at moderate risk of bias (n=54) assessed arm function using the DASH questionnaire and found that, there were non-significant improvements in arm function in both the CDT and compression therapy alone groups.

Compression garments

Lymphoedema (volume)

1 RCT (Duygu-Yildiz et al., 2023) at high risk of bias (n=21) comparing low to high bandage pressure reported medians and minimum and maximum values for:

- The percentage of residual volume at 3 months for people receiving low bandage pressure (Median= 21.6, ranging from 1.4 to 35) compared to people receiving high bandage pressure (Median= 31.4, ranging from 12.4 to 62.3).
- Skin thickness (mm)
    - in the hand dorsum at 3 months for people receiving low bandage pressure (Median= 0.70, ranging from 0.6 to 0.9) compared to people receiving high bandage pressure (Median= 0.75, ranging from 0.6 to 1.0).
    - in the wrist volar at 3 months for people receiving low bandage pressure (Median= 0.70, ranging from 0.7 to 1.0) compared to people receiving high bandage pressure (Median= 0.65, ranging from 0.5 to 1.6).
    - in the forearm volar at 3 months for people receiving low bandage pressure (Median= 0.90, ranging from 0.7 to 1.2) compared to people receiving high bandage pressure (Median= 0.85, ranging from 0.7 to 1.8).
    - in the arm volar at 3 months for people receiving low bandage pressure (Median= 0.90, ranging from 0.7 to 1.3) compared to people receiving high bandage pressure (Median= 0.90, ranging from 0.7 to 1.2).
    - in the forearm dorsum at 3 months for people receiving low bandage pressure (Median= 0.95, ranging from 0.7 to 1.4) compared to people receiving high bandage pressure (Median= 0.85, ranging from 0.7 to 2.7).
    - in the arm dorsum at 3 months for people receiving low bandage pressure (Median= 1.05, ranging from 0.8 to 1.6) compared to people receiving high bandage pressure (Median= 1.10, ranging from 0.9 to 2.6).
- Tissue thickness
    - in the hand dorsum at 3 months for people receiving low bandage pressure (Median= 3.55, ranging from 1.6 to 5.3) compared to people receiving high bandage pressure (Median= 5.6, ranging from 1.1 to 8.5).
    - in the wrist volar at 3 months for people receiving low bandage pressure (Median= 4.5, ranging from 1.6 to 7.6) compared to people receiving high bandage pressure (Median= 4.4, ranging from 1.6 to 8.9).
    - in the forearm volar at 3 months for people receiving low bandage pressure (Median= 4.55, ranging from 2.5 to 6.6) compared to people receiving high bandage pressure (Median= 4.9, ranging from 4.1 to 7.3).
    - in the arm volar at 3 months for people receiving low bandage pressure (Median= 5.3, ranging from 2.3 to 8.7) compared to people receiving high bandage pressure (Median= 5.25, ranging from 4.1 to 7.2).
    - in the forearm dorsum at 3 months for people receiving low bandage pressure (Median= 7.35, ranging from 6.0 to 12.8) compared to people receiving high bandage pressure (Median= 7.95, ranging from 2.5 to 16.7).
    - in the arm dorsum at 3 months for people receiving low bandage pressure (Median= 7.8, ranging from 5.7 to 24.0) compared to people receiving high bandage pressure (Median= 9.05, ranging from 5.8 to 19.3).

Adverse events and quality of life

1 RCT (Mestre 2017) at moderate risk of bias (n=40) compared compression garment (nighttime plus daytime for 90 days) to compression garment (daytime only for 30 days followed by night and daytime compression from day 31 to day 90). They found that:

- 31 people (77.5%) across both arms reported at least one adverse event. There were 36 adverse events in people receiving nighttime compression and 28 adverse events

in people receiving daytime compression. Of these reported adverse events, 11 events (n=8 people [40%] from the night-use group) were considered as device-related. Most frequently related adverse events to MOBIDERM® Autofit arm sleeve were erythema (n=5) and pruritis (n=4), but none of them were severe.

- Nighttime compression showed an improvement in the function domain of quality of life in the LYMQOL arm questionnaire (-0.4 points) in people receiving compression garment (nighttime plus day time for 90 days) compared to (+0.1 points), lower scores on this questionnaire indicate improvement.

3 Exercise and movement

3.1 Summary of studies included in the evidence

Table 16 Summary of studies included in the evidence

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Systematic review					
Lytvyn et al. (2020) 36 RCTs	People diagnosed with unilateral extremity lymphoedema.	Complex Decongestive therapy Manual lymphatic drainage, resistance/aerobic exercise, compression pumps, water-based and yoga/tai-chi exercise.	Standard care	• Lymphoedema volume • Lymphoedema swelling and symptoms • Function • Quality of life • Patient reported outcomes (pain/fatigue)	Low
Rangon et al. (2022) 12 RCTs	Breast cancer survivors with clinical diagnosis of unilateral lymphoedema in the upper limb.	Complex physical therapy Skin care, manual lymphatic drainage, compression and myolymphokinetic exercises.	Multimodal approaches Other conservative treatment modalities or combination of complex physical therapy with other treatment modalities	• Lymphoedema (Reduction in total volume of upper limb) • Patient reported outcomes (pain reduction, function)	Moderate
Yeung and Semicuw (2018)	People with primary or secondary lymphoedema.	Aquatic therapy or hydrotherapy	Standard land-based treatment	• Lymphoedema (Relative change in limb volume)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
4 RCTs		Alone or in combination with other treatments for lymphoedema	Standard land-based treatment (e.g. habitual physical activities, standard care)	• Quality of life (Self-reported psychosocial measure) • Patient-reported outcomes (limb function – strength, range of movement, pain and heaviness symptoms) • Adverse events	
Randomised controlled trials					
Ali et al. (2021) n=50 Location: Egypt	Participants with a history of breast cancer for which they had undergone unilateral excision of the axillary lymph nodes. Mild to moderate degree / stage I-II lymphoedema.	Aqua therapy-resistance exercise program Three 60-minute sessions per week for 8 weeks. Arm exercises and diaphragmatic breathing in a hydrotherapy pool.	Exercise therapy program Three 60-minute sessions per week for 8 weeks. Mobility and stretching exercises, strength and resistance exercise and diaphragmatic breathing. Participants instructed to use a compression garment during sessions.	• Lymphoedema (arm volume) • Patient-reported outcomes (pain) • Arm function (should flexion, abduction)	Low
Kizil et al. (2018) n=32 Location: Turkey	Participants aged 25 to 75, presence of unilateral lymphoedema at least 6 months and up to 8 years after treatment of breast cancer. At least 2cm difference at a point between affected and unaffected arm	Complete decongestive therapy plus continuous passive motion 15 sessions on 15 consecutive days. Self-manual lymphatic drainage	Complete decongestive therapy 15 sessions on 15 consecutive days. Self-manual lymphatic drainage, multilayer short stretch compression bandage,	• Lymphoedema (volumetric measurement) • Mobility (Range of motion - flexion and abduction, internal rotation and external rotation)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
		taught for 20 minutes. Patients given CPM (Kinetec Centura Shoulder CPM) with third-level speed plus flexion-directed exercise up to approximately 90% of the shoulder joint ROM for 20 minutes in the first five sessions and for 30 minutes in the next 10 sessions.	instructions in self-care, therapeutic exercise, and education on skin and nail care.		
Kilbreath et al. (2020) n=89 Location: Australia	Women aged ≥18 years; had undergone surgery for breast cancer that included wide local excision and axillary surgery; reported having breast oedema for longer than 3 months in which the intensity of the breast-related symptoms such as heaviness and/or discomfort were ≥3 on a 10-cm visual analogue scale at enrolment into the study.	Exercise. 3 x 1hr sessions/week for 12 weeks. Low intensity warm up, 30 mins training using free weights and resistance machines, 2x10 minute blocks of aerobic training.	Control No exercise advice provided.	• Adverse events • Function (upper limb strength)	Moderate
Park et al. (2023) n=20	People diagnosed with lymphoedema after mastectomy, who had	Complex decongestive physical therapy	Complex decongestive physical therapy	• Lymphoedema (oedema volume, grip strength, K-DASH questionnaire)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Location: South Korea	completed their courses of chemotherapy or had the plan to receive chemotherapy. People with current or completed radiotherapy after anti-cancer treatment and those who could perform exercise according to the therapist's instructions. People who did not have a problem in cognitive functions, and those without abnormal findings on physical and neurological examinations.	(CDPT): Both groups had 3 sessions/week for 6 weeks: 15 minutes of manual lymphatic drainage, 5 minutes of low elastic compression bandages, and 15 minutes of intermittent pneumatic compression therapy. Progressive resistive exercise intervention: After CDPT completed, 50 minutes of resistance exercise, 3 sessions/week for 6 weeks. Exercises focused on stretching, stabilising scapula and strengthening upper limb muscles.	As for the intervention group. Self-home resistance exercise: After CDPT completed, 50 minutes of "self-home resistive exercise" using Thera-band, 3 sessions/week for 6 weeks. Exercises were the same as for the intervention group, but no progression in Thera-band tension.		
Sener et al. (2017) n=60	Women who developed lymphoedema post breast cancer treatment. Women with a diagnosis of severe heart failure, psychological disorders,	Clinical pilates exercise Exercises performed in groups of 5-8 people 3 times per week for 8 weeks.	Control Participants were taught core stabilisation while performing activities of daily living, and how to	• Mobility (grip strength, shoulder flexion, abduction, external rotation) • Patient-reported outcomes (body image, arm function)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Location: Turkey	severe pain of unknown cause in axillary region and musculoskeletal problems before treatment were excluded.	Supervised by physiotherapists. Focus on spinal stabilisation, and hand-arm-shoulder movements, aiming to accelerate the lymphatic flow. After 4 weeks, resistance band exercises were added. Also completed a home-based program every day, including manual lymphatic drainage training, wall extension, wand exercises used to improve shoulder flexibility and skin care training.	conduct manual lymphatic drainage, skincare, and shoulder exercises. Participants were taught wall extension and Wand exercises, head and neck exercises, and exercises to improve shoulder girdle stability. Pumping activities and breathing exercises were recommended. They were also advised to pay attention to skin care and to walk 1 hour every day.	• Quality of life (QLQ-BR23 questionnaire)	
Singh et al. (2016) N= 39 Location: Australia	Women with unilateral upper extremity lymphoedema stages II and III following breast cancer Lymphoedema present for at least 6 months Completed phase	Aerobic exercise: 12 weeks of home-based aerobic exercise progressing from moderate to high intensity	Resistance exercise: 12 weeks of home-based resistance training progressing in intensity	• Patient-reported outcomes • Quality of life • Function • Lymphoedema volume variation (volume excess variation)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	1 of complex decongestive therapy				

Table 17: Included studies in systematic reviews

Authors Lytvyn et al. 2020	Experimental group	Control group	Duration/follow-up	Outcome measures
Andersen et al. 2000 N= 41	CDT	Standard care	Follow-up at 48 weeks	• Lymphoedema volume
Bergmann et al., 2014 N=57	CDT	Standard care	3-4 weeks	• Lymphoedema volume • Pain
Bok et al, 2016 N= 32	CDT plus resistance exercise	CDT	8 weeks	• Lymphoedema volume
Buchan et al., 2016 N= 40	aerobic exercise	resistance exercise	36 weeks	• Lymphoedema volume
Buragadda et al., 2015 N= 60	CDT	CDT	24 weeks	• Lymphoedema volume
Chmielewska et al., 2016 N= 21	CPs plus resistance exercise	CP	4 Weeks	• Lymphoedema volume
Cormie et al., 2013 N=62	Resistance exercise	Standard care	12 weeks	• Lymphoedema volume, function, pain
Dayes et al., 2013	CDT	Standard care	6 weeks	• Lymphoedema volume, function, quality of life

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
N=95				
Didem et al. 2005 N=53	CDT	Standard care	4 weeks	• Lymphoedema volume, function, pain
Do et al. 2015 N=44	CDT + resistance exercise	CDT	8 weeks	• Lymphoedema volume, fatigue, function, pain, quality of life
Do et al. 2017 N= 40	CDT + CPs + resistance exercise	CDT + CPs	4 weeks	• Lymphoedema volume, fatigue, pain, quality of life
Gradalski et al. 2015 N=51	CDT	Standard care	24 weeks	• Lymphoedema volume, fatigue, symptoms, pain, quality of life
Gurdal et al. 2012 N=30	CDT	CPs	6 weeks	• Lymphoedema volume, quality of life
Haghighat et al. 2010 N=112	CDT + CPs	CDT	15 weeks	• Lymphoedema volume, symptoms, pain
Hayes et al. 2009 N=31	Aerobic + resistance exercise	Standard care	12 weeks	• Lymphoedema volume
Jeffs & Wiseman 2013 N=23	Resistance exercise	Standard care	26 weeks	• Lymphoedema volume
Johansson et al. 1998 N=24	CPs	MLD	4 weeks	• Lymphoedema volume
Johansson et al. 2013 N=25	Water-based + yoga exercise	Standard care	8 weeks	• Lymphoedema volume, function
Letellier et al. 2014 N=18	Water-based + yoga exercise	Standard care	4 weeks	• Lymphoedema volume, function, pain, quality of life
Ligabue et al. 2019 N=34	CDT	CDT	24 weeks	• Lymphoedema volume

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Loudon et al. 2014, 2016 N=23	Water-based + yoga exercise	Standard care	12 weeks	• Lymphoedema volume, fatigue, symptoms, pain, quality of life
Luz et al. 2018 N=42	CDT + resistance exercise	CDT	8 weeks	• Lymphoedema volume, function
McClure et al. 2010 N=21	Water-based + yoga exercise	Standard care	17 weeks	• Lymphoedema volume, function, quality of life
McKenzie & Kalda 2003 N=14	Aerobic + resistance exercise	Standard care	8 weeks	• Lymphoedema volume
McNeely et al. 2004 N=44	MLD	Standard care	4 weeks	• Lymphoedema volume
Park 2017 N=63	Aerobic + resistance exercise	CDT	4 weeks	• Lymphoedema volume, symptoms, pain, function
Paysar et al. 2019 N=27	Water-based + yoga exercise	Standard care	8 weeks	• Lymphoedema volume, fatigue, quality of life
Sanal-Toprak et al. 2019 N=46	CPs	CDT	36 weeks	• Lymphoedema volume, function
Schmitz et al. 2009 N=139	Resistance exercise	Standard care	52 weeks	• Lymphoedema volume, symptoms
Schmitz et al. 2019 N=139	Aerobic + resistance exercise	Standard care	52 weeks	• Lymphoedema volume, symptoms
Sitzia et al. 2002 N=27	CDT	CDT	2 weeks	• Lymphoedema volume
Szolnoky et al. 2009 N=27	CDT + CPs	CDT	8 weeks	• Lymphoedema volume, symptoms

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Szuba et al. 2002 N=23	CDT + CPs	CDT	4 weeks	• Lymphoedema volume
Uzkeser et al. 2011 N=30	CDT + CPs	CDT	7 weeks	• Lymphoedema volume
Wigg 2009 N=11	CDT	CPs	4 weeks	• Lymphoedema volume
Rangon et al. 2022				
Bergmann et al N= 66	Arm 1: Group A: MLD with Vodder technique; skin care; bandaging; remedial exercises. Arm 2: Group B: skin care; bandaging; remedial exercises.	Skin care; exercises; fitted standard or custom-made elastic garments.	Visits without specified time	• Volume • Subjective symptoms
Buragadda et al. N=60	CDT Group: MLD; compression garment; remedial exercises; home program self-lymph drainage, exercises, and skin care	CT Group: MLD; low elastic compression garment; glenohumeral mobilization and deep breathing exercise	Immediate after treatment	• Circumference • Volume • Function • Pain
Dayes et al N= 103	MLD technique Vodder or Foldi; short-stretch compression bandages; maintenance of skin care; exercises	elastic compression garments consisting of a sleeve and glove (30-40mmHg); maintenance of skin care; exercises	52 weeks	• Volume • Quality of life • Function

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Didem et al N= 53	CDP group: MLD with modification of the method Foldi; compression bandage; remedial exercises; skincare; home program with compression	bandage; elevation; head-neck/shoulder exercises; home program with compression	Immediate	• Range of motion • Circumference • Volume
Do et al N=44	resistance exercise program; MLD; compression with garment or multilayer shortstretch bandage; skin care.	MLD; compression with garment or multilayer short-stretch bandage; exercises; skin care.	5 weeks	• Volume • Muscular strength • Function • Quality of life
Ergin et al N=36 Location:	MLD; short-stretch bandages; lymph-reducing exercises; skin care	Kinesio Tape lymphatic correction technique; MLD; short-stretch bandages; lymph-reducing exercises; skin care	Immediate	• Volume
Gradalski et al N= 60	MLD with Vodder II method; multilayer compression bandages; active-assisted exercises; skin care	multilayer compression bandages; active-assisted exercises; skin care.	6 months	• Volume • Quality of life
Haghighat et al N=112	CDT group: MLD with Vodder technique; skin care; remedial exercises; compression applied by multilayered short-stretch bandages.	CDT+IPC: MLD in abdomen, chest, axillary, inguinal, and cervical; IPC (40mmHg); skin care; remedial exercises; compression applied by multilayered short-stretch bandages	3 months	• Volume • Subjective symptom
Kim et al N=40	CDP+ARE group: MLD; compression therapy; remedial exercise; active resistance exercise.	CDP group: MLD; compression therapy; remedial exercise.	8 weeks	• Volume • Quality of life

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Pekyavas et al N=45	Group 1: skin care; MDL; short-stretch multilayer compression bandage; remedial exercise program. Group 2: skin care; MDL; short-stretch multilayer compression bandage; remedial exercise program; Kinesio Tape lymphatic correction method under the bandage	skin care; MDL; remedial exercise program; Kinesio Tape lymphatic correction method.	4 weeks	• Subjective symptoms • Volume • Quality of life
Szolnoky et al N=27	CDP+IPC group: IPC (50mmHg); MLD with Vodder method; skin care; multilayered short-stretch bandaging; exercises	CDP group: MLD with Vodder method; skin care; multilayered short-stretch bandaging; exercises.	2 months	• Volume • Subjective symptoms
Tambour et al N=77	T+MLD group: MLD with Foldi technique; skin care; bandaging (20-30mmHg); guidance on physical activity.	T -MLD group: skin care; bandaging (20-30mmHg); guidance on physical activity	6 months	• Volume • Circumference • Subjective symptoms • Quality of life
Uzkeser et al N=31	Group 1: skin care; MLD; compression bandage or garments; exercises	Group 2: IPC (40mmHg); skin care; MLD; compression bandage or garments; exercises.	1 month	• Circumference • Volume • Dermal thickness • Pain
Yeung et al. 2018				
Hayes et al. N= 32	Aerobic and resistance exercise	Control	24 Weeks	• Lymphoedema status perimetry BIS

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Tidher et al. N=48	Group exercise low resistance	Self-management treatment	12 weeks	• Lymphoedema status RLV • Self-reported adherence and outcomes
Johansson et al. N=29	Aqua lymphatic therapy	Compression sleeve	8 weeks	• Lymphoedema status RLV • Self-reported adherence and outcomes
Letellier et al. N=25	Aqua lymphatic therapy	Compression sleeve	12 weeks	• Lymphoedema status RLV • Grip strength. • Pain • Dash Score • QOL • Self-reported adherence and outcomes

See appendix D for full evidence tables.

3.2 Summary of the effectiveness evidence

Table 18 Resistance exercise vs standard care

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Lymphoedema volume change +-MID 0.5	SMD **0.01 SD higher** (0.48 lower to 0.5 higher)	Not reported (Lytvyn 2020)	Low	Could not differentiate
Shoulder function (higher scores are better)				
Shoulder function DASH score +-MID 0.5	SMD **2.49 SD higher** (1.79 higher to 3.19 higher)	62 (Lytvyn 2020)	Very low	Favours resistance exercise
Quality of life (higher scores are better)				
Quality of life FACTB+4 +-MID 0.5	SMD **0.31 SD higher** (0.23 lower to 0.86 higher)	62 (Lytvyn 2020)	Very low	Could not differentiate
Patient reported outcomes (lower scores are better)				
Pain - BDI +-MID 0.5	SMD **1 SD higher** (1.57 lower to 0.43 lower)	62 (Lytvyn 2020)	Very low	Could not differentiate
Symptom severity scale +-MID 0.5	SMD **0.38 SD lower** (0.72 lower to 0.05 lower)	139 (Lytvyn 2020)	Very low	Favours resistance exercise

Table 19 Aerobic + resistance exercise vs standard care/CDT

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Lymphoedema volume change +-MID 0.5	SMD **0.19 SD higher** (0.34 lower to 0.72 higher)	Not reported (Lytvyn 2020)	Very low	Could not differentiate
Shoulder function (lower scores are better)				
Shoulder abduction DASH scores +-MID 0.5	SMD **1.87 SD higher** (1.27 higher to 2.46 higher)	63 (Lytvyn 2020)	Very low	Favours standard care/CDT
Patient reported outcomes (lower scores are better)				
Pain VAS +-MID 0.5	SMD **2.02 SD lower** (2.63 lower to 1.41 lower)	63 (Lytvyn 2020)	Very low	Favours aerobic + resistance exercise
Lymphoedema swelling and symptoms (self-report score) +-MID 0.5	SMD **0.38 SD lower** (0.72 lower to 0.06 lower)	177 (Lytvyn 2020)	Very low	Favours aerobic + resistance exercise

Table 20 Water-based exercise and yoga vs standard care/CDT

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Lymphoedema volume change +-MID 0.5	SMD **0.29 SD lower** (0.77 lower to 0.19 higher)	Not reported (Lytvyn 2020)	Very low	Could not differentiate
Shoulder function (higher scores are better)				
Shoulder function DASH score +-MID 0.5	SMD **0.18 SD higher** (0.39 lower to 0.74 higher)	87 (Lytvyn 2020)	Very low	Could not differentiate
Quality of life (higher scores are better)				
Quality of life EORTC-QLQ-C30/BDI/FACTB/LYMQOL +-MID 0.5	SMD **0.21 SD higher** (0.42 lower to 0.84 higher)	89 (Lytvyn 2020)	Very low	Could not differentiate
Patient reported outcomes (lower scores are better)				
Pain - EORTC-QLQ-C30/VAS/MPQ +-MID 0.5	SMD **0.58 SD lower** (1.07 lower to 0.09 lower)	68 (Lytvyn 2020)	Very low	Favours water-based + yoga exercise
Fatigue EORTC-QLQ-C30/VAS +-MID 0.5	SMD **0.39 SD lower** (0.099 lower to 0.2 higher)	50 (Lytvyn 2020)	Moderate	Could not differentiate
Sensations - VAS +-MID 0.5	SMD **0.07 SD lower** (0.88 lower to 0.75 higher)	23 (Lytvyn 2020)	Very low	Could not differentiate

Table 21 CDT + resistance exercise vs standard care/CDT

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Shoulder function (higher scores are better)				
Shoulder abduction DASH score +-MID 0.5	SMD **0.33 SD lower** (0.75 lower to 0.1 higher)	86 (Lytvyn 2020)	Very low	Could not differentiate
Quality of life (higher scores are better)				
Quality of life EORTC-QLQ-C30 +-MID 0.5	SMD **0.03 SD higher** (0.56 lower to 0.62 higher)	44 (Lytvyn 2020)	Very low	Could not differentiate
Patient reported outcomes (lower scores are better)				
Pain EORTC-QLQ-C30 +-MID 0.5	SMD **0.05 SD higher** (0.54 lower to 0.65 higher)	44 (Lytvyn 2020)	Very low	Could not differentiate
Fatigue EORTC-QLQ-C30 +-MID 0.5	SMD **0.13 SD higher** (0.46 lower to 0.72 higher)	44 (Lytvyn 2020)	Very low	Could not differentiate

Table 22 CDT + compression pump + resistance exercise vs CDT + compression pump

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (higher scores are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life EORTC-QLQ-C30 +- MID 0.5	SMD **0.27 SD higher** (0.35 lower to 0.89 higher)	40 (Lytvyn 2020)	Low	Could not differentiate
Patient reported outcomes (lower scores are better)				
Fatigue EORTC-QLQ-C30 +-MID 0.5	SMD **0.53 SD lower** (1.17 lower to 0.1 higher)	40 (Lytvyn 2020)	Moderate	Could not differentiate
Pain EORTC-QLQ-C30 +-MID 0.5	SMD **0.21 SD lower** (0.83 lower to 0.41 higher)	40 (Lytvyn 2020)	Low	Could not differentiate

Table 23 Complex physical therapy vs multimodal approaches

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Reducing total volume of upper limb (immediate) +- MID 0.5 SD follow-up: 1 months	SMD **0.12 SD lower** (0.62 lower to 0.39 higher)	60 (Rangon 2022)	Very low	Could not differentiate

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Reducing total volume of upper limb (short term) +-MID 0.5 follow-up: range 1 months to 3 months	SMD **0.2 SD lower** (0.44 lower to 0.04 higher)	60 (Rangon 2022)	Low	Could not differentiate
Reducing total volume of upper limb (long term) +-MID 0.5 follow-up: range 6 months to 12 months	SMD **0.15 SD lower** (0.5 lower to 0.21 higher)	60 (Rangon 2022)	Low	Could not differentiate
Patient reported outcomes (lower scores are better for pain; higher scores better for function)				
Pain reduction of upper limb (immediate) +-MID 0.5 follow-up: 1 months	SMD **0.1 SD higher** (0.17 lower to 0.37 higher)	259 (Rangon 2022)	Low	Could not differentiate
Pain reduction of upper limb (short term) +-MID 0.5 follow-up: range 1 months to 3 months	SMD **0.61 SD lower** (1.19 lower to 0.02 lower)	517 (Rangon 2022)	Very low	Favours complex physical therapy
Pain reduction of upper limb (long term) +-MID 0.5 follow-up: range 6 months to 12 months	SMD **0.33 SD lower** (0.79 lower to 0.13 higher)	73 (Rangon 2022)	Very low	Could not differentiate
Physical function of upper limb (immediate) +-MID 0.5 follow-up: 1 months	SMD **0.14 SD higher** (0.28 lower to 0.57 higher)	90 (Rangon 2022)	Very low	Could not differentiate

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Physical function of upper limb (short term) +-MID 0.5 follow-up: range 1 months to 3 months	SMD **0.67 SD lower** (1.6 lower to 0.26 higher)	409 (Rangon 2022)	Very low	Could not differentiate
Physical function of upper limb (long term) +-MID 0.5 follow-up: range 6 months to 12 months	SMD **0.1 SD lower** (0.42 lower to 0.23 higher)	153 (Rangon 2022)	Low	Could not differentiate

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2 **Table 24 Aquatic therapy vs standard care**

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Arm lymphoedema relative volume change (%) +- MID 0.5 follow-up: 3 months	SMD **0.14 SD higher** (0.37 lower to 0.64 higher)	66 (Yeung 2018)	Low	Could not differentiate
Arm function (higher scores are better)				
Arm physical function (range of tools used) +- MID 0.5 follow-up: 3 months	SMD **0.27 SD lower** (0.78 lower to 0.23 higher)	66 (Yeung 2018)	Low	Could not differentiate

Table 25 Aqua therapy vs exercise

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (arm volume) (lower scores are better)				
Arm volume (ml) +- MID -108.03 to 108.03 follow-up: 8 weeks	MD **160.36 lower** (284.32 lower to 36.4 lower)	50 (Ali 2021)	Low	Favours aquatherapy
Arm function (higher scores are better)				
Shoulder flexion (standard goniometry degrees) +- MID -2.90 to 2.90 follow-up: 8 weeks	MD **22.2 higher** (19.19 higher to 25.21 higher)	50 (Ali 2021)	Moderate	Favours aquatherapy
Shoulder abduction (standard goniometry degrees) +- MID -2.19 to 2.19 follow-up: 8 weeks	MD **19.8 higher** (17.58 higher to 22.02 higher)	50 (Ali 2021)	Moderate	Favours aquatherapy
Patient-reported outcomes (lower scores are better)				
Pain (Visual analogue scale) +- MID -1.3 to 1.3 follow-up: 8 weeks	MD **2.32 lower** (2.83 lower to 1.81 lower)	50 (Ali 2021)	Moderate	Favours aquatherapy

Table 26 Continuous passive motion + CDT vs CDT

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Arm volume change (ml) +- MID -459.08 to 459.08 follow-up: 15 days	MD **62.81 lower** (658.21 lower to 532.59 higher)	30 (Kizil 2018)	Very low	Could not differentiate
Lymphoedema (arm mobility) (higher scores are better)				
Shoulder flexion (standard goniometry degrees) +- MID -10.26 to 10.26 follow-up: 15 days	MD **2.29 higher** (19.43 lower to 24.01 higher)	30 (Kizil 2018)	Very low	Could not differentiate
Shoulder abduction (standard goniometry degrees) +- MID -14.23 to 14.23 follow-up: 15 days	MD **4.91 higher** (19.89 lower to 29.71 higher)	30 (Kizil 2018)	Very low	Could not differentiate
Shoulder internal rotation (standard goniometry degrees) +- MID -6.71 to 6.71 follow-up: 15 days	MD **1.08 higher** (8 lower to 10.16 higher)	30 (Kizil 2018)	Very low	Could not differentiate
Shoulder external rotation (standard goniometry degrees) +- MID -6.63 to 6.63 follow-up: 15 days	MD **0.63 higher** (7.61 lower to 8.87 higher)	30 (Kizil 2018)	Very low	Could not differentiate

Table 27 Pilates vs exercise + self care

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (arm mobility and function) (higher scores are better)				
Grip strength (kg) +- MID -3.05 to 3.05 follow-up: 8 weeks	MD **1.1 higher** (2.08 lower to 4.28 higher)	60 (Sener 2017)	Very low	Could not differentiate
Shoulder flexion (standard goniometry degrees) +- MID -6.13 to 6.13 follow-up: 8 weeks	MD **9.01 higher** (0.54 higher to 17.48 higher)	60 (Sener 2017)	Very low	Favours Pilates
Shoulder abduction (standard goniometry degrees) +- MID -11.36 to 11.36 follow-up: 8 weeks	MD **11.84 higher** (2.39 lower to 26.07 higher)	60 (Sener 2017)	Very low	Could not differentiate
Shoulder external rotation (standard goniometry degrees) +- MID -6.70 to 6.70 follow-up: 8 weeks	MD **7.66 higher** (1.29 lower to 16.61 higher)	60 (Sener 2017)	Very low	Could not differentiate
Arm function (DASH score) +- MID -7 to 7 follow-up: 8 weeks	MD **3.58 lower** (10.51 lower to 3.35 higher)	60 (Sener 2017)	Very low	Could not differentiate
Patient-reported outcomes (lower scores are better)				
Body image (SAA score) +- MID -4.32 to 4.32 follow-up: 8 weeks	MD **3.76 lower** (7.72 lower to 0.2 higher)	60 (Sener 2017)	Very low	Could not differentiate
Pain (Visual analogue scale) +- MID -1.44 to 1.44 follow-up: 8 weeks	MD **1.37 lower** (2.82 lower to 0.08 higher)	60 (Sener 2017)	Very low	Could not differentiate
Quality of life (higher scores are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (QLQ-BR23) +- MID -4.38 to 4.38 follow-up: 8 weeks	MD **1.8 higher** (2.82 lower to 6.42 higher)	60 (Sener 2017)	Very low	Could not differentiate

Table 28 Exercise vs no exercise/info on exercise

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Adverse events (lower scores are better)				
Adverse events (musculoskeletal) +- MID 0.8 to 1.25 follow-up: 12 weeks	**RR 5.49** (0.27 to 110.97)	84 (Kilbreath 2020)	Very low	Could not differentiate
Lymphoedema (arm mobility and function) (higher scores are better)				
Arm strength (chest press, kg) +- MID -2 to 2 follow-up: 12 weeks	MD **4.1 higher** (2.41 higher to 5.79 higher)	84 (Kilbreath 2020)	Low	Favours exercise

Table 29 Progressive resistance exercise vs self-directed resistance exercise

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Oedema volume (cm) +- MID -481.8 to 481.8	MD **34.41 lower** (826.65 lower to 757.83 higher)	16 (Park 2023)	Very low	Could not differentiate
Arm mobility and function (higher scores are better for grip strength; lower scores are better for arm function)				
Grip strength (kg) +- MID -2.05 to 2.05	MD **5.55 higher** (1.74 higher to 9.36 higher)	16 (Park 2023)	Very low	Favours progressive resistance exercise
Arm function K-DASH score +- MID -7.35 to 7.35	MD **23.71 lower** (38.1 lower to 9.32 lower)	16 (Park 2023)	Low	Favours progressive resistance exercise

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4 Skincare

4.1 Summary of studies included in the evidence

No evidence was identified that met the criteria in the protocol for skincare interventions for managing breast cancer-related lymphoedema.

5 Lymphoedema education

5.2 Summary of studies included in the evidence

Table 30 Summary of included studies

Study details	Population	Intervention	Comparator	Outcomes	Follow-up	Risk of bias
Randomised Controlled Trials						
Ligabue et al. (2019) n = 41 Location: Italy	Women with lymphoedema secondary to breast cancer who received CDT treatment	Self-administered CDT: A physiotherapist-led course over 4 weeks, teaching manual lymphatic self-drainage, self-bandage, breathing exercises, mobilisation exercises, muscle reinforcement exercises, muscle contracture management, and the understanding of the changes occurring after suffering from lymphoedema.	Usual care: An educational leaflet and a point-by-point briefing and discussion of the leaflet which included descriptions of specifically designed exercises and behavioural and hygienic standards.	• Lymphoedema (asymmetry, measured using excess limb volume indicator (interlimb discrepancy)) • Pain (measured using Numerical Pain Rating Scale)	6 months (outcomes reported at 1 month and 6 months)	• Low (for lymphoedema outcome) • Moderate (for pain outcome)

Study details	Population	Intervention	Comparator	Outcomes	Follow-up	Risk of bias
		Lifestyle and nutritional recommendations were provided, aiming at preventing weight gain and promoting selfcare activities.				
Omidi et al. (2020) n = 105 Location: Iran	Participants with a history of confirmed breast cancer (stages 0 to IV), lymphoedema established by a physician in the past year, aged 18–65 years old and completion of primary cancer treatments.	Intervention 1: Group-based education: 5 sessions of 60 to 90 min twice a week, held in the form of face-to-face group discussions and Q&A in groups of 5. Intervention 2: Social network-based education: Educational content was uploaded to a Telegram™ messenger channel twice a week for three weeks. 20 audio and photo messages were presented at different times of the day.	Control: No education intervention	• Quality of life (measured using Persian version of the Lymphoedema Life Impact Scale)	3 months (outcomes reported immediately after intervention and at 3 months)	High

Study details	Population	Intervention	Comparator	Outcomes	Follow-up	Risk of bias
Ridner et al. (2020) n = 160 Location: US	People with a history of breast cancer, a diagnosis of Stage II lymphoedema based on the International Society of Lymphoedema and aged 18 or older.	Web-based multimedia intervention: 12 sessions of videos lasting 20–45 minutes, featuring narration, reflective questions, and patients sharing stories about living with lymphoedema. The sessions covered basic physiology of lymphoedema and self-care, goal setting and self-reward, diet and exercise strategies, methods of dealing with negative emotions and stress, body image changes, uncertainty, and enhancing emotional and instrumental social support.	Educational pamphlet: A leaflet with topics including lymphoedema risk reduction, early warning signs, advice regarding lymphoedema treatment, emotions and lymphoedema, and paying for treatment.	• Patient-reported outcomes: Symptom burden (measured using the LSIDS-A tool) • Function (measured using the 11-item Quick-Disabilities of Arm, Shoulder, and Hand (QuickDASH) tool)	12 months (outcomes reported at 1 month and 12 month follow-up)	High

1 Abbreviations: LSIDS-A tool: Lymphoedema Symptom Intensity and Distress Scale–Arm tool

See appendix D for full evidence tables.

5.2 Summary of the effectiveness evidence

Table 31 Education on SLD + lifestyle recs vs usual care

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb volume) (lower scores are better)				
Excess arm volume change (%) +- MID -5.27 to 5.27 follow-up: 6 months	MD **6 lower** (14.34 lower to 2.34 higher)	41 (Ligabue 2019)	Low	Could not differentiate
Excess hand volume change (%) +- MID -7.09 to 7.09 follow-up: 6 months	MD **10 lower** (17.89 lower to 2.11 lower)	41 (Ligabue 2019)	Low	Favours education on SLD & lifestyle recommendations
Patient-reported outcomes (lower scores are better)				
Pain (NPRS) +- MID -1.54 to 1.54 follow-up: 6 months	MD **2.2 lower** (3.93 lower to 0.47 lower)	41 (Ligabue 2019)	Very low	Favours education on SLD & lifestyle recommendations

Table 32 Group education vs control

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (lower scores are better)				
Quality of life-psychosocial (LLIS) +- MID -0.15 to 0.15 follow-up: 3 months	MD **0.03 lower** (0.16 lower to 0.1 higher)	67 (Omidi 2019)	Very low	Could not differentiate
Quality of life-functional (LLIS) +- MID -0.14 to 0.14 follow-up: 3 months	MD **0.13 lower** (0.25 lower to 0.01 lower)	67 (Omidi 2019)	Very low	Favours group education

Table 33 Social network-based education vs control

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (lower scores are better)				
Quality of life-psychosocial (LLIS) +- MID -0.15 to 0.15 follow-up: 3 months	MD **0.05 higher** (0.08 lower to 0.18 higher)	69 (Omidi 2019)	Very low	Could not differentiate

Table 34 Group-based education vs social network education

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (lower scores are better)				
Quality of life-psychosocial (LLIS) +-MID -0.13 to 0.13 follow-up: 3 months	MD **0.08 lower** (0.19 lower to 0.03 higher)	66 (Omidi 2019)	Very low	Could not differentiate

1

5.3 Narrative summary of the effectiveness evidence

For some of the evidence, it was not possible to complete GRADE and as such evidence statements were produced to summarise the evidence narratively.1 RCT (Ridner et al., 2020) at high risk of bias (n=160) found that:

- A web-based multimedia intervention (WBMI) had a significantly lower completion rate compared to an educational pamphlet (58.8% vs 77.5%, p=0.011).
- There were no statistically significant differences between the WBMI and pamphlet groups in reducing most symptoms at 1 or 12 months post-intervention (effect sizes 0.05-0.28, p>0.05), as measured by the Lymphoedema Symptom Intensity and Distress Scale–Arm (LSIDS-A).
- The WBMI group showed a greater reduction in biobehavioral (mood) symptoms compared to the pamphlet group at 1 month (25% of WBMI participants had ≤2 mood symptoms vs. no reduction in the pamphlet group, effect size=0.53, p<0.05). This difference was maintained at 12 months (25% of WBMI participants had ≥2 symptom reduction vs. 25% of pamphlet participants with ≥1 symptom reduction, effect size=0.47, p<0.05).
- There were no significant differences between groups in function as measured by the Quick-Disabilities of Arm, Shoulder, and Hand (QuickDASH) scale (median change from baseline at 12 months: -2.3 for both groups, effect size=-0.04, p>0.05).
- The WBMI required significantly more time to complete than the pamphlet (median 525 vs 60 minutes, p<0.001).

6 Pneumatic compression devices

6.1 Summary of studies included in the evidence

Table 35 Summary of included studies

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Randomised Controlled Trials (RCTs)					
Rockson et al. (2022) N = 50 Location: United States	Women with unilateral breast cancer-related lymphoedema were included. Women with any systemic disorder, those with lipoedema, active or recurrent cancer were excluded. Follow-up: 28 days.	NPCD	APCD	• Limb volume • QoL (LYMQoL)	Moderate
Sanal-Toprak et al. (2019) N=46 Location: Turkey	Women with moderate-severe lymphoedema were included. Women with any systemic disorder, those with active infections or metastases were excluded. Follow-up: 3 months	IPC + CB + exercise	MLD + CB + exercise	• ROM	High

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Uzkeser et al. (2013) N=25 Location: Turkey	Women with upper limb lymphoedema, caused by BC and its treatment. No restrictions by BC stage, lymphoedema grade, age, or country.	IPC + usual care	Usual care (includes: skin care, MLD, compression, exercises)	• Limb volume • ROM • Shoulder dysfunction (CMS) • Pain (VAS)	Moderate

Abbreviations: APCD: Advanced Pneumatic Compression Device; CB: compression bandaging; CMS: Constant Murley Score; IPC; Intermittent Pneumatic Compression; MLD: Manual Lymphatic Drainage; NPCD; Non-Pneumatic Compression Device; QoL: Quality of Life; ROM: Range of Motion; VAS: Visual Analogue Scale.

See appendix D for full evidence tables.

6.2 Summary of the effectiveness evidence

Table 36 Novel pneumatic compression devices vs traditional advanced pneumatic compression devices

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Lymphoedema (limb volume) (lower scores are better)				
Arm oedema volume change (%) +- MID -34.97 to 34.97 follow-up: 28 days	MD **36.9 higher** (3.26 lower to 77.06 higher)	50 (Rockson 2022)	Very low	Could not differentiate
Quality of life (higher scores are better)				
Quality of life (LYMQOL) +- MID -0.90 to 0.90 follow-up: 28 days	MD **2.45 higher** (1.48 higher to 3.42 higher)	50 (Rockson 2022)	Low	Favours novel pneumatic compression device

Table 37 Intermittent pneumatic CB + bandaging vs MLD + CB

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Lymphoedema (arm mobility) (higher scores are better)				
Shoulder abduction (standard goniometry degrees) +- MID -10.57 to 10.57 follow-up: 3 months	MD **0.38 lower** (11.7 lower to 10.94 higher)	46 (Sanal-Toprak 2018)	Very low	Could not differentiate

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Shoulder adduction (standard goniometry degrees) +- MID -3.71 to 3.71 follow-up: 3 months	MD **1.85 lower** (5.91 lower to 2.21 higher)	46 (Sanal-Toprak 2018)	Very low	Could not differentiate
Shoulder flexion (standard goniometry degrees) +- MID -9.96 to 9.96 follow-up: 3 months	MD **1.88 higher** (9.56 lower to 13.32 higher)	46 (Sanal-Toprak 2018)	Very low	Could not differentiate
Shoulder extension (standard goniometry degrees) +- MID -4.75 to 4.75 follow-up: 3 months	MD **2.8 lower** (6.97 lower to 1.37 higher)	46 (Sanal-Toprak 2018)	Very low	Could not differentiate
Shoulder internal rotation (standard goniometry degrees) +- MID -4.57 to 4.57 follow-up: 3 months	MD **1.12 lower** (5.21 lower to 2.97 higher)	46 (Sanal-Toprak 2018)	Very low	Could not differentiate
Shoulder external rotation (standard goniometry degrees) +- MID -8.1 to 8.1 follow-up: 3 months	MD **2.93 higher** (5.08 lower to 10.94 higher)	46 (Sanal-Toprak 2018)	Very low	Could not differentiate

6.3 Narrative summary of the effectiveness evidence

For some of the evidence, it was not possible to complete GRADE and as such evidence statements were produced to summarise the evidence narratively.

1. 1 RCT (Uzkeser et al., 2013) at low risk of bias (n=25) found that:
    - pneumatic compression therapy significantly improved shoulder flexion (median 152° to 170°, p=0.018), abduction (130° to 165°, p=0.017), and internal rotation (57° to 70°, p=0.01) at 1-month follow-up compared pre-treatment scores.
    - Manual lymphatic drainage combined with bandaging and exercise (control group) significantly improved shoulder flexion (median 160° to 170°, p=0.018), abduction (160° to 170°, p=0.018), internal rotation (60° to 80°, p=0.008), and external rotation (75° to 90°, p=0.041) at 1-month follow-up compared to pre-treatment scores.
    - pneumatic compression therapy significantly reduced shoulder dysfunction (as measured by the Constant-Murley scale; median 54 to 59, p=0.002) and self-reported pain (as measured by the Visual Analogue Scale; 20 to 5, p=0.01) at 1-month follow-up compared to pre-treatment scores.
    - manual lymphatic drainage combined with bandaging and exercise (control group) significantly reduced shoulder dysfunction (as measured by the Constant-Murley scale; 52 to 57, p=0.001) and self-reported pain (as measured by the Visual Analogue Scale; 40 to 20, p=0.004) at 1-month follow-up compared to pre-treatment scores.
    - no statistically significant differences between pneumatic compression therapy and manual lymphatic drainage combined with bandaging and exercise in terms of improving shoulder range of motion, reducing shoulder dysfunction, or reducing self-reported pain either immediately after treatment or at 1-month follow-up.

7 Complementary therapy

7.1 Summary of studies included in the evidence

Table 38 Summary of included studies

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Systematic review					
Gao et al. (2021) 14 RCTs	Women with BCRL and its treatment procedures (surgery and/or radiotherapy). No restrictions by BC stage, lymphoedema grade, age, or country.	Acupuncture or moxibustion Only needle acupuncture was included for acupuncture studies and moxibustion studies had to burn *Artemisia vulgaris* moxa.	Any other treatment except acupuncture or moxibustion.	• Changes in oedema (limb volume/circumference, UEL index) • Swelling/pain • ROM	Moderate

Abbreviations: BCRL – breast cancer-related lymphoedema, , ROM – range of motion, UEL – Upper Extremity Lymphoedema

Table 39: Included studies in Gao et al. 2021

Authors	Experimental group	Course of treatment	Retention time	Control group	Outcome measures
Ba et al. (2019)	AM	Qid lasts 14 d (Nt = 7)	30 min	Diosmin tablets 450 mg, Bid for 14 d (Nt = 28).	The circumference at 10, 20, 30, and 40 cm above the ulnar styloid process.

Authors	Experimental group	Course of treatment	Retention time	Control group	Outcome measures
N= 30/28 Location: China					
Bao et al. (2018) N= 40/42 Location: USA	Acupuncture	2 × per week for 6 wk (Nt = 12)	30 min	Wait-list. 2 × per week for 6 wk (Nt = 12).	1. The maximum difference between the circumference of the affected arm and that of the contralateral arm. 2.Bioimpedance.
Huang et al. (2014) N= 31/31 Location: China	Moxibustion + Functional exercises	5 × per week for 6 wk (Nt = 30)	20 min	Functional exercises for 6 wk (Nt-UK) + Hydrochlorothiazide 50 mg, Tid for 6 wk (Nt = 126) + Spironolactone 20 mg, Tid for 6 wk (Nt = 126).	The circumference at elbow crease.
Jiao et al. (2017) N=15/15 Location: China	AM	5 × per week for 9 wk (Nt = 45)	20 min	Usual care for 9 wk (Nt-UK).	The circumference at elbow crease.

Authors	Experimental group	Course of treatment	Retention time	Control group	Outcome measures
Liu et al. (2019a) N= 40/40 Location: China	AM	Qid lasts 28 d (Nt = 14)	30 min	Diosmin tablets 900 mg, Tid for 28 d (Nt = 84).	1. EIL (10 cm proximal to elbow crease). 2. Shoulder joint ROM. 3. QOL-UK.
Liu et al. (2019b) N= 30/30 Location: China	AM + Manual lymphatic drainage	Qd for 42 d (Nt = 42)	30 min	Manual lymphatic drainage, 10 min at a time, Tid for 42 d (Nt = 126).	1. The difference between the circumference of the affected arm and that of the contralateral arm (10 cm proximal to elbow crease). 2. VAS for swelling 3.QOL-UK.
Shen et al. (2019) N= 24/24 Location: China	Moxibustion.	6 × per month for 2 mo (Nt = 12)	5-15 min	Pneumatic circulation, 30 min at a time, 6 × per month for 2 mo (Nt = 12).	1. The circumference at wrist crease, 10 cm proximal to wrist crease, elbow crease, and 10cm proximal to elbow crease. 2 VAS for swelling. 3. EORTC - QLQ.
Smith et al. (2014) N= 10/10	Acupuncture	2 × per week for 4 wk, then 1 × per week for 4 wk (Nt = 12)	20 min	Usual care for 8 wk (Nt-UK).	Bioimpedance

Authors	Experimental group	Course of treatment	Retention time	Control group	Outcome measures
Location: Australia					
Wang et al. (2019) N= 24/24 Location: China	Moxibustion	Qid lasts 28 d (Nt = 14)	30 min	Pneumatic circulation, 30 min at a time, Qid lasts 28 d (14 total).	1. The circumference at wrist crease, 10cm proximal to wrist crease, elbow crease, and 10 cm proximal to elbow crease. 2.The affected limb circumference mean value. 3. VAS for swelling
Wu et al. (2018) N= 30/30 Location: China	Acupuncture + Functional exercises	Qd for 28 d (Nt = 28)	UK	Functional exercises, 3 to 4 times a week, for 4 wk (Nt = 12-16).	1. The difference between the total circumference (add the values measured at 20, 15, 10, and 5 cm above and below the elbow, as well as at the middle of the palm and the wrist) of the affected arm and that of the contralateral arm. 2. VAS for pain.
Yao et al. (2016) N= 15/15 Location: China	AM	Qid lasts 30 d (Nt = 15)	30 min	Diosmin tablets 900 mg, Tid for 30 days (Nt = 90).	1. EIL (wrist crease, 10 cm proximal to wrist crease, elbow crease, 10 cm proximal to elbow crease, and overall). 2. Shoulder joint ROM. 3. QLQ- Likert
Zhan and Lou (2017) N=30/30	Acupuncture + Functional exercises	Qd for 28 d (Nt = 28)	UK	Functional exercises, 3 to 4 times a week, for 4 wk (Nt = 12-16).	1. The difference between the total circumference (the sum of the measured values at the elbow and 10 cm, 20 cm, 30 cm and 40 cm above the elbow) of the affected arm and that of the contralateral arm.

Authors	Experimental group	Course of treatment	Retention time	Control group	Outcome measures
Location: China					2. VAS for pain.
Zhang et al. (2020) N= 14/14 Location: China	Moxibustion	2 × per week for 4 wk (Nt = 8)	30 min	Pneumatic circulation, 30 min at a time, 2 × per week for 4 wk (Nt = 8).	1. The affected limb circumference mean value. 2. VAS for swelling. 3. QLQ - CCC.
Zhao et al. (2012) N= 46/46 Location: China	AM	5 × per week for 3 wk (Nt = 15)	20 min	Usual care for 3 wk (Nt-UK).	The circumference at elbow crease.

Abbreviations: AM: Acupuncture and Moxibustion; Qid: four times a day; Qd once a day; Nt: number of treatments; Tid; three times a day; UK: Unknown

See appendix D for full evidence table.

7.2 Summary of the effectiveness evidence

Table 40 Moxibustion vs pneumatic circulation

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Mean arm circumference (cm)+- MID -0.8 to 0.8	MD **0.66 cm lower** (2.63 lower to 1.31 higher)	76 (Gao 2021)	Very low	Could not differentiate
Circumference at wrist crease (cm) +-MID -0.55 to 0.55	MD **0.2 cm lower** (1.25 lower to 0.85 higher)	96 (Gao 2021)	Very low	Could not differentiate
Circumference at proximal 10cm of wrist crease (cm) +-MID -1.2 to 1.2	MD **0.17 cm lower** (2.13 lower to 1.78 higher)	96 (Gao 2021)	Very low	Could not differentiate
Circumference at proximal 10cm of elbow crease (cm) +- MID -1.3 to 1.3	MD **0.48 cm lower** (5.07 lower to 4.12 higher)	96 (Gao 2021)	Very low	Could not differentiate
Circumference at elbow crease (cm) +- MID -1.4 to 1.4	MD **0.24 cm lower** (3.44 lower to 2.96 higher)	96 (Gao 2021)	Very low	Could not differentiate

Table 41 Acupuncture plus moxibustion vs usual care

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Circumference at elbow crease (cm) +- MID -1.4 to 1.4	MD **7.26 cm lower** (8.3 lower to 6.21 lower)	122 (Gao 2021)	Low	Favours acupuncture plus moxibustion

Table 42 Acupuncture plus moxibustion vs diosmin

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (lower scores are better)				
Effective index for upper limb lymphoedema: +- MID -4 to 4	MD **27.68 cm higher** (24.82 higher to 30.53 higher)	90 (Gao 2021)	Low	Favours diosmin

8 Psychological interventions

8.1 Summary of studies included in the evidence

No evidence was identified that met the criteria in the protocol for psychological interventions for managing breast cancer-related lymphoedema.

9 Kinesiotaping

9.1 Summary of studies included in the evidence

Table 43 Summary of included studies included

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Systematic review					
Kasawara et al. (2018) 7 RCTs N=303	Women with upper limb lymphoedema, caused by BC and its treatment. No restrictions by BC stage, lymphoedema grade, age, or country.	KT	No intervention or compression bandaging and complex decongestive therapy	• Severity of lymphoedema (change in limb volume/circumference) • Quality of life	Moderate
Randomised controlled trials					
Basoglu et al. (2021) N=36 Location: Turkey	Women with moderate, unilateral breast cancer-related lymphoedema. Women with mild/severe lymphoedema, pre-existing shoulder disability, BMI >35 kg/m^2 were excluded. Follow-up: 1 month	KT + skin care + exercise	CDT (including compression bandage, MLD, skin care and therapeutic exercises)	• Lymphoedema (Upper extremity circumference, arm volume) • Arm function (grip strength, arm and shoulder function DASH scores) • Arm function (Q-DASH) • QoL (FACT-B, LYMQoL)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
Ergin et al. (2019) N=32 Location: Turkey	Women with severe, unilateral breast cancer-related lymphoedema. Women with paralysis on part of the arm were excluded. Follow-up: 1 month	KT + CDT	CDT (including compression bandage, MLD, skin care and therapeutic exercises)	• Limb volume	Moderate
Ozsoy-Unbol et al. (2019) N=35 Location: Turkey	Women with mild, unilateral breast cancer-related lymphoedema. Participants must have completed 3 months of follow-up post breast surgery and did not receive lymphoedema treatment before. Participants must have completed 3 months of follow-up post breast surgery and did not receive lymphoedema treatment before. Women were also excluded if they have uncontrolled systemic and psychiatric diseases or were undergoing diuretic therapy.	KT	Compression garments	• Range of motion • Patient reported outcomes (pain, heaviness, tightness VAS scores)	Moderate

Study details	Population	Intervention	Comparator	Outcomes	Risk of bias
	Follow-up: 3 months				
Selcuk-Yilmaz (2023) N=30 Location: Turkey	Women with moderate, unilateral lymphoedema and stage I-III breast cancer were included. Women with advanced breast cancer (stage IV), bilateral breast cancer and lymphoedema were excluded. Follow-up: 3 months	KT	MLD	• Arm circumference • Volume • Disability (Q-DASH) • Range of motion (ROM) • QoL (LYMQoL) • Pain (PDQ)	Moderate

1

Tantawy (2019) N=59 Location: Egypt	Women with moderate-severe, unilateral breast cancer-related lymphoedema. Participants must have completed 3 months of follow-up post breast surgery and did not receive lymphoedema treatment before. Follow-up: No regular follow-up	KT	Compression garments	• Limb circumference • Handgrip strength • Disability (SPADI) • QoL (EORTC-QLQC30)	Moderate
Torres-Lacomba (2020) N=146 Location: Spain	Women with moderate, unilateral breast cancer-related lymphoedema. Participants must have completed 3 months of follow-up post breast surgery and did not receive lymphoedema treatment before. Follow-up: No regular follow-up depends on patient adherence.	KT+MLD	Bandaging + MLD	• Limb volume • Patient reported outcomes (comfort)	High

Abbreviations: CDT: Complete Decongestive Therapy; EORTC: European Organisation for Research and Treatment of Cancer; KT: Kinesiotaping; MLD: Manual Lymphatic Drainage; QoL: Quality of Life; Q-DASH: Quick Disabilities of Arm, Shoulder and Hand; ROM: Range of Motion; VAS: Visual Analogue Scale.

Table 44: Included studies in Kasawara et al. 2018

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Malicka et al. (2014) N= 28	KT	Control (no anti-oedema treatments)	4 weeks	• Circumference differences
Melgaard et al. (2016) N= 10	KT + standard treatment	Standard treatment + bandaging	4 weeks	• Circumference, Quality of Life
Pekyavas et al. (2014) N= 45	Arm 1: CDT + Bandage + KT Arm 2: CDT + KT	CDT +Bandage	4 weeks	• Lymphoedema volume, pain, heaviness, tension, stiffness, numbness, QoL
Pop et al. (2014) N= 44	KT + exercise	Control group (exercise)	3 weeks	• Reduction in lymphoedema, grip strength, range of motion
Smykla et al. (2013) N=65	KT	Multilayered compression therapy	4 weeks	• Reduction in lymphoedema
Taradaj et al. (2016)	Arm 1: KT Arm 2: Quasi KT	Bandaging	4 weeks	• Limb volume, shoulder range of motion, grip strength

N= 70				
Tsai et al. (2009) N= 41	Modified CDT + KT	CDT + bandage	12 weeks	• Limb volume, pain, heaviness, tightness, HRQoL

See appendix D for full evidence tables

9.2 Summary of the effectiveness evidence

Table 45 KT vs control

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb circumference and volume) (lower scores are better)				
Lymphoedema reduction +-MID 0.5 follow-up: range 4 weeks to 3 months	SMD **0.04 SD higher** (0.24 lower to 0.33 higher)	196 (Kasawara 2018)	Moderate	Could not differentiate

Table 46 KT vs usual care

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb circumference and volume) (lower scores are better)				
Lymphoedema reduction +- MID 0.5 follow-up: range 4 weeks to 3 months	SMD **0.12 SD higher** (0.16 lower to 0.41 higher)	199 (Kasawara 2018)	Moderate	Could not differentiate

Table 47 KT vs CDT

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb circumference and volume) (lower scores are better)				
Arm circumference change (cm) +- MID - 2.1 to 2.1 follow-up: 1 months	MD **1.3 higher** (0.81 higher to 3.41 higher)	36 (Basoglu 2021)	Low	Favours CDT
Arm volume change (ml) +- MID - 53.95 to 53.95 follow-up: 1 months	MD **1.58 lower** (213.14 higher to 103.46 lower)	36 (Basoglu 2021)	Low	Could not differentiate
Lymphoedema (arm function) (higher scores are better for grip strength; lower scores are better for DASH)				
Grip strength change (kg) +- MID - 0.75 to 0.75 follow-up: 1 months	MD **0.4 lower** (1.15 lower to 0.35 higher)	36 (Basoglu 2021)	Low	Could not differentiate
Arm and shoulder function DASH scores +- MID - 2.85 to 2.85 follow-up: 1 months	MD **2.1 lower** (8.05 lower to 3.85 higher)	36 (Basoglu 2021)	Very low	Could not differentiate
Quality of life (higher scores are better)				
Quality of Life FACT-B scores +- MID -7 to 8 follow-up: 1 months	MD **1.8 lower** (6.66 lower to 3.06 higher)	36 (Basoglu 2021)	Moderate	Could not differentiate

Table 48 KT vs compression garment (Ozsoy-Unbol 2019)

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (arm mobility) (higher scores are better)				
Shoulder abduction (standard goniometry degrees) +- MID - 9.13 to 9.13 follow-up: 3 months	MD **1.18 lower** (15.36 lower to 13 higher)	35 (Ozsoy-Unbol 2019)	Very low	Could not differentiate
Shoulder adduction (standard goniometry degrees) +- MID - 3.51 to 3.51 follow-up: 3 months	MD **1.15 higher** (2.49 lower to 4.81 higher)	35 (Ozsoy-Unbol 2019)	Low	Could not differentiate
Shoulder flexion (standard goniometry degrees) +- MID - 7.64 to 7.64 follow-up: 3 months	MD **4.06 higher** (9.19 lower to 17.29 higher)	35 (Ozsoy-Unbol 2019)	Very low	Could not differentiate
Shoulder extension (standard goniometry degrees) +- MID -2.93 to 2.93 follow-up: 3 months	MD **0.33 lower** (4.6 lower to 3.94 higher)	35 (Ozsoy-Unbol 2019)	Very low	Could not differentiate
Shoulder internal rotation (standard goniometry degrees) +- MID - 7.04 to 7.04 follow-up: 3 months	MD **5.62 higher** (3.27 lower to 14.51 higher)	35 (Ozsoy-Unbol 2019)	Low	Could not differentiate
Shoulder external rotation (standard goniometry degrees) +- MID - 2.85 to 2.85 follow-up: 3 months	MD **1.54 higher** (5.49 lower to 8.57 higher)	35 (Ozsoy-Unbol 2019)	Very low	Could not differentiate
Patient-reported outcomes (lower scores are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Pain VAS +- MID -0.57 to 0.57 follow-up: 3 months	MD **0.23 higher** (0.61 lower to 1.07 higher)	35 (Ozsoy-Unbol 2019)	Very low	Could not differentiate
Tightness VAS +- MID -0.59 to 0.59 follow-up: 3 months	MD **0.25 lower** (1.1 lower to 0.6 higher)	35 (Ozsoy-Unbol 2019)	Very low	Could not differentiate
Heaviness VAS +- MID - 0.56 to 0.56 follow-up: 3 months	MD **0.25 lower** (0.49 lower to 0.6 higher)	35 (Ozsoy-Unbol 2019)	Low	Could not differentiate

1

2 **Table 49 KT vs compression garments (Tantawy 2019)**

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Lymphoedema (limb circumference) (lower scores are better)				
Limb circumference (cm) +- MID -8.06 to 8.06 follow-up: 3 weeks	MD **15.2 lower** (22.78 lower to 7.62 lower)	59 (Tantawy 2019)	Very low	Favours kinesiotaping
Lymphoedema (arm function) (lower scores are better)				
Disability SPADI scores +- MID -34.21 to 34.21 follow-up: 3 weeks	MD **82.19 lower** (107.33 lower to 57.05 lower)	59 (Tantawy 2019)	Low	Favours kinesiotaping

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Handgrip strength change (kg) +- MID - 2.82 to 2.82 follow-up: 3 weeks	MD **21.25 higher** (14.87 higher to 27.63 higher)	59 (Tantawy 2019)	Low	Favours compression garments
Quality of life (higher scores are better)				
Quality of Life EORTC-QLQC30 +- MID - 8.52 to 12 follow-up: 3 weeks	MD **10.6 higher** (2.39 higher to 18.81 higher)	59 (Tantawy 2019)	Very low	Favours kinesiotaping

1

2 **Table 50 KT vs MLD**

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Lymphoedema (limb volume) (lower scores are better)				
Arm volume change (%) +- MID - 5.34 to 5.34 follow-up: 3 months	MD **2.1 lower** (8.63 lower to 4.43 higher)	30 (Selcuk-Yilmaz 2023)	Very low	Could not differentiate
Quality of life (higher scores are better)				
Quality of life scores LYMQoL +- MID - 3.85 to 3.85 follow-up: 3 months	MD **3.97 lower** (11.26 lower to 3.32 higher)	30 (Selcuk-Yilmaz 2023)	Very low	Could not differentiate
Lymphoedema (arm function) (lower scores are better)				

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Arm function Q-DASH +- MID -8 to 8 follow-up: 3 months	MD **8.13 lower** (22.84 lower to 6.58 higher)	30 (Selcuk-Yilmaz 2023)	Very low	Could not differentiate

1

9.3 Narrative summary of the effectiveness evidence

For some of the evidence, it was not possible to complete GRADE and as such evidence statements were produced to summarise the evidence narratively.

Bandaging vs CDT

Lymphoedema (excess limb volume)

1. 1 RCT (Torres-Lacomba et al., 2020) at high risk of bias (n=150) found that compared to adhesive bandages and kinesio tape, cohesive bandages significantly reduced excess limb volume after 3 weeks of complex decongestive therapy (median reduction: 46.3% vs. 21.7% and 4.9%, respectively, p<0.001) in women with breast cancer-related lymphoedema.
2. 1 RCT (Torres-Lacomba et al., 2020) at high risk of bias (n=150) found that compared to traditional multilayer bandages, simplified multilayer bandages significantly reduced excess limb volume after 3 weeks of complex decongestive therapy (median reduction: 59.5% vs. 36.3%, p<0.001) in women with breast cancer-related lymphoedema.

Patient reported outcomes

3. 1 RCT (Torres-Lacomba et al., 2020) at high risk of bias (n=150) found that compared to traditional multilayer bandages, simplified multilayer bandages significantly improved perceived comfort (median score: 5.0 vs. 6.7 on a 0-10 scale, p<0.001) after 3 weeks of complex decongestive therapy in women with breast cancer-related lymphoedema.
4. 1 RCT (Torres-Lacomba et al., 2020) at high risk of bias (n=150) found that compared to multilayer, simplified multilayer, cohesive, and adhesive bandages kinesio tape did not significantly reduce excess limb volume (median reduction: 4.9% vs. 36.3%, 59.5%, 46.3%, and 21.7%, respectively, p<0.001) but significantly improved perceived comfort (median score: 1.4 vs. 6.7, 5.0, 4.8, and 4.3 on a 0-10 scale, respectively, p<0.001) after 3 weeks of complex decongestive therapy in women with breast cancer-related lymphoedema

10 Wired vs non-wired bras, foam inserts, spaghetti foam

10.1 Summary of studies included in the evidence

No evidence was identified that met the criteria in the protocol for bras, foam inserts or spaghetti foam for managing breast cancer-related lymphoedema.

11 Surgical interventions

11.1 Summary of studies included in the evidence

Table 51 Summary of included studies

Study details	Population	Intervention (s)	Comparator	Outcomes	Risk of bias
Systematic review					
Winters et al. (2021) 8 RCTs 9 cohort studies	Women >18 years with breast cancer-related lymphoedema, caused by BC and its treatment procedures (surgery and/or radiotherapy). No restrictions by BC stage, lymphoedema grade, age, or country.	Vascularised lymph node transfer Lymphaticovenous Anastomosis	Any other treatment (including conservative management, microsurgical breast reconstruction)	• Changes in oedema (limb volume/upper extremity lymphoedema index score) • QoL • Skin infections • Complication rates	High
Randomised controlled trial					
Jonis et al. (2024) N= 46 Location: The Netherlands	Women >18 years treated for early breast cancer and have mild-moderate breast cancer-related lymphoedema. People with severe, bilateral and primary congenital lymphoedema were excluded. Males were also excluded from this study.	Lymphaticovenous Anastomosis	Conservative therapy (includes skin care, manual lymphatic drainage, exercises and compression)	• Changes in oedema (limb volume reduction, circumference reduction) • Adverse events • QoL (Lymph-ICF)	Low

Abbreviations: BC – breast cancer, NA: Not applicable; QoL – quality of life

Table 52: Included studies in Winters et al. 2021

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Akita et al. (2017) N= 27	VLNT + DIEP flap (from groin to axilla)	VLNT alone	19.1 ± 1.7 months	• UEL index reduction, compression garment usage
Aljaaly et al. (2018) N= 15	VLNT (from submental to wrist)	NA (cohort)	17 months	• Arm volume difference • QoL • Infections
Becker et al. (2006) N= 24	VLNT (from groin to axilla)	NA (cohort study)	8.3 years	• Arm perimeter difference • Infections
De Brucker et al. (2016) N= 25	VLNT (from groin to axilla)	NA (cohort)	29 ± 14 months	• QoL • Incidence of lymphoedema • Infections • Compression garment use
Dionyssiou et al. (2016) N= 36	VLNT (from groin to axilla)	Physiotherapy alone	18 months	• Arm volume difference • Infections • Pain/heaviness/function
Engel et al. (2017) N= 87	LVA/VLNT ± breast reconstruction (from	Complete decongestive therapy	47.8 months	• Arm volume difference • Infections

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
	groin/submental to wrist/elbow)			
Gharb et al. (2011) N= 11	VLNT (from groin to wrist/forearm)	Free groin flap	39.5 months	• Arm volume difference • Complications • Secondary procedures • Lymphoedema symptoms
Granzow et al. (2014) N= 8 LVA N= 8 VLNT	LVA VLNT (from groin to axilla)	Suction assisted protein lipectomy	25 months	• Volume reduction • Compression garments use • Lymphoedema therapy • Infections
Gratzon et al. (2017) N= 50 Location: United States	VLNT (from lower abdomen/chest wall/neck to axilla)	NA (cohort study)	12 months	• Arm volume difference • Pain/heaviness • QoL • Infections
Lin et al. (2009) N= 13	VLNT (from groin to wrist)	NA (cohort study)	56.3 ±27.1 months	• Arm volume difference, morbidity
Liu et al. (2018) N= 30	VLNT (from groin to wrist)	NA (cohort study)	22.1 ± 7.8 months	• Arm volume difference • Lymphatic drainage
Maruccia et al. (2019) N= 39	VLNT ± scar release (from groin/gastroepiploic to wrist)	VLNT	30.5 months	• Arm volume difference • QoL • Infections

Authors	Experimental group	Control group	Duration/follow-up	Outcome measures
Montag et al. (2019) N= 24	VLNT (from groin to axilla) + DIEP	VLNT (from groin to wrist) + inguinal lymph node flap	18 months	• Arm volume difference • Infections
Nguyen et al. (2015) N= 29	VLNT (from groin to axilla) + breast reconstruction	NA (cohort study)	11 months	• Arm volume difference • Complications
Patel et al. (2014) N= 25	VLNT (from groin/submental to wrist)	NA (cohort study)	12 months	• Limb circumference • Infections • QoL
Saaristo et al. (2012) N= 9	VLNT + breast reconstruction (from groin to axilla)	Breast reconstruction	6 months	• Arm volume difference • Incidence of lymphoedema/seroma
Yang et al. (2017) N= 10	VLNT + breast reconstruction (from groin to axilla)	Physiotherapy	12 months	• Arm circumference • Upper limb movement • Pain/swelling/numbness

Abbreviations: DIEP- deep inferior epigastric perforator; LVA – Lymphaticovenous anastomosis; NA: Not applicable; QoL: Quality of life; UEL – Upper extremity lymphoedema; VLNT – Vascularised lymph node transfer

See appendix D for full evidence tables.

11.2 Summary of the effectiveness evidence

Table 53 LVA vs CDT

Outcomes	Effect estimate (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Quality of life (lower scores are better)				
Quality of life scores - Lymph-ICF +-MID - 9.1 to 9.1 follow-up: 6 months	MD **5.92 lower** (14.31 lower to 2.47 higher)	92 (Jonis 2024)	Low	Could not differentiate
Lymphoedema (limb volume and circumference) (lower scores are better)				
Volume reduction (ml) +-MID -94.99 to 94.99 follow-up: 6	MD **13.94 lower** (92.2 lower to 65.02 higher)	92 (Jonis 2024)	Moderate	Could not differentiate
Limb circumference (upper extremity lymphoedema index) +-MID - 7.3 to 7.3 follow-up: 6 months	MD **2.68 SD higher** (3.29 lower to 8.65 higher)	92 (Jonis 2024)	Low	Could not differentiate
Adverse events (RR of less than 1 represents fewer adverse events)				
Adverse events MID +/- 0.8 to 1.25 follow-up: 6 months	**RR 0.60** (0.15 to 2.37)	92 (Jonis 2024)	Low	Could not differentiate
Serious Adverse events MID +/- 0.8 to 1.25 follow-up: 6 months	**RR 3.07** (0.12 to 77.24)	92 (Jonis 2024)	Very low	Could not differentiate

11.3 Narrative summary of the effectiveness evidence

For some of the evidence, it was not possible to complete GRADE and as such evidence statements were produced to summarise the evidence narratively.

1. One systematic review of 8 RCTs and 9 cohort studies (Winters et al., 2021), at high risk of bias found data from:
    - 8 studies at unclear risk of bias (N not reported) found that vascularised lymph node transfer (VLNT) reduced the arm volume difference between healthy and affected arms by an average of 40.31% (95% CI 31.44% to 49.17%).
    - 5 studies at unclear risk of bias (N not reported) found that VLNT significantly improved quality of life scores on various assessment tools, but pooled analysis was not possible due to heterogeneity in measurement methods.
    - 3 studies at unclear risk of bias (N not reported) found that VLNT significantly reduced annual skin infection rates compared to pre-surgical rates.
    - 3 studies at unclear risk of bias (N=60) found that 45% of patients were able to discontinue compression garment use after VLNT.
    - 16 studies at unclear risk of bias (N=369 for recipient site, N=338 for donor site) reported overall complication rates of 12.1% at the donor site and 7.3% at the recipient site following VLNT.

12 Economic evidence

12.1 Included studies

A search was performed to identify published economic evaluations of relevance to this guideline update (Appendix G) This search retrieved 121 studies. Based on title and abstract screening, 118 of the studies were excluded for this question. Following the full-text review, we excluded a further study. Thus, the review for this question includes 2 studies from the existing literature.

12.2 Excluded studies

1 study was included due to inapplicability and very serious limitations. See Appendix J – Excluded studies for detailed reasons for exclusion.

12.3 Summary of included economic evidence

Table 54: Lymphovenous bypass vs complete decongestive therapy

Study	Applicability	Limitations	Interventions	Incremental			Uncertainty[1]
				Cost	Effects (QALYs)	ICER (Cost/ QALY)	
Linden 2019 (Canada)	Partially applicable (Table 95, Appendix H – Economic evidence tables)	Potentially serious limitations (Table 96, Appendix H – Economic evidence tables)	1: Complete decongestive therapy 2: Lymphovenous bypass	2-1: -£1,986	NA	NA	Several one-way sensitivity analyses conducted. Only in 37% of the simulated scenario complete decongestive therapy was cheaper than surgery. No probabilistic analysis was done.

Table 55: Complete decongestive therapy with Kinesio tape vs complete decongestive therapy with low-stretch bandages

Study	Applicability	Limitations	Interventions	Incremental			Uncertainty[1]
				Cost	Effects (QALYs)	ICER (Cost/QALY)	
Melgaard 2016 (Denmark)	Partially applicable (Table 95, Appendix H – Economic evidence tables)	Potentially serious limitations (Table 96, Appendix H – Economic evidence tables)	1: Complete decongestive therapy with low-stretch bandages 2: Complete decongestive therapy with Kinesio tape	2-1: -£558	NA[(a)]	NA	No sensitivity analysis was conducted.

a) see Table 55 in Appendix H – Economic evidence tables for lymphoedema circumference outcomes

12.4 Economic model

No economic model was developed for this review question.

12.5 Unit costs

Table 56 Service planning recommended guide for treatment pathways

Treatment (TX) Category and elements	A. SIMPLE/EARLY Mild lymphoedema with no complications requiring compression hosiery and education only		B.MODIFIED Moderate lymphoedema requiring TX, possibly 1 element of Decongestive Lymphoedema Treatment (DLT), then maintenance		C. COMPLEX Complex lymphoedema requiring intensive TX (DLT)		D. VERY COMPLEX Very Complex lymphoedema requiring intensive, possibly repeated DLT and prolonged TX	
Initial Assessment Cost	3 units £61.50	£184.50	3 units £61.50	£184.50	3 units £61.50	£184.50	3 units £61.50	£184.50
TX Schedule Costs	2 units £61.50 to include	£123	1 unit initial TX £61.50 + 20 units modified	£1291.50	1 unit initial TX £61.50 + 60 units DLT per	£3751.50	1 unit initial TX £61.50 + 200 units modified	£61.50 + negotiated cost

Treatment (TX) Category and elements	**A. SIMPLE/EARLY Mild lymphoedema with no complications requiring compression hosiery and education only**		**B.MODIFIED Moderate lymphoedema requiring TX, possibly 1 element of Decongestive Lymphoedema Treatment (DLT), then maintenance**		**C. COMPLEX Complex lymphoedema requiring intensive TX (DLT)**		**D. VERY COMPLEX Very Complex lymphoedema requiring intensive, possibly repeated DLT and prolonged TX**	
	garment fitting		DLT per site of oedema		site of oedema		DLT. TX & duration to be negotiated with referrer before commencing	
Follow up the first 12 months	3 x 2 units £61.50	£369	3 x 2 units £61.50	£369	3 x 2 units £61.50	£369	To be negotiated according to length of treatment agreed	
Total cost of treatment first 12 months		**£676**		**£1845**		**£4305**	To be negotiated according to length of treatment agreed	
Ongoing Follow Up Annually	2x 2 units until stable or discharged to the GP	£246	2x 2 units until stable or discharged to the GP	£246	2x 2 units until stable or discharged to the GP	£246	Review and consider further treatment needed	
Total cost for 2 year package		**£922**		**£2091**		**£4551**	To be negotiated according to treatment agreed	

1 Source: British Lymphology Society (BLS) 2021

12.6 Evidence statements

- One cost-comparison from Denmark found that complete decongestive therapy with Kinesiotaping is less expensive than a complete decongestive therapy with low-stretch bandages. The analysis was assessed as partially applicable with potentially serious limitations.

- One cost-comparison analysis from Canada found that lymphovenous bypass is less expensive than complete decongestive therapy. The analysis was assessed as partially applicable with potentially serious limitations.

13.1 The committee's discussion and interpretation of the evidence

13.1.1 The outcomes that matter most

The committee discussed the range of outcomes and agreed that measures of the severity of lymphoedema, including reduction in upper limb, breast or chest wall volume and adverse events such as infections or surgical complications were the most important in decision making for lymphoedema management.

They also recognised the importance of patient-centred outcomes such as quality of life, pain, psychological well-being, and skin/tissue changes for example, softening, hardening, tension.

Reducing acute inflammatory episodes or cellulitis is an important outcome to consider in lymphoedema management. The committee noted by minimising these acute complications, effective lymphoedema management can improve patient comfort, reduce the risk of long-term lymphatic damage, and enhance overall quality of life. However this was not commonly reported in the evidence.

The committee also wanted to consider cosmetic impact (changes in tissues and skin condition) of lymphoedema and its effect on people's body image as potential outcomes, but these were not reported in the available literature. This suggests a need for future research to better understand and address these aspects of the patient experience.

13.1.2 The quality of the evidence

The evidence summarised for the review was heterogeneous, both in terms of intervention and comparator characteristics and also in terms of the outcome measures used. Although most of the studies reported some measure of limb circumference or volume, they were inconsistent in the ways that they measured and reported this. Therefore, no meta-analysis was performed and GRADE was used for some of the outcomes to determine confidence where possible. Some of the systematic reviews reported narratively in this review did undertake meta-analysis and this is reported where relevant. For all papers reported in this review the quality of the evidence is based on critical appraisal of the study using the appropriate checklist as set out in the NICE manual.

While the quality of the evidence varied, most of the papers identified were at moderate to high risk of bias. This was mainly due to lack of blinding, imbalanced baseline characteristics, selective reporting of outcomes, and unclear definitions of outcome measures.

The committee noted significant inconsistencies in how the severity of lymphoedema was measured and reported across studies. This variability made it extremely challenging to pool, analyse, and interpret the evidence effectively. Furthermore, the committee recognized the importance of stratifying evidence by baseline lymphoedema severity. However, this stratification was rarely possible due to inadequate reporting in the included studies, which prevented the committee from fully considering severity in their discussions.

This led to the committee's decision to make a research recommendation for the development of a core outcome set for lymphoedema studies. The committee believed a core outcome set would establish a standardized approach to measuring and reporting lymphoedema severity, addressing the current inconsistencies that hinder data synthesis and

interpretation. The committee also highlighted that only one study in this review included people with breast lymphoedema, whereas the remaining studies focused on upper limb lymphoedema. They were in agreement that this underscored a significant gap in the current evidence base. The committee concluded that there is a pressing need for future research specifically targeting interventions for breast lymphoedema management and therefore made a research recommendation. There were several challenges and limitations with the included studies. The committee were cautious that across all of the studies there were no definitive diagnostic criteria for lymphoedema; studies used different methods to diagnose and recruit people into the studies (such as circumference measurements, volume displacement, bioimpedance), and different cut-off points to diagnose lymphoedema, and therefore there was significant heterogeneity in the population making it very difficult to compare the evidence. The committee were concerned that the majority of the studies had a small sample size.

There was variability in measurement techniques for example the location of circumference measurements and timing of assessment, some studies reported follow-ups for up to 3 months while other studies recorded the outcomes immediately after treatment. The committee noted that many of the studies did not report long-term follow-up. This also indicates that there is a need for longitudinal studies to understand the natural history of the BCRL and the long-term effects of different management strategies.

The committee were also concerned that the studies did not report detailed information on the interventions, such as the type of compression therapies provided, the components of complete decongestive therapy, or the duration and frequency of treatments, which made it difficult to make detailed recommendations.

13.1.3 Benefits and harms

Complete decongestive therapy

The committee were presented with evidence on a range of interventions including, complete decongestive therapy (CDT) which includes manual lymphatic drainage (MLD) and compression therapy) The evidence was limited to 5 RCTs with small sample sizes and varied in treatment protocols. There were uncertain effects for reducing excess arm volume in early lymphoedema, the committee also had concerns about the validity and reproducibility of this outcome due to the time point and the definitions of excess arm volume used. For most outcomes the committee had low confidence in the evidence. There was no clear benefit of CDT with regards to incidence of lymphoedema and quality of life. The committee noted that for many of the outcomes, the evidence could not differentiate between effectiveness of the intervention and comparators because the 95% confidence intervals for the outcomes crossed the line of no effect.

The committee also discussed the evidence for the effectiveness of the individual components of CDT. They discussed the effectiveness of skin and nail care and noted that while the literature did not directly compare, or explicitly report on the benefit of skin and nail care in terms of managing lymphoedema, the committee noted that it is widely used in practice and was included in the treatment regimens of all studies because it is important for protecting skin integrity and preventing infection.

Manual lymphatic drainage (MLD):

The committee discussed types of manual lymphatic drainage, including self-lymphatic drainage, and agreed that the evidence did not show any clear effect of this on breast cancer related lymphoedema (BCRL). A systematic review suggested that use of longer term MLD (more than 20 sessions, or more than 2 weeks of daily sessions) might provide some volume

reduction. However no significant difference between MLD and control for arm volume if less than 20 sessions are completed. 3 studies with a small sample size also found MLD significantly reduced pain, The committee were concerned that that the number of required sessions would make the treatment difficult both for the patient to commit to and for the service to have capacity to maintain this service. They were not convinced that there is a benefit from MLD, so they did not make recommendations.

Compression therapy:

The committee were convinced by the evidence supporting the efficacy of compression therapy. However, they also acknowledged that sometimes compression therapy may not be appropriate for instance for patients who experience significant discomfort, skin irritation, or allergic reactions to compression garments and where the affected area is difficult to compress effectively using standard garments such as the breast. In these examples , alternative options such as kinesiology tape may be considered. The committee, after reviewing the available evidence, made a strong recommendation for compression therapy as the first-line treatment for the management of lymphoedema

Education

The committee discussed lymphoedema education was reported in most studies as usual care or as part of usual care. The committee agreed with the standard use of education in the literature. The committee acknowledged that evidence on education is mixed. However, they considered that providing comprehensive information represents a low-risk intervention with potential benefits for people with lymphoedema They agreed that, as part of their lymphoedema education, people undergoing breast cancer treatment receive comprehensive information about lymphoedema risk and management. This approach aims to empower people with knowledge and tools for self-management and monitoring.

The committee noted that maintaining healthy body weight, reducing infection risk, and proper skincare were included in the recommendation because it was important that people aremade aware of the importance of skin and nail care, and to understand and recognise the signs of infection (for example cellulitis) or other serious sequelae of lymphoedema and to know who to contact for urgent help. The committee retained the previous recommendation on advice on movement and exercise, aswell as addressing common concerns (e.g., air travel, medical procedures) to reduce unnecessary anxiety and restrictions. The committee retained both parts of the recommendations from previous guidelines (NG101) and this was supported by some evidence of benefit for exercise with respect to quality of life.

There was some evidence that early intervention for lymphoedema leads to better outcomes and quality of life (see evidence review C) but the committee agreed regular hospital monitoring where baseline measurements for people can be recorded, and any early changes can be identified would be difficult to implement in practice. The committee wanted to emphasise self-monitoring as a crucial component of lymphoedema management. They therefore recommended that the information people are given should include advice on how to self-monitor and to detect changes in their condition early on, information to increase awareness of early signs and symptoms of lymphoedema and advice on how to collect baseline measurements.

Kinesiology taping

There was some evidence on kinesiology tape for the management of lymphoedema that showed although the effectiveness of this treatment varied compared to other compression garments, there was improvement in patient quality of life, pain and discomfort levels. The committee noted that some people may prefer kinesiology tape because of its convenience, ease of application and comfort. However, they noted that this may not be as effective as

compression garments and would have differing results depending on the area of oedema. The committee carefully considered the potential economic impact of different lymphoedema management options on patients. They discussed while some people may prefer kinesiology tape the committee noted that this option often requires people to purchase their own tape. They were concerned that this additional cost could create a barrier to access, particularly for individuals from lower socioeconomic backgrounds. This disparity in access could potentially exacerbate existing inequalities.

Complementary therapies

The committee reviewed the available evidence on acupuncture and moxibustion as part of complementary therapies for lymphoedema management but decided not to make recommendations for their use in the NHS setting. This decision was based on several factors. Firstly, while some studies showed potential benefits (reduced elbow circumference and improved range of motion), the overall evidence was limited, low quality and included very few people. Secondly, the evidence primarily focuses on patient acceptance of acupuncture and moxibustion, rather than their clinical effectiveness. The committee agreed that introducing acupuncture and moxibustion as recommended treatments could require significant resource allocation for training, equipment, and staffing, which may not be justified given the current evidence base.

Pneumatic compression devices (PCDs)

The committee considered the use of pneumatic compression devices (PCDs) in lymphoedema management. They noted that the evidence base for the use of PCDs is limited. There was some evidence that intermittent pneumatic compression with compression bandaging showed significant improvement in arm circumference and improve range of motion (ROM). The committee also noted they can make the affected limb more comfortable potentially enhancing overall treatment efficacy. However, PCDs are primarily used as an adjunct to other treatments and are not available in all clinics, which impacts access to this treatment option across different healthcare settings.

The committee also noted that PCDs are more commonly used and potentially more beneficial for lower limb lymphoedema. The committee emphasised that while PCDs may provide benefits for some patients, they were not convinced by evidence to make any recommendations.

Exercise

The committee reviewed the evidence and their clinical experience regarding exercise, complex physical therapy, and aquatic therapy for people with breast cancer-related lymphoedema. High-quality evidence from 7 studies suggested that complex physical reduced total upper limb volume

Some studies showed improvements in limb volume, shoulder flexion and abduction, pain scores, and upper limb strength with exercise interventions. The committee agreed that exercise generally does not worsen clinical outcomes for people with BCRL and can improve outcomes such as pain and function.

The committee recognized that some people with BCRL might some misconceptions against certain types of exercise for example, high intensity, weight training) following breast cancer treatment. They emphasized the importance of making people aware of the benefits of exercise for long-term lymphoedema management. In the committee's experience, making people aware of the benefits of exercise was important in the long-term management of lymphoedema.

The committee discussed concerns around aquatic therapy, noting that it alone is not sufficient for lymphoedema management. They considered the balance of potential benefits versus the practical limitations within the NHS. For example issues around pool size and staffing requirements would make recommending aquatic therapy challenging. The committee's views were aligned with previous guidance stating that exercise does not prevent, cause, or worsen lymphoedema and may improve quality of life. They decided to retain the previous recommendations however they did not find any strong evidence to update an include specific exercise regimens.

Surgery

The committee considered the evidence on surgical interventions such as lymphaticovenous anastomosis (LVA) and vascularised lymph node transfer (VLNT) for the treatment of lymphoedema. Evidence from a systematic review showed a benefit to arm volume following VLNT, and evidence for LVA at 6 months showed improved quality of life. However, lack of strong high-quality evidence made it difficult to draw definitive conclusions about the efficacy, safety, and long-term outcomes of these surgical interventions compared to other treatments or no treatment at all. The committee highlighted that there are disparities in research between upper and lower limb lymphoedema that may be due to the higher prevalence of lower limb lymphoedema and indeed, the concentration of studies from East Asian countries and the lack of English translations has limited the accessibility and dissemination of research findings.

The committee discussed surgical interventions for secondary lymphoedema, recognising that the included studies in NICE's interventional procedures guidance were not UK-based and primarily focused on lower limb lymphoedema. While lower limb lymphoedema is well studied there is an evidence gap for truncal and upper limb lymphoedema. which are more relevant to breast cancer patients. Therefore, they made a research recommendation for surgical interventions including Lymphovenous anastomosis during axillary as well as vascularised lymph node transfer which is not covered by the NICE interventional procedure’s guidance.

Other interventions

No evidence was identified for psychological interventions or for bras, foam inserts or spaghetti foam for managing breast cancer-related lymphoedema.

13.1.4 Cost effectiveness and resource use

Two health economic studies were included for this review.

The first study compared CDT with Kinesio taping and CDT with low-stretch bandages and was assessed as partially applicable (Denmark) and with potentially serious limitations. The main limitations were the extremely small sample size of the pilot study (10 people), the lack of clarity regarding the source of unit costs and the short time horizon (4 weeks). The study assumed that a Kinesio taping therapy would require 8 sessions (twice a week for 4 weeks), whereas “standard” CDT would require 20 sessions (5 days a week for 4 weeks). As a result, Kinesio taping was found to be cost saving, as it costed £558 (2015/2016) less than standard CDT. The systematic review included in the analysis reported a significant heterogeneity in Kinesio taping protocols, with some requiring 9 and other 20 sessions. Therefore, it is uncertain whether consistent cost savings would occur. Unit costs were presented to the committee. The NHS Supply Chain catalogue reports a cost of £2.76 for standard 5cm x 5 m Kinesio tape. The corresponding cost for a 6cm x 5m compression bandage is £0.39 making Kinesio tape almost 10 times more expensive than the compression bandage. The committee noted that people are often required to buy their own tape/bandage after their

CDT session, and therefore, part of the cost is borne by them. In addition, the committee highlighted that CDT is not typically delivered in the UK in the same manner as in the study, and services do not currently support CDT being given at this intensity. Therefore, there were also concerns regarding the generalisability of the study

The second economic study was a cost-comparison analysis looking at lifetime savings of lymphaticovenous anastomosis (LVA). The analysis was assessed as partially applicable (Canada) with potentially serious limitations. Treatment effects were estimated from a meta-analysis that included a few studies on congenital non-cancer related lymphoedema, that do not match the population specified in the protocol. Moreover, the size of the effect, 56.3% of people discontinuing compression garments therapy, was well above the treatment effect reported in the studies included in the clinical review, around 40%. Notably, the latter figure is just above the threshold of 36% identified by the authors as the minimum treatment effect for LVA to be cost-saving. Finally, the analysis did not include potentially important outcomes such as adverse events of surgery and recurrence. Given the study's limitations, the cost-effectiveness of LVA in the UK remains uncertain.

The committee noted that LVA and Vascularized Lymph Node Transfer (VLNT) differ considerably, as the first requires around 3 hours in surgery and can be conducted out either under local or general anaesthesia, while the second requires most of the day in surgery and is performed under general anaesthesia. The clinical review found no statistically significant improvement with LVA but statistically significant benefits to arm volume following VLNT. The studies also reported that 41% of people partially or completely discontinue compression therapy after LVA, with a comparable figure of 45% following VLNT. Although this could potentially reduce future costs associated with future management of lymphoedema and improve quality of life, it remains unclear whether these benefits would offset the considerably large initial investment necessary for two types of microsurgeries, particularly if performed in isolation. The committee also acknowledged that, in current practice, management or preventive lymphoedema surgeries are done alongside other interventions, such as breast reconstruction or axillary lymph node dissection. In such scenarios, the cost of a lymphoedema surgery could be significantly lower, making this procedure more cost-effective if performed alongside other surgeries. Given the lack of strong economic and clinical evidence, the committee made a research recommendation for surgery, acknowledging the importance, particularly for people living with lymphoedema, of providing a variety of treatments, including surgery for severe cases. As there are currently only a few centres in the country providing lymphoedema microsurgery, any recommendation would potentially require more investment to make this service equally accessible for people across the country. Downstream NHS savings due to a reduced need for compression therapy would be expected to be approximately 40% of those undergoing surgery.

There was no economic evidence for manual lymphatic drainage (MLD) and the clinical review did not find any clear effect on lymphoedema. The committee acknowledged that MLD is labour intensive and is often carried out by specialist lymphoedema practitioners for several sessions, and therefore, could bear a significant cost for the NHS. Given the lack of strong evidence and the potential cost for the public healthcare, the committee decided not to make any recommendation on MLD.

The committee acknowledged that there is wide variability in access to lymphoedema services, noting that people are often required to buy their own garments and tapes. Of particular concern are items like Kinesio tapes, which are often not available on prescription, potentially exacerbating inequality and limiting access to treatments.

13.1.5 Other factors the committee took into account

The committee acknowledged the variable provision of lymphoedema services across the UK and recognised potential equality issues beyond just geography and cost. While access to services and the affordability of treatments like kinesiology tape are crucial concerns, the committee also considered other potential barriers identified in the EHIA. The committee considered that kinesiology tape is necessary to consider as an alternative, which allows for access of treatment for when compression therapy is inappropriate.

The committee considered that all the included studies only included women in their studies, they highlighted that men also are at risk of lymphoedema, however they decided it would be appropriate to extrapolate the findings for men.

13.2 Recommendations supported by this evidence review

This evidence review supports recommendations 2.1.1 to 2.1.7 and the research recommendations on developing lymphoedema core outcomes set, breast oedema management and surgical techniques for the management of lymphoedema.

13.3 References – included studies

13.3.1 Effectiveness

Randomised controlled trials and Randomised clinical trials included in systematic reviews

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Cormie, Prue, Pumpa, Kate, Galvao, Daniel A et al. (2013) Is it safe and efficacious for women with lymphoedema secondary to breast cancer to lift heavy weights during exercise: a randomised controlled trial. Journal of cancer survivorship : research and practice 7(3): 413-24

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Systematic reviews

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13.3.2 Economic

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lymphoedema

Appendices

Appendix A – Review protocols

Review protocol for the non-pharmacological management of lymphoedema in people who have, or have had, breast cancer.

ID	Field	Content
0.	PROSPERO registration number	CRD42024521515
1.	Review title	The non-pharmacological management of lymphoedema in people who have, or have had, breast cancer.
2.	Review question	In people who have, or have had, breast cancer and have lymphoedema, what non-pharmacological strategies are effective and cost-effective, for managing it?
3.	Objective	To determine effective non-pharmacological strategies for the management of lymphoedema in people who have, or have had, breast cancer. This will include assessing existing interventions, their efficacy and their impact on patient outcomes.
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • HTA (Health Technology Assessment) • DARE (Database of Abstracts of Reviews of Effectiveness) • Embase • Emcare • MEDLINE ALL • INAHTA • Epistemonikos • AMED (Allied and Complementary Medicine)

		For the economics review the following databases will be searched: • Embase* • MEDLINE ALL* • Econlit • INAHTA • HTA (Health Technology Assessment) • NHS EED Searches will be restricted by: • Date of last search (October 2013) • English language • Human studies • Abstracts, conference presentations and theses will be excluded. • Systematic reviews and RCTs and observational studies. The full search strategies for MEDLINE database will be published in the final review. The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion.
5.	Condition or domain being studied	Lymphoedema in all people who have, or have had, breast cancer.
6.	Population	Inclusion: All adults (aged 18 or over) who have, or have had, breast cancer and have lymphoedema of the upper limb (including axilla, hands and fingers), chest wall or breast. Exclusion: none identified.

7.	Intervention	**A) Non-surgical** Any conservative non-pharmacological interventions/strategies: 1. Complete Decongestive Therapy (CDT) (for example, manual lymphatic drainage (MLD), compression, skin care and exercise, deep oscillation therapy) 2. Exercise and Movement (for example, Pilates, yoga, Tai Chi, range of motion exercises and breathing intervention) 3. Skincare (for example, keeping skin clean and use of moisturisers) 4. Lymphoedema Education (for example, self-management advice, simple lymphatic drainage (SLD), weight management advice, information on lymphoedema complications like cellulitis and sepsis) 5. Pneumatic Compression Devices (for example, intermittent pneumatic compression (IPC)) 6. Complementary therapy (for example, acupuncture, reflexology) 7. Psychological interventions (for example, acceptance and commitment therapy (ACT), cognitive behavioural therapy (CBT)) 8. Kinesiotaping (for example, K-Tape, elastic therapeutic tape) 9. Wired vs non-wired bras, foam inserts, spaghetti foam

		B) Surgical The following surgical interventions/strategies: 1 Vascularised Lymph Node Transfer (VLNT) 2 Lymphovenous Bypass 3 Reconstructive Lymphatic Microsurgery 4 Lymphaticovenous Anastomosis (LVA) Exclusions: Liposuction as it is covered by IPG723: liposuction for chronic lymphoedema.
8.	Comparator	• No intervention/education only • Each other • Contralateral arm or breast
9.	Types of study to be included	We will search for • SRs of RCTs • SRs of cohort studies • RCTs • Prospective cohort studies. Due to time and resource restraints, the best evidence will be included for each intervention and evidence from lower categories in the hierarchy of evidence will be excluded, so for example we will only include cohort studies for an intervention if there is no/poor RCT evidence for that intervention. Adequacy of evidence will be discussed on an intervention-by-intervention basis between the team and QA lead.
10.	Other exclusion criteria	• Abstracts, conference presentations and theses • Non-human studies • Non-English language studies

11.	Context	The NICE surveillance review (June 2023) identified some studies that showed that various interventions such as laser therapy, extracorporeal shockwave therapy and vascularised lymph node transfer may decrease lymphoedema in people with breast cancer. The current recommendations in NG101 and CG81 focus on managing lymphoedema in people with advanced breast cancer and do not include people with early breast cancer. As such, there is a need to expand the evidence reviews to cover all people with breast cancer, as well as review any new evidence on the management and treatment of lymphoedema in people with breast cancer.
12.	Primary outcomes (critical outcomes)	At all reported timepoints in 6-monthly intervals where applicable (e.g. 0-6 months, 7-12 months): • Severity of lymphoedema (for example, change from baseline in limb or breast volume/swelling using ultrasound/tissue dielectric constant, arm mobility (including DASH scores), bioimpedance) • Adverse events (for example, infection, surgical complications) For surgery only: • Recurrence of lymphoedema or need for further intervention • Need for further intervention after surgery

13.	Secondary outcomes (important outcomes)	At all reported timepoints in 6-monthly intervals where applicable (e.g. 0-6 months, 7-12 months): • Quality of life (for example, LYMQOL, FACT B+4, EQ-5D and EORTC-QoL-C30) • Patient reported outcomes (for example pain, psychological distress) • Changes in tissues and skin condition (for example, softening, hardening, tension) • Reduction in acute inflammatory episodes or cellulitis • Cosmetic impact and body image
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4).
15.	Risk of bias (quality) assessment	Risk of bias for RCTs and systematic reviews will be assessed using the Cochrane Risk of Bias v.2.0 or ROBIS respectively. Risk of bias for cohort and non-randomised studies will be assessed using the ROBINS-I tool (Risk Of Bias In

		Non-randomised Studies - of Interventions).
16.	Strategy for data synthesis	Where possible, meta-analyses of outcome data will be conducted for all comparators that are reported by more than one study, with reference to the Cochrane Handbook for Systematic Reviews of Interventions. Where data can be disaggregated it will also be separated into the subgroups identified in section 17 (below). Pooled relative risks will be calculated for dichotomous outcomes (using the Mantel–Haenszel method) reporting numbers of people having an event. Absolute risks will be presented where possible. Continuous outcomes will be analysed as mean differences unless multiple scales are used to measure the same factor. In these cases, standardised mean differences will be used instead. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all comparators, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models will be deemed to be inappropriate if one or both of the following conditions is met: • Significant between study heterogeneity in methodology, population, intervention or comparator was identified by the reviewer in advance of data analysis. • The presence of significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$.

		GRADE will be used to assess the quality of the outcomes. Data from randomised controlled trials will be initially rated as high quality, with the quality of the evidence for each outcome then downgraded or not from this initial point. Where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically (visually) assess the potential for publication bias. Imprecision will be based on default values of 0.8 and 1.25 for dichotomous outcomes, and 0.5*median SD of the control groups for continuous outcomes.
17.	Analysis of sub-groups	Where disaggregation is possible/applicable: • Axillary intervention • Type of treatment (surgery or radiotherapy) • Severe lymphoedema • Duration/intensity of treatment • Risk factors for lymphoedema (for example, age, obesity, comorbidities)
18.	Type and method of review	☒ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative ☐ Epidemiologic ☐ Service Delivery ☐ Other (please specify)
19.	Language	English
20.	Country	England
21.	Anticipated or actual start date	February 2024
22.	Anticipated completion date	June 2024

1

Appendix B – Literature search strategies

Background and development

Search design and peer review

A NICE Senior Information Specialist (SIS) conducted the literature searches for the evidence review. The searches were run on 19 February 2024 (effectiveness search) and 22 February 2024 (cost effectiveness search).

This search report is compliant with the requirements of the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (for further details see: Rethlefsen M et al. PRISMA-S. *Systematic Reviews*, 10(1), 39).

The MEDLINE strategies below were quality assured (QA) by a trained NICE SIS. All translated search strategies were peer reviewed by another SIS to ensure their accuracy. Both procedures were adapted from the Peer Review of Electronic Search Strategies Guideline Statement (for further details see: McGowan J et al. PRESS 2015 Guideline Statement. *Journal of Clinical Epidemiology*, 75, 40-46).

The principal search strategies were developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage.

Review management

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess "low-probability" matches. All decisions made for the review can be accessed via the deduplication history.

Prior work

The search strategy was based on the strategies used for NG101 and CG81.The strategy was updated to include additional lymphoedema terms.

Search limits and other restrictions

Formats

Limits were applied in adherence to standard NICE practice and the review protocol to exclude:

- Animal studies

- Editorials, letters, news items and commentaries
- Conference abstracts and posters
- Papers not published in the English language.

The limit to remove animal studies in the searches was the standard NICE practice, which has been adapted from:

Dickersin K, Scherer R & Lefebvre C. (1994) Systematic Reviews: Identifying relevant studies for systematic reviews. *BMJ*, 309(6964), 1286.

Date limits

A date limit of October 2013 to February 2024 was applied, as stated in the review protocol, because the last update search for GG81 was in October 2013. The update search for NG101 was carried out in 2017. We were aware that there would be some duplicate records for the NG101 population (2013-2017).

Allied and Complementary Medicine (AMED) was searched up until October 2023. This is due to the British Library cyberattack. Full access to AMED has yet to be restored.

Search filters and classifiers

Effectiveness searches

Randomised controlled trials filter

The MEDLINE RCT filter was McMaster Therapy – Medline - "best balance of sensitivity and specificity" version.

The standard NICE modifications were used: the MeSH heading *randomized controlled trial/*, which is equivalent *to randomized controlled trial.pt* was exploded to capture newer, narrower *terms equivalence trial/ and pragmatic clinical trial*. The free-text term *randomized.mp* was also changed to the (more inclusive) alternative *randomi?ed.mp.* to capture both UK and US spellings.

The Embase RCT filter was McMaster Therapy – Embase "best balance of sensitivity and specificity" version.

Systematic reviews filters:

Lee, E. et al. (2012) An optimal search filter for retrieving systematic reviews and meta-analyses. BMC Medical Research Methodology, 12(1), 51.

- In MEDLINE, the standard NICE modifications were used: pubmed.tw added; systematic review.pt added from MeSH update 2019.
- In Embase, the standard NICE modifications were used: pubmed.tw added to line medline.tw.

Observational studies

The terms used for observational studies are standard NICE practice that have been developed in house.

Cost effectiveness searches

In line with the review protocol, the sensitive version of the validated NICE cost utility filter was used in the MEDLINE and Embase strategies without amendment.

> Hubbard W et al. (2022) Development and validation of paired MEDLINE and Embase search filters for cost-utility studies. *BMC Medical Research Methodology*, 22(1), 310.

Note: Several modifications have been made to these filters over the years that are standard NICE practice.

Effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
Allied and Complementary Medicine (AMED)	19/02/24	Ovid	1985 to October 2023	69
Cochrane Central Register of Controlled Trials (CENTRAL)	19/02/24	Wiley	Issue 2 of 12, February 2024	560
Cochrane Database of Systematic Reviews (CDSR)	19/02/24	Wiley	Issue 2 of 12, February 2024	11
Database of Abstracts of Reviews of Effectiveness (DARE)	19/02/24	CRD	-	13
Embase	19/02/24	Ovid	1996 to 2024 February 16	2,400
Emcare	19/02/24	Ovid	1995 to 2024 Week 06	882
Epistemonikos	19/02/24	Epistemonikos		503
Health Technology Assessment (HTA)	19/02/24	CRD	-	4
International Health Technology Assessment Database (INAHTA)	19/02/24	https://database.inahta.org/	-	9
Medline ALL	19/02/24	Ovid	1946 to February 16, 2024	1,938

Search strategy history

Database name: Allied and Complementary Medicine (AMED)

Searches	
1	exp breast neoplasms/ 1933
2	exp Breast/ 104
3	breast*.ti,ab. 2872
4	2 or 3 2908
5	(breast adj milk).ti,ab. 37
6	(breast adj tender*).ti,ab. 5
7	5 or 6 42
8	4 not 7 2866
9	exp neoplasms/ 18086
10	8 and 9 2213
11	(breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab. 2470
12	(mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab. 101
13	10 or 11 or 12 2630
14	1 or 13 2799
15	(duct* carcinoma* in situ or DCIS).ti,ab. 2
16	14 or 15 2799
17	exp lymphoedema/ 289
18	(lymphed* or lymphoed*).ti,ab. 344
19	elephantiasis.ti,ab. 15
20	((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab. 1317
21	(breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab. 27
22	(lymph* adj4 (oedema* or edema*)).ti,ab. 37
23	or/17-22 1707
24	16 and 23 197
25	limit 24 to english 175
26	limit 25 to yr="2013 -Current" 69

Database name: Cochrane Central Register of Controlled Trials (CENTRAL)

Searches	
#1	MeSH descriptor: [Breast Neoplasms] explode all trees 19974
#2	MeSH descriptor: [Neoplasms, Ductal, Lobular, and Medullary] explode all trees 1001
#3	MeSH descriptor: [Carcinoma, Lobular] this term only 217
#4	MeSH descriptor: [Carcinoma, Medullary] this term only 21
#5	MeSH descriptor: [Carcinoma, Intraductal, Noninfiltrating] this term only 305
#6	{OR #1-#5} 20272
#7	MeSH descriptor: [Breast] explode all trees 1142
#8	breast*:ti,ab 60058

Searches
#9 #7 or #8 60167 #10 (breast NEXT milk):ti,ab 2709 #11 (breast NEXT tender*):ti,ab 261 #12 #10 or #11 2969 #13 #9 not #12 57198 #14 MeSH descriptor: [Neoplasms] explode all trees 123386 #15 #13 and #14 20312 #16 (breast* NEAR/5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)):ti,ab 43053 #17 (mammar* near/5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)):ti,ab 282 #18 MeSH descriptor: [Paget's Disease, Mammary] explode all trees 3 #19 (paget* and (breast* or mammary or nipple*)):ti,ab 18 #20 {OR #15-#19} 44070 #21 #6 or #20 45463 #22 ((duct* carcinoma* in situ or DCIS)):ti,ab,kw 1013 #23 #21 or #22 45560 #24 MeSH descriptor: [Lymphoedema] explode all trees 906 #25 (lymphoed* or lymphed*):ti,ab,kw 1896 #26 (elephantiasis):ti,ab,kw 182 #27 (((arm* or hand* or finger* or upper limb* or "chest wall" or trunc* or trunk* or axilla* or thoracic) NEAR/4 (morbidity or swell* or swollen or pain* or oedema* or edema*))):ti,ab,kw 11433 #28 ((breast* NEAR/4 (morbidity or swell* or swollen or oedema* or edema*))):ti,ab,kw 371 #29 ((lymph* NEAR/4 (oedema* or edema*))):ti,ab,kw 237 #30 #24 OR #25 OR #26 OR #27 OR #28 OR #29 13511 #31 #23 AND #30 1762 #32 MeSH descriptor: [Breast Cancer Lymphoedema] this term only 155 #33 #31 OR #32 1766 #34 (((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp))):an (Word variations have been searched) 494506 #35 #33 NOT #34 1236 #36 ("conference"):pt 236547 #37 #35 NOT #36 with Cochrane Library publication date Between Oct 2013 and Feb 2024, in Cochrane Reviews 11 #38 #35 NOT #36 with Publication Year from 2013 to 2024, in Trials 560

1 **Database name: Cochrane Database of Systematic Reviews (CDSR)**

Searches
#1 MeSH descriptor: [Breast Neoplasms] explode all trees 19974

Searches
#2 MeSH descriptor: [Neoplasms, Ductal, Lobular, and Medullary] explode all trees 1001
#3 MeSH descriptor: [Carcinoma, Lobular] this term only 217
#4 MeSH descriptor: [Carcinoma, Medullary] this term only 21
#5 MeSH descriptor: [Carcinoma, Intraductal, Noninfiltrating] this term only 305
#6 {OR #1-#5} 20272
#7 MeSH descriptor: [Breast] explode all trees 1142
#8 breast*:ti,ab 60058
#9 #7 or #8 60167
#10 (breast NEXT milk):ti,ab 2709
#11 (breast NEXT tender*):ti,ab 261
#12 #10 or #11 2969
#13 #9 not #12 57198
#14 MeSH descriptor: [Neoplasms] explode all trees 123386
#15 #13 and #14 20312
#16 (breast* NEAR/5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)):ti,ab 43053
#17 (mammar* near/5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)):ti,ab 282
#18 MeSH descriptor: [Paget's Disease, Mammary] explode all trees 3
#19 (paget* and (breast* or mammary or nipple*)):ti,ab 18
#20 {OR #15-#19} 44070
#21 #6 or #20 45463
#22 ((duct* carcinoma* in situ or DCIS)):ti,ab,kw 1013
#23 #21 or #22 45560
#24 MeSH descriptor: [Lymphoedema] explode all trees 906
#25 (lymphoed* or lymphed*):ti,ab,kw 1896
#26 (elephantiasis):ti,ab,kw 182
#27 (((arm* or hand* or finger* or upper limb* or "chest wall" or trunc* or trunk* or axilla* or thoracic) NEAR/4 (morbidity or swell* or swollen or pain* or oedema* or edema*))):ti,ab,kw 11433
#28 ((breast* NEAR/4 (morbidity or swell* or swollen or oedema* or edema*))):ti,ab,kw 371
#29 ((lymph* NEAR/4 (oedema* or edema*))):ti,ab,kw 237
#30 #24 OR #25 OR #26 OR #27 OR #28 OR #29 13511
#31 #23 AND #30 1762
#32 MeSH descriptor: [Breast Cancer Lymphoedema] this term only 155
#33 #31 OR #32 1766
#34 (((clinicaltrials or trialsearch* or trial-registry or trials-registry or clinicalstudies or trialsregister* or trialregister* or trial-number* or studyregister* or study-register* or controlled-trials-com or current-controlled-trial or AMCTR or ANZCTR or ChiCTR* or CRiS or CTIS or CTRI* or DRKS* or EU-CTR* or EUCTR* or EUDRACT* or ICTRP or IRCT* or JAPIC* or JMCTR* or JRCT or ISRCTN* or LBCTR* or NTR* or ReBec* or REPEC* or RPCEC* or SLCTR or TCTR* or UMIN*):so or (ctgov or ictrp))):an (Word variations have been searched) 494506
#35 #33 NOT #34 1236
#36 ("conference"):pt 236547
#37 #35 NOT #36 with Cochrane Library publication date Between Oct 2013 and Feb 2024, in Cochrane Reviews 11

Searches		
#38	#35 NOT #36 with Publication Year from 2013 to 2024, in Trials	560

Database name: Database of Abstracts of Reviews of Effectiveness (DARE)

Searches
1 MESH DESCRIPTOR Breast Neoplasms EXPLODE ALL TREES
2 MESH DESCRIPTOR Neoplasms, Ductal, Lobular, and Medullary EXPLODE ALL TREES
3 MESH DESCRIPTOR Carcinoma, Lobular
4 MESH DESCRIPTOR Carcinoma, Medullary
5 MESH DESCRIPTOR Carcinoma, Intraductal, Noninfiltrating
6 #1 OR #2 OR #3 OR #4 OR #5
7 MESH DESCRIPTOR Breast EXPLODE ALL TREES
8 breast*
9 #7 or #8
10 (breast NEXT milk)
11 (breast NEXT tender*)
12 #10 or #11
13 #9 not #12
14 MESH DESCRIPTOR Neoplasms EXPLODE ALL TREES
15 #13 and #14
16 (breast* NEAR5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*))
17 (mammar* near5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*))
18 MESH DESCRIPTOR Paget's Disease, Mammary EXPLODE ALL TREES
19 (paget* and (breast* or mammary or nipple*))
20 #15 OR #16 OR #17 OR #18 OR #19
21 #6 or #20
22 ((duct* carcinoma* in situ or DCIS))
23 #21 or #22
24 MESH DESCRIPTOR Lymphoedema EXPLODE ALL TREES
25 (lymphoed* or lymphed*)
26 (elephantiasis)
27 (((arm* or hand* or finger* or upper limb* or "chest wall" or trunc* or trunk* or axilla* or thoracic) NEAR4 (morbidity or swell* or swollen or pain* or oedema* or edema*)))
28 ((breast* NEAR4 (morbidity or swell* or swollen or oedema* or edema*)))
29 ((lymph* NEAR4 (oedema* or edema*)))
30 #24 OR #25 OR #26 OR #27 OR #28 OR #29
31 #23 AND #30
32 MESH DESCRIPTOR Breast Cancer Lymphoedema
33 #31 OR #32
34 * IN DARE FROM 2013 TO 2015
35 #33 AND #34
36 * IN HTA FROM 2013 TO 2018
37 #33 AND #36
34 * IN DARE FROM 2013 TO 2015
35 #33 AND #34

1 Database name: Embase

Searches	
1	exp breast cancer/ 529909
2	exp breast carcinoma/ 76840
3	exp medullary carcinoma/ 10990
4	ductal breast carcinoma in situ/ 2803
5	exp breast tumor/ 592337
6	lobular carcinoma/ 3428
7	or/1-6 601890
8	exp breast/ 90238
9	breast*.ti,ab,kf. 707921
10	8 or 9 723315
11	(breast adj milk).ti,ab,kf. 18056
12	(breast adj tender*).ti,ab,kf. 642
13	11 or 12 18692
14	10 not 13 704623
15	exp neoplasm/ 4809452
16	14 and 15 543759
17	(breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 559182
18	(mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 30184
19	exp Paget nipple disease/ 7002
20	(paget* and (breast* or mammary or nipple*)).ti,ab,kf. 1496
21	or/16-20 610142
22	7 or 21 720727
23	(duct* carcinoma* in situ or DCIS).ti,ab,kf. 15980
24	ductal breast carcinoma in situ/ 2803
25	23 or 24 17216
26	22 or 25 721602
27	lymphoedema/ 17927
28	hand edema/ or arm edema/ 2843
29	(lymphed* or lymphoed*).ti,ab,kf. 16315
30	elephantiasis.ti,ab,kf. 968
31	elephantiasis/ 1104
32	((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab,kf. 29338
33	(breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab,kf. 2543
34	(lymph* adj4 (oedema* or edema*)).ti,ab,kf. 2558
35	or/27-34 56148
36	26 and 35 9822
37	breast cancer-related lymphoedema/ 1026
38	36 or 37 9909
39	limit 38 to english language 9267
40	nonhuman/ not (human/ and nonhuman/) 4078001
41	39 not 40 9181
42	41 not (letter or editorial).pt. 8841

Searches
43 42 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6199
44 limit 43 to dc=20131028-20240219 3924
45 random:.tw. 1891142
46 placebo:.mp. 454874
47 double-blind:.tw. 203299
48 or/45-47 2106089
49 44 and 48 657
50 (MEDLINE or pubmed).tw. 428339
51 exp systematic review/ or systematic review.tw. 533668
52 meta-analysis/ 299840
53 intervention$.ti. 260952
54 or/50-53 988821
55 44 and 54 455
56 Clinical study/ 114620
57 Case control study/ 208200
58 Family study/ 23056
59 Longitudinal study/ 198747
60 Retrospective study/ 1538275
61 comparative study/ 833607
62 Prospective study/ 884095
63 Randomized controlled trials/ 268881
64 62 not 63 873100
65 Cohort analysis/ 1104832
66 cohort analy$.tw. 19876
67 (Cohort adj (study or studies)).tw. 483757
68 (Case control$ adj (study or studies)).tw. 167323
69 (follow up adj (study or studies)).tw. 61088
70 (observational adj (study or studies)).tw. 265849
71 (epidemiologic$ adj (study or studies)).tw. 107694
72 (cross sectional adj (study or studies)).tw. 356283
73 case series.tw. 151642
74 prospective.tw. 1070934
75 retrospective.tw. 1266191
76 or/56-61,64-75 5181172
77 44 and 76 1466
78 49 or 55 934

1 **Database name: Emcare**

Searches
1 exp breast cancer/ 87822
2 exp breast carcinoma/ 10647
3 exp medullary carcinoma/ 1186
4 ductal breast carcinoma in situ/ 47
5 exp breast tumor/ 91820
6 lobular carcinoma/ 292
7 or/1-6 92792
8 exp breast/ 19500
9 breast*.ti,ab,kf. 173755

Searches
10 8 or 9 175714
11 (breast adj milk).ti,ab,kf. 6979
12 (breast adj tender*).ti,ab,kf. 215
13 11 or 12 7191
14 10 not 13 168523
15 exp neoplasm/ 586574
16 14 and 15 78895
17 (breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 119680
18 (mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 3570
19 exp Paget nipple disease/ 1094
20 (paget* and (breast* or mammary or nipple*)).ti,ab,kf. 254
21 or/16-20 127587
22 7 or 21 146722
23 (duct* carcinoma* in situ or DCIS).ti,ab,kf. 3191
24 ductal breast carcinoma in situ/ 47
25 23 or 24 3195
26 22 or 25 147059
27 lymphoedema/ 3290
28 hand edema/ or arm edema/ 601
29 (lymphed* or lymphoed*).ti,ab,kf. 4027
30 elephantiasis.ti,ab,kf. 234
31 elephantiasis/ 202
32 ((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab,kf. 8658
33 (breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab,kf. 742
34 (lymph* adj4 (oedema* or edema*)).ti,ab,kf. 477
35 or/27-34 14711
36 26 and 35 2696
37 breast cancer-related lymphoedema/ 199
38 36 or 37 2702
39 limit 38 to english language 2550
40 nonhuman/ not (human/ and nonhuman/) 366923
41 39 not 40 2539
42 41 not (letter or editorial).pt. 2428
43 42 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 2390
44 limit 43 to dc=20131028-20240219 1549
45 random:.tw. 617894
46 placebo:.mp. 124509
47 double-blind:.tw. 61710
48 or/45-47 673244
49 44 and 48 306
50 (MEDLINE or pubmed).tw. 168156
51 exp systematic review/ or systematic review.tw. 196322
52 meta-analysis/ 60710

Searches	
53	intervention$.ti. 127911
54	or/50-53 386930
55	44 and 54 192
56	Clinical study/ 43682
57	Case control study/ 30075
58	Family study/ 9975
59	Longitudinal study/ 52483
60	Retrospective study/ 173031
61	comparative study/ 93270
62	Prospective study/ 138331
63	Randomized controlled trials/ 52706
64	62 not 63 136396
65	Cohort analysis/ 146137
66	cohort analy$.tw. 5531
67	(Cohort adj (study or studies)).tw. 162921
68	(Case control$ adj (study or studies)).tw. 46523
69	(follow up adj (study or studies)).tw. 19973
70	(observational adj (study or studies)).tw. 82242
71	(epidemiologic$ adj (study or studies)).tw. 31731
72	(cross sectional adj (study or studies)).tw. 148946
73	case series.tw. 40415
74	prospective.tw. 305265
75	retrospective.tw. 305940
76	or/56-61,64-75 1192781
77	44 and 76 458
78	49 or 55 424

1 **Database name: Epistemonikos**

Searches
(advanced_title_en:((breast* AND (neoplasm* OR cancer* OR tumor* OR tumour* OR carcinoma* OR adenocarcinoma* OR sarcoma* OR leiomyosarcoma* OR dcis OR duct* OR infiltrat* OR intraduct* OR lobul* OR medullary OR tubular OR malignanc*)) OR (mammar* AND (neoplasm* OR cancer* OR tumor* OR tumour* OR carcinoma* OR adenocarcinoma* OR sarcoma* OR leiomyosarcoma* OR dcis OR duct* OR infiltrat* OR intraduct* OR lobul* OR medullary OR tubular OR malignan*)) OR (paget* AND (breast* OR mammary OR nipple*)) OR (duct* carcinoma* in situ OR dcis)) OR advanced_abstract_en:((breast* AND (neoplasm* OR cancer* OR tumo?r* OR carcinoma* OR adenocarcinoma* OR sarcoma* OR leiomyosarcoma* OR dcis OR duct* OR infiltrat* OR intraduct* OR lobul* OR medullary OR tubular OR malignan*)) OR (mammar* AND (neoplasm* OR cancer* OR tumo?r* OR carcinoma* OR adenocarcinoma* OR sarcoma* OR leiomyosarcoma* OR dcis OR duct* OR infiltrat* OR intraduct* OR lobul* OR medullary OR tubular OR malignanc*)) OR (paget* AND (breast* OR mammary OR nipple*)) OR (duct* carcinoma* in situ OR dcis))) AND (advanced_title_en:((lymphoed* OR lymphed*) OR (elephantiasis) OR (((arm* OR hand* OR finger* OR upper limb* OR "chest wall" OR trunc* OR trunk* OR axilla* OR thoracic) AND (morbidity OR swell* OR swollen OR pain* OR oedema* OR edema*))) OR ((breast* AND (morbidity OR swell* OR swollen OR oedema* OR edema*))) OR ((lymph* AND (oedema* OR edema*)))) OR advanced_abstract_en:((lymphoed* OR lymphed*) OR (elephantiasis) OR (((arm* OR hand* OR finger* OR upper limb* OR "chest wall" OR trunc* OR trunk* OR axilla* OR

Searches
thoracic) AND (morbidity OR swell* OR swollen OR pain* OR oedema* OR edema*))) OR ((breast* AND (morbidity OR swell* OR swollen OR oedema* OR edema*))) OR ((lymph* AND (oedema* OR edema*))))) [Filters: classification=systematic-review, cochrane=missing, protocol=no, min_year=2013, max_year=2024]

1 **Database name: Health Technology Assessment (HTA)**

Searches
1 MESH DESCRIPTOR Breast Neoplasms EXPLODE ALL TREES 2 MESH DESCRIPTOR Neoplasms, Ductal, Lobular, and Medullary EXPLODE ALL TREES 3 MESH DESCRIPTOR Carcinoma, Lobular 4 MESH DESCRIPTOR Carcinoma, Medullary 5 MESH DESCRIPTOR Carcinoma, Intraductal, Noninfiltrating 6 #1 OR #2 OR #3 OR #4 OR #5 7 MESH DESCRIPTOR Breast EXPLODE ALL TREES 8 breast* 9 #7 or #8 10 (breast NEXT milk) 11 (breast NEXT tender*) 12 #10 or #11 13 #9 not #12 14 MESH DESCRIPTOR Neoplasms EXPLODE ALL TREES 15 #13 and #14 16 (breast* NEAR5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)) 17 (mammar* near5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)) 18 MESH DESCRIPTOR Paget's Disease, Mammary EXPLODE ALL TREES 19 (paget* and (breast* or mammary or nipple*)) 20 #15 OR #16 OR #17 OR #18 OR #19 21 #6 or #20 22 ((duct* carcinoma* in situ or DCIS)) 23 #21 or #22 24 MESH DESCRIPTOR Lymphoedema EXPLODE ALL TREES 25 (lymphoed* or lymphed*) 26 (elephantiasis) 27 (((arm* or hand* or finger* or upper limb* or "chest wall" or trunc* or trunk* or axilla* or thoracic) NEAR4 (morbidity or swell* or swollen or pain* or oedema* or edema*))) 28 ((breast* NEAR4 (morbidity or swell* or swollen or oedema* or edema*))) 29 ((lymph* NEAR4 (oedema* or edema*))) 30 #24 OR #25 OR #26 OR #27 OR #28 OR #29 31 #23 AND #30 32 MESH DESCRIPTOR Breast Cancer Lymphoedema 33 #31 OR #32 34 * IN DARE FROM 2013 TO 2015 35 #33 AND #34 36 * IN HTA FROM 2013 TO 2018 37 #33 AND #36

Database name: International Health Technology Assessment Database (INAHTA)

Searches
(((((paget* and (breast* or mammary or nipple*)))[Title] OR ((paget* and (breast* or mammary or nipple*)))[abs]) OR ("Paget's Disease, Mammary"[mh]) OR (((duct* carcinoma* in situ or DCIS))[Title] OR ((duct* carcinoma* in situ or DCIS))[abs]) OR (((breast* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[Title] OR ((breast* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[abs]) OR (((mammar* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[Title] OR ((mammar* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[abs]) OR (("Carcinoma, Intraductal, Noninfiltrating"[mh]) OR ("Carcinoma, Medullary"[mh]) OR ("Carcinoma, Lobular"[mh]) OR ("Neoplasms, Ductal, Lobular, and Medullary"[mhe]) OR ("Breast Neoplasms"[mhe]))) AND ((((lymph* AND (oedema* or edema*)))[Title] OR ((lymph* AND (oedema* or edema*)))[abs]) OR (((breast* AND (morbidity or swell* or swollen or oedema* or edema*)))[Title] OR ((breast* AND (morbidity or swell* or swollen or oedema* or edema*)))[abs]) OR ((((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) AND (morbidity or swell* or swollen or pain* or oedema* or edema*)))[Title] OR (((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) AND (morbidity or swell* or swollen or pain* or oedema* or edema*)))[abs]) OR ((elephantiasis)[Title] OR (elephantiasis)[abs]) OR ((Lymphoedema)[mh]) OR ((lymphed* or lymphoed*)[Title] OR (lymphed* or lymphoed*)[abs]))) OR ("Breast Cancer Lymphoedema"[mh])

Database name: Medline ALL

Searches
1 exp Breast Neoplasms/ 350560
2 exp "Neoplasms, Ductal, Lobular, and Medullary"/ 47659
3 Carcinoma, Lobular/ 6144
4 Carcinoma, Medullary/ 3414
5 Carcinoma, Intraductal, Noninfiltrating/ 10797
6 or/1-5 370386
7 exp Breast/ 54252
8 breast*.ti,ab,kf. 572489
9 7 or 8 582466
10 (breast adj milk).ti,ab,kf. 16563
11 (breast adj tender*).ti,ab,kf. 591
12 10 or 11 17151
13 9 not 12 565315
14 exp Neoplasms/ 3937769
15 13 and 14 367555
16 (breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 431026

Searches
17 (mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 37160
18 Paget's Disease, Mammary/ 819
19 (paget* and (breast* or mammary or nipple*)).ti,ab,kf. 1539
20 or/15-19 483927
21 6 or 20 541054
22 (duct* carcinoma* in situ or DCIS).ti,ab,kf. 9660
23 21 or 22 541289
24 exp Lymphoedema/ 14418
25 (lymphed* or lymphoed*).ti,ab,kf. 13195
26 elephantiasis.ti,ab,kf. 1679
27 ((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab,kf. 20575
28 (breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab,kf. 1955
29 (lymph* adj4 (oedema* or edema*)).ti,ab,kf. 1976
30 or/24-29 42155
31 23 and 30 6171
32 Breast Cancer Lymphoedema/ 464
33 31 or 32 6184
34 animals/ not humans/ 5164263
35 33 not 34 6147
36 limit 35 to ed=20131028-20240219 2743
37 limit 35 to dt=20131028-20240219 3272
38 36 or 37 3381
39 limit 38 to english language 3235
40 limit 39 to (letter or historical article or comment or editorial or news or case reports) 463
41 39 not 40 2772
42 exp Randomized Controlled Trial/ 610711
43 randomi?ed.mp. 1105735
44 placebo.mp. 253935
45 or/42-44 1172955
46 41 and 45 510
47 (MEDLINE or pubmed).tw. 348643
48 systematic review.tw. 291515
49 systematic review.pt. 252884
50 meta-analysis.pt. 195422
51 intervention$.ti. 210163
52 or/47-51 727387
53 41 and 52 364
54 Observational Studies as Topic/ 9480
55 Observational Study/ 152445
56 Epidemiologic Studies/ 9493
57 exp Case-Control Studies/ 1483235
58 exp Cohort Studies/ 2575193
59 Cross-Sectional Studies/ 493306
60 Controlled Before-After Studies/ 748
61 Historically Controlled Study/ 231

Searches		
62	Interrupted Time Series Analysis/	1999
63	Comparative Study.pt.	1913680
64	case control$.tw.	164265
65	case series.tw.	108819
66	(cohort adj (study or studies)).tw.	341314
67	cohort analy$.tw.	12718
68	(follow up adj (study or studies)).tw.	57657
69	(observational adj (study or studies)).tw.	173410
70	longitudinal.tw.	339087
71	prospective.tw.	744373
72	retrospective.tw.	791851
73	cross sectional.tw.	547954
74	or/54-73	5666064
75	41 and 74	1206
76	46 or 53	732

1

Cost-effectiveness searches

Database results

Databases	Date searched	Database platform	Database segment or version	No. of results downloaded
EconLit	22/02/24	Ovid	Econlit 1886 to February 15, 2024	0
(NHS) EED	22/02/24	CRD	-	0
Embase	22/02/24	Ovid	Embase 1996 to 2024 February 21	96
Health Technology Assessment (HTA)	22/02/24	CRD	-	4
International Health Technology Assessment Database (INAHTA)	22/02/24	https://database.inahta.org/	-	9
Medline ALL	22/02/24	Ovid	MEDLINE(R) ALL 1946 to February 21, 2024	79

Search strategy history

Database name: Econlit

Searches	
1	(breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kw. 396
2	(mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kw. 1
3	(duct* carcinoma* in situ or DCIS).ti,ab,kw. 3
4	(paget* and (breast* or mammary or nipple*)).ti,ab,kw. 0
5	or/1-4 398
6	(lymphed* or lymphoed*).ti,ab,kw. 0

Searches
7 elephantiasis.ti,ab,kw. 0
8 ((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab,kw. 11
9 (breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab,kw. 5
10 (lymph* adj4 (oedema* or edema*)).ti,ab,kw. 0
11 or/6-10 16
12 5 and 11 2
13 limit 12 to english 2
14 limit 13 to yr="2013 -Current" 0

Database name: NHS EED

Searches
1 MESH DESCRIPTOR Breast Neoplasms EXPLODE ALL TREES 1798
2 MESH DESCRIPTOR Neoplasms, Ductal, Lobular, and Medullary EXPLODE ALL TREES 65
3 MESH DESCRIPTOR Carcinoma, Lobular 7
4 MESH DESCRIPTOR Carcinoma, Medullary 7
5 MESH DESCRIPTOR Carcinoma, Intraductal, Noninfiltrating 13
6 #1 OR #2 OR #3 OR #4 OR #5 1820
7 MESH DESCRIPTOR Breast EXPLODE ALL TREES 97
8 breast* 3002
9 #7 or #8 3002
10 (breast NEXT milk) 58
11 (breast NEXT tender*) 14
12 #10 or #11 72
13 #9 not #12 2930
14 MESH DESCRIPTOR Neoplasms EXPLODE ALL TREES 12016
15 #13 and #14 2071
16 (breast* NEAR5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)) 2414
17 (mammar* near5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)) 7
18 MESH DESCRIPTOR Paget's Disease, Mammary EXPLODE ALL TREES 1
19 (paget* and (breast* or mammary or nipple*)) 4
20 #15 OR #16 OR #17 OR #18 OR #19 2455
21 #6 or #20 2477
22 ((duct* carcinoma* in situ or DCIS)) 46
23 #21 or #22 2477
24 MESH DESCRIPTOR Lymphoedema EXPLODE ALL TREES 50
25 (lymphoed* or lymphed*) 77
26 (elephantiasis) 6
27 (((arm* or hand* or finger* or upper limb* or "chest wall" or trunc* or trunk* or axilla* or thoracic) NEAR4 (morbidity or swell* or swollen or pain* or oedema* or edema*))) 82
28 ((breast* NEAR4 (morbidity or swell* or swollen or oedema* or edema*))) 15
29 ((lymph* NEAR4 (oedema* or edema*))) 3

Searches		
30	#24 OR #25 OR #26 OR #27 OR #28 OR #29	168
31	#23 AND #30	64
32	MESH DESCRIPTOR Breast Cancer Lymphoedema	0
33	#31 OR #32	64
34	* IN NHSEED FROM 2013 TO 2015	3345
35	#33 AND #34	0

Database name: Embase

Searches		
1	exp breast cancer/	530109
2	exp breast carcinoma/	76856
3	exp medullary carcinoma/	10993
4	ductal breast carcinoma in situ/	2810
5	exp breast tumor/	592548
6	lobular carcinoma/	3430
7	or/1-6	602104
8	exp breast/	90259
9	breast*.ti,ab,kf.	708228
10	8 or 9	723627
11	(breast adj milk).ti,ab,kf.	18068
12	(breast adj tender*).ti,ab,kf.	642
13	11 or 12	18704
14	10 not 13	704923
15	exp neoplasm/	4815765
16	14 and 15	544005
17	(breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf.	559419
18	(mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf.	30192
19	exp Paget nipple disease/	7002
20	(paget* and (breast* or mammary or nipple*)).ti,ab,kf.	1496
21	or/16-20	610395
22	7 or 21	720985
23	(duct* carcinoma* in situ or DCIS).ti,ab,kf.	15984
24	ductal breast carcinoma in situ/	2810
25	23 or 24	17223
26	22 or 25	721860
27	lymphoedema/	17932
28	hand edema/ or arm edema/	2844
29	(lymphed* or lymphoed*).ti,ab,kf.	16320
30	elephantiasis.ti,ab,kf.	968
31	elephantiasis/	1104
32	((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab,kf.	29351
33	(breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab,kf.	2544

Searches
34 (lymph* adj4 (oedema* or edema*)).ti,ab,kf. 2560 35 or/27-34 56168 36 26 and 35 9827 37 breast cancer-related lymphoedema/ 1027 38 36 or 37 9914 39 limit 38 to english language 9271 40 nonhuman/ not (human/ and nonhuman/) 4079755 41 39 not 40 9185 42 41 not (letter or editorial).pt. 8845 43 42 not (conference abstract* or conference review or conference paper or conference proceeding).db,pt,su. 6202 44 limit 43 to dc=20131028-20240222 3927 45 cost utility analysis/ 12719 46 quality adjusted life year/ 36546 47 cost*.ti. 170922 48 (cost* adj2 utilit*).tw. 12813 49 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. 366211 50 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 64840 51 (qualit* adj2 adjust* adj2 life*).tw. 27688 52 QALY*.tw. 27269 53 (incremental* adj2 cost*).tw. 29195 54 ICER.tw. 13436 55 utilities.tw. 14726 56 markov*.tw. 39567 57 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. 67998 58 ((utility or effective*) adj2 analys*).tw. 37326 59 (willing* adj2 pay*).tw. 14913 60 (EQ5D* or EQ-5D*).tw. 26893 61 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 5431 62 (european* adj2 quality adj3 ("5" or five)).tw. 1026 63 or/45-62 591958 64 44 and 63 96

1 **Database name: Health Technology Assessment (HTA)**

Searches
1 MESH DESCRIPTOR Breast Neoplasms EXPLODE ALL TREES 1798 2 MESH DESCRIPTOR Neoplasms, Ductal, Lobular, and Medullary EXPLODE ALL TREES 65 3 MESH DESCRIPTOR Carcinoma, Lobular 7 4 MESH DESCRIPTOR Carcinoma, Medullary 7 5 MESH DESCRIPTOR Carcinoma, Intraductal, Noninfiltrating 13 6 #1 OR #2 OR #3 OR #4 OR #5 1820 7 MESH DESCRIPTOR Breast EXPLODE ALL TREES 97 8 breast* 3002 9 #7 or #8 3002

Searches
10 (breast NEXT milk) 58 11 (breast NEXT tender*) 14 12 #10 or #11 72 13 #9 not #12 2930 14 MESH DESCRIPTOR Neoplasms EXPLODE ALL TREES 12016 15 #13 and #14 2071 16 (breast* NEAR5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)) 2414 17 (mammar* near5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)) 7 18 MESH DESCRIPTOR Paget's Disease, Mammary EXPLODE ALL TREES 1 19 (paget* and (breast* or mammary or nipple*)) 4 20 #15 OR #16 OR #17 OR #18 OR #19 2455 21 #6 or #20 2477 22 ((duct* carcinoma* in situ or DCIS)) 46 23 #21 or #22 2477 24 MESH DESCRIPTOR Lymphoedema EXPLODE ALL TREES 50 25 (lymphoed* or lymphed*) 77 26 (elephantiasis) 6 27 (((arm* or hand* or finger* or upper limb* or "chest wall" or trunc* or trunk* or axilla* or thoracic) NEAR4 (morbidity or swell* or swollen or pain* or oedema* or edema*))) 82 28 ((breast* NEAR4 (morbidity or swell* or swollen or oedema* or edema*))) 15 29 ((lymph* NEAR4 (oedema* or edema*))) 3 30 #24 OR #25 OR #26 OR #27 OR #28 OR #29 168 31 #23 AND #30 64 32 MESH DESCRIPTOR Breast Cancer Lymphoedema 0 33 #31 OR #32 64 34 * IN DARE FROM 2013 TO 2015 17124 35 #33 AND #34 13 36 * IN HTA FROM 2013 TO 2018 4606 37 #33 AND #36 4

Database name: International Health Technology Assessment Database (INAHTA)

Searches
(((((paget* and (breast* or mammary or nipple*)))[Title] OR ((paget* and (breast* or mammary or nipple*)))[abs]) OR ("Paget's Disease, Mammary"[mh]) OR (((duct* carcinoma* in situ or DCIS))[Title] OR ((duct* carcinoma* in situ or DCIS))[abs]) OR (((breast* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[Title] OR ((breast* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[abs]) OR (((mammar* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)))[Title] OR ((mammar* AND (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or

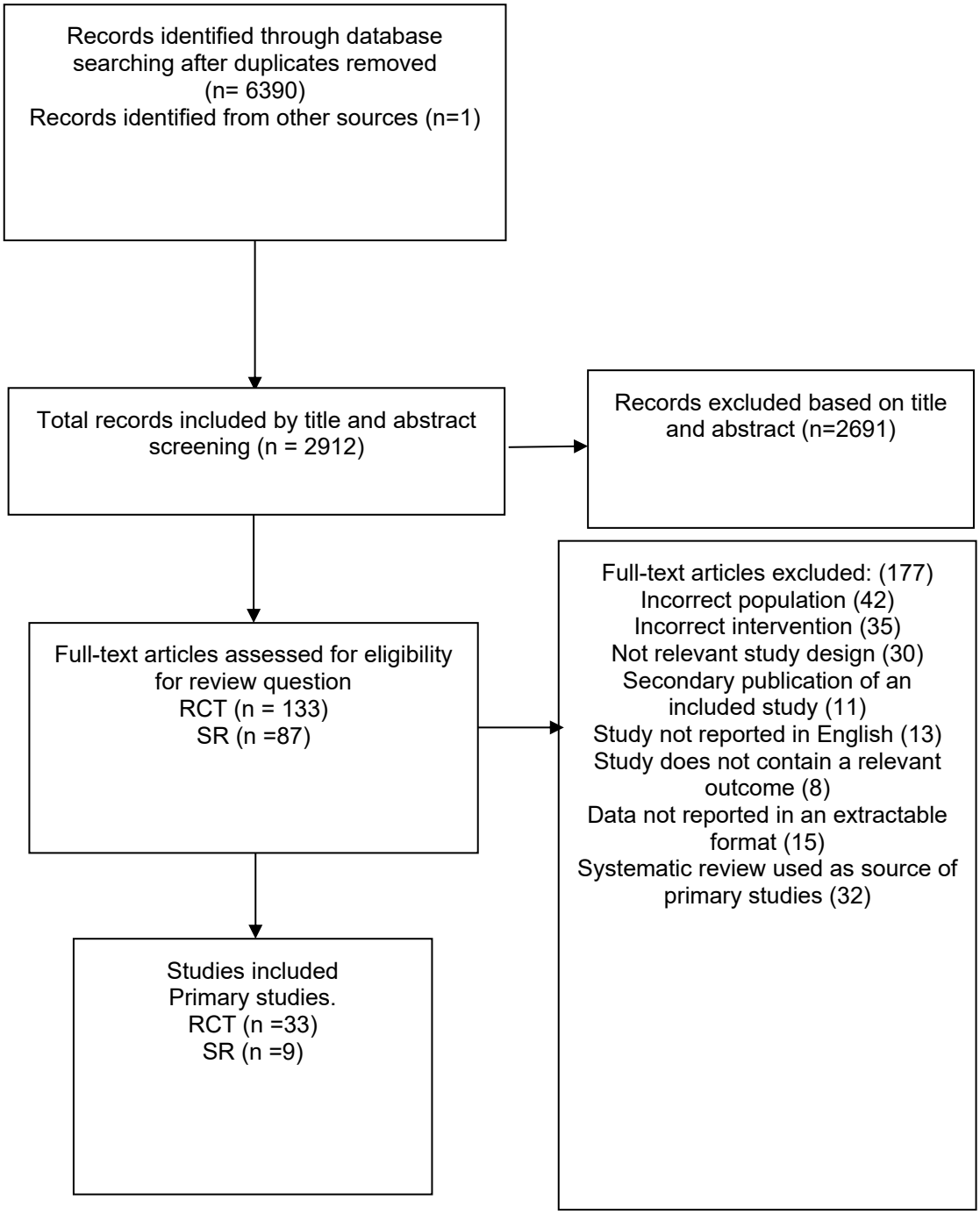
Searches
medullary or tubular or malignan*)))[abs]) OR (("Carcinoma, Intraductal, Noninfiltrating"[mh]) OR ("Carcinoma, Medullary"[mh]) OR ("Carcinoma, Lobular"[mh]) OR ("Neoplasms, Ductal, Lobular, and Medullary"[mhe]) OR ("Breast Neoplasms"[mhe])) AND ((((lymph* AND (oedema* or edema*)))[Title] OR ((lymph* AND (oedema* or edema*)))[abs]) OR (((breast* AND (morbidity or swell* or swollen or oedema* or edema*)))[Title] OR ((breast* AND (morbidity or swell* or swollen or oedema* or edema*)))[abs]) OR ((((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) AND (morbidity or swell* or swollen or pain* or oedema* or edema*)))[Title] OR (((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) AND (morbidity or swell* or swollen or pain* or oedema* or edema*)))[abs]) OR ((elephantiasis)[Title] OR (elephantiasis)[abs]) OR ((Lymphoedema)[mh]) OR ((lymphed* or lymphoed*)[Title] OR (lymphed* or lymphoed*)[abs])))) OR ("Breast Cancer Lymphoedema"[mh])

1 **Database name: Medline ALL**

Searches
1 exp Breast Neoplasms/ 350464
2 exp "Neoplasms, Ductal, Lobular, and Medullary"/ 47625
3 Carcinoma, Lobular/ 6142
4 Carcinoma, Medullary/ 3414
5 Carcinoma, Intraductal, Noninfiltrating/ 10794
6 or/1-5 370256
7 exp Breast/ 54248
8 breast*.ti,ab,kf. 572438
9 7 or 8 582416
10 (breast adj milk).ti,ab,kf. 16564
11 (breast adj tender*).ti,ab,kf. 591
12 10 or 11 17152
13 9 not 12 565264
14 exp Neoplasms/ 3937191
15 13 and 14 367429
16 (breast* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 430956
17 (mammar* adj5 (neoplasm* or cancer* or tumo?r* or carcinoma* or adenocarcinoma* or sarcoma* or leiomyosarcoma* or dcis or duct* or infiltrat* or intraduct* or lobul* or medullary or tubular or malignan*)).ti,ab,kf. 37150
18 Paget's Disease, Mammary/ 819
19 (paget* and (breast* or mammary or nipple*)).ti,ab,kf. 1538
20 or/15-19 483859
21 6 or 20 540948
22 (duct* carcinoma* in situ or DCIS).ti,ab,kf. 9658
23 21 or 22 541183
24 exp Lymphoedema/ 14413
25 (lymphed* or lymphoed*).ti,ab,kf. 13192
26 elephantiasis.ti,ab,kf. 1678
27 ((arm* or hand* or finger* or upper limb* or chest wall or trunc* or trunk* or axilla* or thoracic) adj4 (morbidity or swell* or swollen or pain* or oedema* or edema*)).ti,ab,kf. 20586

Searches
28 (breast* adj4 (morbidity or swell* or swollen or oedema* or edema*)).ti,ab,kf. 1954
29 (lymph* adj4 (oedema* or edema*)).ti,ab,kf. 1977
30 or/24-29 42160
31 23 and 30 6168
32 Breast Cancer Lymphoedema/ 463
33 31 or 32 6181
34 animals/ not humans/ 5163561
35 33 not 34 6144
36 limit 35 to ed=20131028-20240222 2739
37 limit 35 to dt=20131028-20240222 3269
38 36 or 37 3378
39 limit 38 to english language 3231
40 limit 39 to (letter or historical article or comment or editorial or news or case reports) 464
41 39 not 40 2767
42 Cost-Benefit Analysis/ 94087
43 Quality-Adjusted Life Years/ 16166
44 Markov Chains/ 16084
45 exp Models, Economic/ 16263
46 cost*.ti. 148113
47 (cost* adj2 utilit*).tw. 7946
48 (cost* adj2 (effective* or assess* or evaluat* or analys* or model* or benefit* or threshold* or quality or expens* or saving* or reduc*)).tw. 285690
49 (economic* adj2 (evaluat* or assess* or analys* or model* or outcome* or benefit* or threshold* or expens* or saving* or reduc*)).tw. 48640
50 (qualit* adj2 adjust* adj2 life*).tw. 18401
51 QALY*.tw. 14916
52 (incremental* adj2 cost*).tw. 17979
53 ICER.tw. 6297
54 utilities.tw. 9693
55 markov*.tw. 32699
56 (dollar* or USD or cents or pound or pounds or GBP or sterling* or pence or euro or euros or yen or JPY).tw. 55441
57 ((utility or effective*) adj2 analys*).tw. 25775
58 (willing* adj2 pay*).tw. 10210
59 (EQ5D* or EQ-5D*).tw. 14021
60 ((euroqol or euro-qol or euroquol or euro-quol or eurocol or euro-col) adj3 ("5" or five)).tw. 4066
61 (european* adj2 quality adj3 ("5" or five)).tw. 742
62 or/42-61 515254
63 41 and 62 79

Appendix C –Effectiveness evidence study selection



Appendix D –Effectiveness evidence

Systematic review evidence

Gao, 2021

Bibliographic Reference	Gao, Yu; Ma, Tingting; Han, Mei; Yu, Mingwei; Wang, Xiuhui; Lv, Yiren; Wang, Xiaomin; Effects of Acupuncture and Moxibustion on Breast Cancer-Related Lymphoedema: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.; Integrative cancer therapies; 2021; vol. 20; 15347354211044107

Study Characteristics

Study design	Systematic review
Study details	Dates searched Until January 2021 Databases searched English/Chinese medical literature in the MEDLINE (via PubMed), EMBASE, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Chongqing VIP Chinese Science and Technology Periodical (VIP), and Wanfang databases. Sources of funding Beijing Science and Technology Plan Project Grant
Inclusion criteria	Population: women with lymphoedema caused by breast cancer and its treatment (surgery/raditotherapy) Intervention: needle acupuncture was allowed for acupuncture and only burning Artemisia vulgaris was allowed for moxibustion
Exclusion criteria	Unavailable original full text; duplicates of published literature; incomplete or missing research data; studies without comparable baselines; animal experiments, letters, reviews or commentaries
Intervention(s)	Intervention: acupuncture and/or moxibustion without any restriction of manipulation techniques Comparator: routine care; oral drug therapy (diosmin tablets, hydrochlorothiazide and spironolactone), pneumatic circulation, functional exercises and wait-list control
Outcome(s)	Severity of lymphoedema (changes in arm circumference at difference points) Adverse events related to acupuncture and moxibustion Range of motion of shoulder Visual analoguescale (VAS) for swelling and pain Quality of life
Number of studies included in	14 studies

the systematic review	
Studies from the systematic review that are relevant for use in the current review	Ba 2019, Bao 2018, Huang 2014, Jiao 2017, Liu 2019a, Liu 2019b, Shen 2019, Smith 2014, Wang 2019, Wu 2018, Yao 2016, Zhan and Lou 2017, Zhang 2020, Zhao 2012

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(Some issues with blinding of participants and selective reporting of results)*
Overall study ratings	Applicability as a source of data	Fully applicable

Jeffs, 2018

Bibliographic Reference	Jeffs, Eunice; Ream, Emma; Taylor, Cath; Bick, Debra; Clinical effectiveness of decongestive treatments on excess arm volume and patient-centered outcomes in women with early breast cancer-related arm lymphoedema : a systematic review.; JBI database of systematic reviews and implementation reports; 2018; vol. 16 (no. 2); 453-506

Study Characteristics

Study design	Systematic review
Study details	Dates searched Until July 2016 Databases searched Allied and Contemporary Medicine (AMED), Biomed Central, BIOSIS, British Nursing Index, CINAHL, Cochrane Library (Wiley Online Library), Embase, HMIC, MEDLINE, Physiotherapy Evidence Database (PEDro), PsycARTICLES, PsycINFO, PubMed, Scopus, Turning Research into Practice (TRIP), Web of Science and WorldCat Sources of funding National Institute for Health Research

Inclusion criteria	Population: women with unilateral BCRL of the arm who received lymphoedema treatment within 12 months of developing arm swelling Intervention: Any conservative non-drug treatment where the goal was to decongest the arm, that is, reduce lymphoedema , whether delivered by lymphoedema therapist or patient self-management
Exclusion criteria	Studies reporting participants with other forms of lymphoedema (e.g. leg lymphoedema , breast/ truncal edema) Unless BCRL outcomes were reported separately People with bilateral lymphoedema, or people at risk of developing BCRL People receiving concurrent cancer treatment Men with BCRL Studies evaluating surgical or drug therapy interventions, treatment of progressive lymphoedema due to uncontrolled active cancer, safety assessment of treatment, interventions used without the intention of lymphoedema decongestion, evaluation of a single session of treatment (such as compression bandaging or hosiery, manual lymph drainage or exercise), interventions to reduce the risk of developing BCRL, or assessment techniques
Intervention(s)	Intervention: Any conservative non-drug treatment where the goal was to decongest the arm Delivered by therapist or patient self-management Comparator: Another form of lymphoedema treatment, placebo or no treatment
Outcome(s)	Assessment of lymphoedema Relative change in excess arm volume compared to the non-swollen arm, measured by water displacement, perometry or circumference measurements Quality of life Using an appropriate, validated tool or visual analogue scale
Number of studies included in the systematic review	7 (5 RCTs)
Studies from the systematic review that are relevant for use in the current review	Dayes et al. 2013, Gradalski et al. 2015, Kaviani et al. 2006, Kim et al. 2010, McNeely et al. 2014

Studies from the systematic review that are not relevant for use in the current review	Haghighat et al. 2013a, Haghighat et al. 2013b
Additional comments	Originally planned to exclude studies with women who had symptoms for more than 12 months (assumed that sufficient skin and tissue changes would have occurred by 12 months to affect the outcome of treatment), but due to lack of data for symptoms less than 12 months, these studies were included. No meta-analysis performed due to heterogeneity. Results summarised for each study instead

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low *(good quality systematic review)*
Overall study ratings	Applicability as a source of data	Fully applicable

Kasawara, 2018

Bibliographic Reference	Kasawara, Karina Tamy; Mapa, Jessica Monique Rossetti; Ferreira, Vilma; Added, Marco Aurelio Nemitalla; Shiwa, Silvia Regina; Carvas, Nelson Jr; Batista, Patricia Andrade; Effects of Kinesio Taping on breast cancer-related lymphoedema : A meta-analysis in clinical trials.; Physiotherapy theory and practice; 2018; vol. 34 (no. 5); 337-345

Study Characteristics

Study design	Systematic review
Study details	Dates searched search was conducted in SCIELO, LILACS, MEDLINE (via PubMed), and PEDro databases Databases searched from 2009 to 2016. Sources of funding not reported

Inclusion criteria	Adults with upper limb lymphoedema secondary to breast cancer treatment.
Exclusion criteria	Case reports and case series Duplicate studies Studies using KT for other types of lymphoedema (congenital, primary, lower limb) Non-English, Portuguese or Spanish language Studies without a comparison group
Intervention(s)	Kinesio Taping (KT) Comparators: no intervention or compression bandaging and complex decongestive therapy.
Outcome(s)	Quality of life severity of lymphoedema (change in limb volume/circumference).
Number of studies included in the systematic review	7 clinical trials with a total of 303 participants
Studies from the systematic review that are relevant for use in the current review	Tsai, 2009 Smykla, 2013 Pekyavas, 2014 Pop, 2014 Malicka, 2014 Taradaj, 2016 Melgaard, 2016
Studies from the systematic review that are not relevant for use in the current review	0

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(some concerns with selective reporting of results and selection of included studies)*
Overall study ratings	Applicability as a source of data	Fully applicable

Lin, 2022

Bibliographic Reference	Lin, Yan; Yang, Yan; Zhang, Xiaoyu; Li, Wandi; Li, Haoran; Mu, Dali; Manual Lymphatic Drainage for Breast Cancer-related Lymphoedema: A Systematic Review and Meta-analysis of Randomized Controlled Trials.; Clinical breast cancer; 2022; vol. 22 (no. 5); e664-e673

Study Characteristics

Study design	Systematic review
Study details	Dates searched Up until April 2021 Databases searched Cochrane Library, the Cochrane Central Register of Controlled Trials, PubMed, EMBASE, Web of Science, ClinicalTrials.gov were systematically searched. Sources of funding None
Inclusion criteria	Population: Women with breast cancer and lymphoedema Intervention: Manual lymphatic drainage
Exclusion criteria	Studies without related outcomes, and studies without RCT design.
Intervention(s)	Intervention: Manual lymphatic drainage Comparator: Another form of lymphoedema treatment, placebo or no treatment
Outcome(s)	Assessment of lymphoedema Incidence of lymphoedema, volumetric changes in lymphoedema Visual analoguescale (VAS) for swelling and pain Quality of life
Number of studies	11 RCTs

included in the systematic review	
Studies from the systematic review that are relevant for use in the current review	Anderson 2000, Cho 2016, Devoogdt 2011, Devoogdt 2018, Gol 2020, Gradalski 2015, McNeely 2004, Sen 2020, Tambour 2018, Zhang 2016
Studies from the systematic review that are not relevant for use in the current review	Anderson 2000, Cho 2016, Devoogdt 2011, Devoogdt 2018, Gol 2020, Gradalski 2015, McNeely 2004, Sen 2020, Tambour 2018, Zhang 2016
Additional comments	Uses AMSTAR for RoB assessments of RCTs

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low *(no concerns)*
Overall study ratings	Applicability as a source of data	Fully applicable

Lytvyn, 2020

Bibliographic Reference	Lytvyn, Lyubov; Conservative intervention strategies for adult cancer-related lymphoedema : a systematic review and network meta-analysis; Number 5/September 2020; 2020; vol. 47 (no. 5); e171-e189

Study Characteristics

Study design	Systematic review
Study details	Dates searched Studies published from database to October 31, 2019 were searched.

	Databases searched CINAHL, Embase, and MEDLINE. Clinical trial registries (clinicaltrials.gov and WHO ICTRP) were also searched for grey literature. Sources of funding 12 studies did not report funding source 18 studies reported university, hospital, and/or government funding 4 studies reported no funding 2 studies reported university, hospital, and/or government funding and in-kind industry donation
Inclusion criteria	Randomised trials Adult participants (≥18 years) with cancer-related secondary lymphoedema in extremities Conservative treatment strategies of at least 2 weeks duration English language
Exclusion criteria	Trials examining truncal, breast, and head and neck lymphoedema Mixed populations (e.g., primary and secondary lymphoedema) that did not report study population separately Surgical treatments, pharmacological treatments, laser therapy, kinesio tape, shock-wave therapy, electrical stimulation, aromatherapy
Intervention(s)	Intervention: Resistance or aerobic exercises Intervention: lymphatic drainage, lymphtape, compression bandage or sleeve, intermittent pneumatic compression (ICP) or exercise Intervention: Manual lymphatic drainage Comparator: Compression bandaging or other standard treatment
Outcome(s)	Patient-reported outcomes Adverse events severity of lymphoedema (change in limb volume/circumference). Quality of life
Number of studies included in the systematic review	36 randomised controlled trials with 1,651 participants
Studies from the systematic review that are relevant for use in the current review	Andersen, 2000 Bergmann, 2014 Bok, 2016 Buchan, 2016 Buragadda, 2015 Chmielewska, 2016 Cormie, 2013 Dayes, 2013 Didem, 2005 Do, 2015 Do, 2017 Gradalski, 2015 Gurdal, 2012 Haghighat, 2010 Hayes, 2009 Jeffs, 2013 Johansson, 1998 Johansson, 2013 Letellier, 2014 Ligabue, 2019 Loudon, 2014 Luz, 2018 McClure, 2010 McKenzie, 2003 McNeely, 2004 Park, 2017 Pasyar, 2019 Sanal-Toprak, 2019 Schmitz, 2009 Schmitz, 2019 Sitzia, 2002 Szolnoky, 2009 Szuba, 2002 Tambour, 2018 Uzkeser, 2011 Wigg, 2009
Studies from the	None

systematic review that are not relevant for use in the current review	
Additional comments	1,651 total participants across 36 studies

Study arms

Complete Decongestive Therapy (CDT): (N = 388)

Manual Lymphatic Drainage (MLD) (N = 35)

Compression pumps (N = 146)

Aerobic exercise (N = 35)

Resistance exercise (N = 170)

Aerobic + resistance exercise (N = 113)

Water-based/yoga exercise (N = 83)

Standard care (maintenance phase of CDT): (N = 364)

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low *As a network meta-analysis was conducted, this was appraised against the modified PRISMA -NMA checklist, based on this the NMA fully addresses and details most criteria well. However there were concerns around network geometry as despite the network diagram being provided, there was limited discussion of potential biases related to the network structure. There were also some issues surrounding the justification for merging some interventions.*
Overall study ratings	Applicability as a source of data	Fully applicable

Qiao, 2023

Bibliographic Reference	Qiao, Jia; Yang, Li-Ning; Kong, Yu-Han; Huang, Xin; Li, Yi; Bai, Ding-Qun; Effect of Manual Lymphatic Drainage on Breast Cancer-Related Postmastectomy Lymphoedema: A Meta-analysis of Randomized Controlled Trials.; Cancer nursing; 2023; vol. 46 (no. 2); 159-166

Study Characteristics

Study design	Systematic review
Study details	Dates searched Until January 2020 Databases searched PubMed, EMBASE, Web of science, and the Cochrane Library Sources of funding Chongqing Health Commission and Science and Technology Bureau Joint Research Project of Traditional Chinese Medicine
Inclusion criteria	Population: Patients aged 18 or over with BCRL diagnostic criteria: an increase in arm volume by at least 150 mL compared with preoperatively, an increase in arm circumference by at least 2 cm, or an increase in arm volume of the affected arm by at least 10% compared with the unaffected arm Intervention: Manual lymphatic drainage
Exclusion criteria	Patients with serious complications (vital signs unstable)
Intervention(s)	Intervention: Manual lymphatic drainage Comparator: Compression bandaging or other standard treatment
Outcome(s)	Assessment of lymphoedema Change from baseline (measured by volume change or arm circumference change) Quality of life Patient-reported outcomes Pain, anxiety, mobility
Number of studies included in the systematic review	8
Studies from the systematic review that are relevant	Andersen 2000, Bergmann 2014, Johansson 1999, Sitzia 2002, Tambour 2018, Dayes 2013, McNeely 2004, Williams 2002

for use in the current review	
Studies from the systematic review that are not relevant for use in the current review	None

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(Some concerns about sensitivity analysis methods and publication bias)*
Overall study ratings	Applicability as a source of data	Fully applicable

Rangon, 2022

Bibliographic Reference	Rangon, Flavia Belavenuto; da Silva, Jessica; Dibai-Filho, Almir Vieira; Guirro, Rinaldo Roberto de Jesus; Guirro, Elaine Caldeira de Oliveira; Effects of Complex Physical Therapy and Multimodal Approaches on Lymphoedema Secondary to Breast Cancer: A Systematic Review and Meta-analysis of Randomized Controlled Trials.; Archives of physical medicine and rehabilitation; 2022; vol. 103 (no. 2); 353-363

Study Characteristics

Study design	Systematic review
Study details	Dates searched Until August 2020 Databases searched MEDLINE, Embase, Cochrane Library, and Physiotherapy Evidence Database Sources of funding None reported
Inclusion criteria	Population: Breast cancer survivors with clinical diagnosis of unilateral lymphoedema in the upper limb
Exclusion criteria	Studies in languages other than English Other conditions that cause oedema of the upper limb, however it is not diagnosed as lymphoedema

Intervention(s)	Intervention: Complex physical therapy Complex physical therapy: Gold standard treatment for lymphoedema control, consisting of skin care, manual lymphatic drainage, compression and myolymphokinetic exercises. Comparator: Multimodal approaches Other conservative treatment modalities or combination of complex physical therapy with other treatment modalities
Outcome(s)	Assessment of lymphoedema Reducing total volume of the upper limb Patient-reported outcomes Pain reduction, function
Number of studies included in the systematic review	12
Studies from the systematic review that are relevant for use in the current review	Bergmann et al. 2014, Buragadda et al. 2015, Dayes et al. 2013, Do et al. 2015, Ergin et al. 2019, Gradalski et al. 2015, Haghighat et al. 2010, Kim et al. 2010, Pekyavas et al. 2014, Tambour et al. 2018, Tastaban et al. 2020, Uzkeser et al. 2015
Studies from the systematic review that are not relevant for use in the current review	Didem et al. 2005, Szolnoky et al. 2009
Additional comments	Outcomes separated into shorter- and longer-term outcomes (less than 1 month, 1-3 months and 6-12 months)

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(Limited reporting of study baseline characteristics and high heterogeneity for pain and physical functioning outcomes)*

Section	Question	Answer
Overall study ratings	Applicability as a source of data	Fully applicable

1

2 **Winters, 2021**

Bibliographic Reference	Winters, H; Tielemans, HJP; Paulus, V; Hummelink, S; Slater, NJ; Ulrich, DJO; A Systematic Review and Meta-Analysis of Vascularised Lymph Node Transfer for Breast Cancer Related Lymphoedema.; Journal of vascular surgery. Venous and lymphatic disorders; 2021

3

4 **Study Characteristics**

Study design	Systematic review
Study details	Dates searched The last search date was June 27, 2019 Databases searched Sources of funding Not reported
Inclusion criteria	Studies describing the use of vascularized lymph node transfer (VLNT) in the treatment of breast cancer-related lymphoedema (BCRL) Studies including female patients aged >18 years Studies with at least 5 patients
Exclusion criteria	Not reported
Intervention(s)	vascularized lymph node transfer (VLNT) Comparators: no intervention/physiotherapy alone or compare VLNT plus breast reconstruction to breast reconstruction alone.
Outcome(s)	Quality of life Patient-reported outcomes Severity of lymphoedema (change in volume difference between arms) Adverse events Skin infections, complication rates
Number of studies included in the systematic review	17
Studies from the systematic	Akita, 2017 Aljaaly, 2018 Becker, 2006 De Brucker, 2016 Dionyssiou, 2016 Engel, 2017 Gharb, 2011 Granzow, 2014

review that are relevant for use in the current review	Gratzon, 2017 Lin, 2009 Liu, 2018 Maruccia, 2019 Montag, 2019 Nguyen, 2015 Patel, 2014 Saaristo, 2012 Yang, 2017
Studies from the systematic review that are not relevant for use in the current review	0
Additional comments	

Study arms

Vascularised Lymph Node Transfer (N = NR)

No intervention/physiotherapy alone (N = NR)

Some included studies compare VLNT to no intervention/physiotherapy alone or compare VLNT plus breast reconstruction to breast reconstruction alone.

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	High *(publication bias, selective reporting of results from included studies, high heterogeneity between baseline characteristics)*
Overall study ratings	Applicability as a source of data	Partially applicable *(includes cohort studies)*

Yeung, 2018

Bibliographic Reference	Yeung, Wai; Semciw, Adam I; Aquatic Therapy for People with Lymphoedema: A Systematic Review and Meta-analysis.; Lymphatic research and biology; 2018; vol. 16 (no. 1); 9-19

Study Characteristics

Study design	Systematic review
Study details	Dates searched Until January 2016 Databases searched

	PubMed, CINAHL, EMBASE, COCHRANE, and physiotherapy evidence database [PEDro) Sources of funding None reported
Inclusion criteria	Population: People with primary or secondary lymphoedema Intervention: Aquatic therapy or hydrotherapy Defined as the therapeutic use of water for the maintenance of health or the treatment of disease with various temperatures, pressure, duration, and site
Exclusion criteria	Not reported
Intervention(s)	Intervention: Aquatic therapy or hydrotherapy Alone or in combination with other treatments for lymphoedema Comparator: Standard land-based treatment Standard land-based treatment (e.g. habitual physical activities, standard care)
Outcome(s)	Assessment of lymphoedema relative change in limb volume (% difference in volume between affected and unaffected limb) as measured by water displacement, opto-electronic perometry or circumference measurements or relative change to tissue fluid status as measured by tissue dielectric constant (TDC) or bioelectrical impedance spectroscopy (BIS) Quality of life psychosocial patient self-report outcome measure Patient-reported outcomes Limb function (including strength, range of movement, and symptoms such as pain and sensation of heaviness in affected limb) Adverse events
Number of studies included in the systematic review	4
Studies from the systematic review that are relevant for use in the current review	Tidhar 2010, Letellier 2014

Studies from the systematic review that are not relevant for use in the current review	Hayes 2009, Johansson 2013
Additional comments	Inclusion criteria for the review is anyone who has primary or secondary lymphoedema. However, both studies included in the review were for people with breast cancer and therefore relevant to this review Adverse events were included in the protocol, but no study compared these between arms

Critical appraisal - RQ2AB - Systematic reviews RoB

Section	Question	Answer
Overall study ratings	Overall risk of bias	Moderate *(Limited information about search terms and exclusion criteria. RE model used for physical function outcome)*
Overall study ratings	Applicability as a source of data	Fully applicable

Randomised clinical trial evidence

Ali, 2021

Bibliographic Reference	Ali, Khadra Mohamed; El Gammal, Eid Rizk; Eladl, Hadaya Mosaad; Effect of Aqua Therapy Exercises on Postmastectomy Lymphoedema: A Prospective Randomized Controlled Trial.; Annals of rehabilitation medicine; 2021; vol. 45 (no. 2); 131-140

Study details

Trial registration number and/or trial name	NCT04257643
Study type	Randomised controlled trial (RCT)
Study location	Egypt
Study setting	Community setting
Study dates	July 2018 to November 2019
Sources of funding	Not reported. No conflicts of interest were reported.
Inclusion criteria	Patients with a history of breast cancer for which they had undergone unilateral excision of the axillary lymph nodes Mild to moderate degree / stage I-II lymphoedema (a difference in circumference up to 2 cm compared to the other arm for mild; of 2–5 cm for moderate)
Exclusion criteria	Cancer recurrence, ongoing active oncological treatment, functional disorders impeding participation in the exercise programs, and open wounds in any part of the body
Intervention(s)	Aqua therapy-resistance exercise program. Three 60 minute sessions per week for 8 consecutive weeks. Hydrotherapy pool. Arm exercises and diaphragmatic breathing. No compression garment specified. Infection prevention measures (pool cleanliness) carried out.
Comparator	Exercise therapy program. Three 60 minute sessions per week for 8 consecutive weeks. Mobility and stretching exercises, strength exercises, resistance exercise and diaphragmatic breathing. Participants instructed to use a compression garment during sessions consistently.
Outcome measures	Patient-reported outcomes Swelling Mobility

Number of participants	N=50 Aqua therapy: 25 Exercise therapy: 25
Duration of follow-up	8 weeks
Loss to follow-up	0
Methods of analysis	The mean, standard deviation, and frequencies were calculated for the descriptive statistics. The Shapiro-Wilk test was used to check the normal distribution of data, and homogeneity between the groups was tested using Levene test for homogeneity of variances. Within- and between-group comparisons were performed using a mixed-design MANOVA.
Additional comments	Study was limited by a short term follow up.

Study arms

Aqua exercise therapy (N = 25)

Exercises as for exercise therapy group, but in water

Exercise therapy (N = 25)

8 week programme

Characteristics

Arm-level characteristics

Characteristic	Aqua exercise therapy (N = 25)	Exercise therapy (N = 25)
% Female No of events	n = 25 ; % = 100	n = 25 ; % = 100
Mean age (SD) Mean (SD)	51.36 (9.15)	49.84 (8.57)
BMI Mean (SD)	29.97 (3.36)	29.78 (4)
Type of surgery: modified radical mastectomy No of events	n = 12 ; % = 48	n = 9 ; % = 36
Type of surgery: Partial mastectomy and lymph node resection No of events	n = 13 ; % = 52	n = 16 ; % = 64
Lymphoedema stage I No of events	n = 11 ; % = 44	n = 10 ; % = 40
Lymphoedema stage II	n = 14 ; % = 56	n = 15 ; % = 60

Characteristic	Aqua exercise therapy (N = 25)	Exercise therapy (N = 25)
No of events		
Number of lymph node resection Mean (SD)	11.88 (3.98)	11.8 (4.07)
Time since surgery (years) Mean (SD)	2.64 (1.37)	2.88 (1.76)

Critical appraisal - RQ2AB – RCT RoB – STUDY LEVEL

Section	Question	Answer
Overall study ratings	Overall risk of bias	Low
Overall study ratings	Applicability as a source of data	Fully applicable

Bahtiyarca, 2019

Bibliographic Reference	Bahtiyarca, Zeynep Tuba; Can, Asli; Eksioglu, Emel; Cakci, Aytul; The addition of self-lymphatic drainage to compression therapy instead of manual lymphatic drainage in the first phase of complex decongestive therapy for treatment of breast cancer-related lymphoedema : A randomized-controlled, prospective study.; Turkish journal of physical medicine and rehabilitation; 2019; vol. 65 (no. 4); 309-317

Study details

Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Community
Study dates	January 2015 to January 2017
Sources of funding	No financial support received.
Inclusion criteria	(i) Stage I-II unilateral BCRL, (ii) aged over 18 years, (iii) >3 months after breast cancer treatment, and (iv) willingness to participate in the study.

Exclusion criteria	Patients with Stage 3-4 breast cancer related lymphoedema, those undergoing current radiotherapy (RT) or chemotherapy (CT), patients with an evidence of distant cancer metastasis or cancer recurrence, bilateral breast cancer, congestive heart failure, renal insufficiency, venous or arterial obstruction in the affected arm, infection in the affected arm, and pregnancy.
Intervention(s)	Self-lymphatic drainage (SLD) + compression therapy. Duration: until no changes were observed in the weekly limb circumference measurements obtained. All patients were given information about lymphoedema , skin care, and physical exercises. Compression bandaging was applied to all patients. Short stretch bandages were used to achieve continuous pressure during work as well as during rest periods. The bandage was kept on for 23 h and replaced the next day. The clinician applied all the compression bandages five days per week. SLD: A clinician instructed participants for 10-15 minutes each day prior to SLD (unclear for how many days total), and an information leaflet was given. SLD applied to neck, non-affected axilla, anterior chest wall, affected inguinal region, lateral trunk, affected shoulder, affected upper arm, affected forearm, affected hand and fingers. Movements repeated 10 times in various positions. At every visit, the patients were asked to indicate whether they performed SLD regularly. Their technique was monitored weekly during the study and each participant kept a diary recording the areas covered and time taken each day for SLD
Comparator	Compression therapy. Duration: until no changes were observed in the weekly limb circumference measurements obtained. All patients were given information about lymphoedema, skin care, and physical exercises. Compression bandaging was applied to all patients. Short stretch bandages were used to achieve continuous pressure during work as well as during rest periods. The bandage was kept on for 23 h and replaced the next day. The clinician applied all the compression bandages five days per week.
Outcome measures	Lymphoedema -Circumference and limb volume Patient-reported outcomes -Anxiety and depression Quality of life
Number of participants	N=40 SLD + compression therapy: 20 Compression therapy: 20
Duration of follow-up	6 months after end of treatment. Treatment duration: LD + compression therapy: median 6 (range 4 to 20) weeks

	Compression therapy: median 5 (range 4 to 8) weeks
Loss to follow-up	N=16/40 (40%) SLD + compression therapy: 10/20 (50%). (10 did not complete intervention because they were dissatisfied with the treatment response [n=3], were lost to follow up [n=3], did not use compression garment [n=2] or had tumour recurrence [n=2]). Compression therapy: 6/20 (30%). (6 did not complete intervention because they were lost to follow up [n=2], did not use compression garment [n=2] or had discomfort compression bandaging [n=2]).
Methods of analysis	Per protocol approach used. The independent sample t-test and Mann Whitney U test were used for inter-group comparisons of continuous and discrete variables. The Pearson chi-square and Fisher's exact tests were used to compare the categorical variables. Repeated measures analysis of variance (ANOVA) and Friedman test were used for intra-group comparisons of the repeated measures.
Additional comments	Baseline characteristics and results presented for participants who completed the study (Intervention: n=10; Control: n=14). Circumference measurement and limb volume: The circumferential measurements of both arms were taken at four points: the metacarpophalangeal (MCP) joints, the wrist, 10-cm distal to the lateral epicondyle, and 10-cm proximal to the lateral epicondyle. Calculation of the limb volume was undertaken using the simplified Frustum Formula (summed truncated cone). Quality of life: Short Form-36 (SF-36) health survey, split into the physical component summary (PCS) and mental component summary (MCS). Higher scores indicate better health status. Anxiety and depression: Hospital Anxiety and Depression Scale (HADS). Upper extremity function: Quick Disabilities of Arm, Shoulder, and Hand (Q-DASH) questionnaire. Total score ranges from 0 to 100. Higher scores indicate lower functional level.

Study arms

Self-lymphatic drainage + compression therapy (N = 20)

Compression therapy (N = 20)

Characteristics

Arm-level characteristics

Characteristic	Self-lymphatic drainage + compression therapy (N = 20)	Compression therapy (N = 20)
% Female No of events	n = 10 ; % = 100	n = 14 ; % = 100

Characteristic	Self-lymphatic drainage + compression therapy (N = 20)	Compression therapy (N = 20)
% Female Sample size	n = 10	n = 14
Mean age (SD) Mean (SD)	55.2 (7.15)	61.64 (11.69)
BMI Mean (SD)	30.88 (3.62)	32.73 (5.8)
Comorbidities Comorbidities present No of events	n = 7 ; % = 70	n = 11 ; % = 78.6
Type of surgery - BCS+ALND No of events	n = 1 ; % = 10	n = 1 ; % = 7.1
Type of surgery - MRM+ALND No of events	n = 9 ; % = 90	n = 13 ; % = 92.9
Cancer stage - 1 No of events	n = 2 ; % = 20	n = 3 ; % = 21.4
Cancer stage - 2 No of events	n = 4 ; % = 40	n = 4 ; % = 28.6
Cancer stage - 3 No of events	n = 4 ; % = 40	n = 7 ; % = 50
Lymphoedema stage - 1 No of events	n = 2 ; % = 20	n = 3 ; % = 21.4
Lymphoedema stage - 2 No of events	n = 8 ; % = 80	n = 11 ; % = 78.6

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Per protocol analysis, no protocol identified, no blinding in outcome assessment for patient-reported outcomes.)*
Overall bias and Directness	Overall Directness	Directly applicable

Basoglu, 2021

Bibliographic Reference	Basoglu, C; Sindel, D; Corum, M; Oral, A; Comparison of complete decongestive therapy and kinesiology taping for unilateral upper limb breast cancer-related lymphoedema : A randomized controlled trial.; Lymphology; 2021; vol. 54 (no. 1); 41-51

Study details

Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Hospital/Outpatient
Study dates	September 2014 to March 2015
Sources of funding	**NR**
Inclusion criteria	Women >18 years; unilateral grade 2 BCRL; radiotherapy treatment ended over 3 months prior; difference of >2cm between circumference of two arms
Exclusion criteria	Patients with stage 1 and 3 lymphoedema; active cancer; skin infection; radiation burns; severely affected upper extremity ROM; structural disorders of the upper limbs; kidney failure; heart failure; history of untreated deep venous thrombosis; BMI >35kg/m2; received CDT program within last 3 months; bandage allergy
Intervention(s)	Kinesiotaping including skin care, exercise and no MLD or bandaging
Comparator	CDT including compression bandage, MLD, skin care and therapeutic exercises
Outcome measures	Lymphoedema Limb circumference measurements at four points, the metacarpophalangeal joints, the wrists, 10 cm distal to the lateral epicondyles, and 12 cm proximal to the lateral epicondyle. Limb volume using circumferential measurements of Frustum formula and difference between volume of two limbs Quality of life Using FACT-B Function Range of motion (DASH score), grip strength
Number of participants	36
Duration of follow-up	One month

Loss to follow-up	4 participants excluded due to non-adherence, adverse effects or refusal of treatment
Methods of analysis	The Statistical Package for the Social Sciences (SPSS) software (Version 22.0, IBM Corp., Armonk, NY, USA) was used for statistical analysis. The descriptive statistics of the data are expressed as mean, standard deviation (SD) and median values for continuous variables, and counts and percentages for categorical variables. Chi-square test was used in the analysis of qualitative independent data. The Kolmogorov-Smirnov test was used to analyze the normality of distribution of quantitative variables. The Mann-Whitney-U test was used to compare the means between groups, and the Wilcoxon test was used to evaluate the parameters within the groups. A p value of less than 0.05 was considered statistically significant.
Additional comments	

Study arms
CDT group (N = 19)

KT (N = 17)

Characteristics
Arm-level characteristics

Characteristic	**CDT group (N = 19)**	**KT (N = 17)**
Mean age (SD) Mean (SD)	53.4 (8.3)	29.7 (4.4)
Breast conservation surgery No of events	n = 13 ; % = 68.4	n = 15 ; % = 88.2
Modified radical mastectomy No of events	n = 6 ; % = 31.6	n = 2 ; % = 11.8
Right arm No of events	n = 14 ; % = 73.7	n = 8 ; % = 47
Left arm No of events	n = 5 ; % = 26.3	n = 9 ; % = 52.9

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	**Question**	**Answer**
Overall bias and Directness	Risk of bias judgement	Moderate *(imbalanced baseline characteristics, no blinding of participants from intervention)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Blom, 2022

Bibliographic Reference	Blom, Katarina Y; Johansson, Karin I; Nilsson-Wikmar, Lena B; Brogardh, Christina B; Early intervention with compression garments prevents progression in mild breast cancer-related arm lymphoedema : a randomized controlled trial.; Acta oncologica (Stockholm, Sweden); 2022; vol. 61 (no. 7); 897-905

Study details

Trial registration number and/or trial name	ISRCTN51918431
Study location	Sweden
Study setting	Community
Study dates	Not reported
Sources of funding	Swedish Cancer Foundation and the Swedish Breast Cancer Association
Inclusion criteria	Mild breast cancer-related arm lymphoedema defined as increased skin and subcutis thickness compared to the non-affected arm in addition to either a threshold Tissue Dielectric Constant (TDC) ratio ≥1.45 in the upper arm, and/or ≥1.3 in the forearm), and/or LRV ≥5–≤8%.
Exclusion criteria	Recurrent cancer, concurrent diseases, cognitive disability or unable to understand or speak Swedish
Intervention(s)	Compression garment (CG) Participants received circular knitted compression sleeves (ccl 1) or if needed, individually adjusted compression sleeves (ccl 2) for daily wearing for six months, and counselling in self-care about exercise, weight control, skin care and instructions in self-massage. The self-massage comprised instructions on light strokes over the shoulder and arm in a proximal direction for about 10–15 min a day. If the self-massage was perceived as effective, participants were encouraged to continue, otherwise to stop.
Comparator	No compression garment (NCG) Participants received instructions in self-care only (unclear whether self-care is at same intensity and with same content as intervention group)

Outcome measures	Lymphoedema -progression, arm volume, local tissue water
Number of participants	Randomised: N=75 CG: 37 NCG: 38
Duration of follow-up	6 months from baseline
Loss to follow-up	N=75 CG: 6/37 (16%) - 1 participant had a progression in lymphoedema and so discontinued intervention, 3 had a recurrence of cancer, 1 did not use the compression garment, remaining 1 unclear). NCG: 22/38 (55%) - 1 participant had a recurrence in cancer, the remaining 21 had a progression in lymphoedema and so were excluded (note that progression in lymphoedema outcome includes these participants)
Methods of analysis	Number of participants not sufficient to be able to detect an arm volume difference of 20% between the groups. Differences between groups were calculated with Pearson Chi square test for nominal data, Mann–Whitney test for ordinal data and t-test for continuous data. The TDC data were not normally distributed and therefore presented as both median (min-max) and mean ± SD, to be able to compare results with other studies. The participants in the NCG who progressed in LRV >2%, and those in both groups that exceeded 10% were defined as having progression and the remaining as having no progression. They were not included in the LRV analysis, local tissue water, subjective symptoms, and self-care after the time-point when they progressed.
Additional comments	Due to ethical reasons, the participants in the NCG who increased in LRV >2% from baseline dropped out from their group allocation and started to wear compression garments. If LRV exceeded 10% the participants from both groups dropped out and received extended treatment. Arm volume: Water Displacement Method (WDM). LRV values were obtained by calculating the edema volume divided by the total arm volume of the nonaffected arm and were adjusted for hand dominance. Local tissue water: measured by the MoistureMeterD. Subjective symptoms: participants self-rated experiences of heaviness, tension and pain in the affected arm were rated on a horizontal 100 mm visual analogue scale. Data not presented in paper (reportedly low at all timepoints with no significant differences between groups).

Study arms

Compression garment (N = 33)

No compression garment (N = 37)

Characteristics

Arm-level characteristics

Characteristic	Compression garment (N = 33)	No compression garment (N = 37)
% Female No of events	n = 33 ; % = 100	n = 37 ; % = 100
Mean age (SD) Mean (SD)	57.9 (13.8)	57 (12.5)
BMI Mean (SD)	26.1 (4.8)	27.2 (5.4)
Type of cancer surgery: mastectomy and ALND No of events	n = 20 ; % = 61	n = 13 ; % = 35
Type of cancer surgery: lumpectomy and ALND No of events	n = 13 ; % = 39	n = 24 ; % = 65
Lymphoedema duration months Mean (SD)	1 (1.3)	1 (1.5)

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Unblinded assessment of outcomes, trial registered retrospectively. High risk of bias for outcomes other than progression due to high rates of exclusions in control arm.)*
Overall bias and Directness	Overall Directness	Directly applicable

De Vrieze, 2022

Bibliographic Reference	De Vrieze, Tessa; Gebruers, Nick; Nevelsteen, Ines; Fieuws, Steffen; Thomis, Sarah; De Groef, An; Tjalma, Wiebren Aa; Belgrado, Jean-Paul; Vandermeeren, Liesbeth; Monten, Chris;

Hanssens, Marianne; Devoogdt, Nele; Manual lymphatic drainage with or without fluoroscopy guidance did not substantially improve the effect of decongestive lymphatic therapy in people with breast cancer-related lymphoedema (EFforT-BCRL trial): a multicentre randomised trial.; Journal of physiotherapy; 2022; vol. 68 (no. 2); 110-122

Study details

Study type	Randomised controlled trial (RCT)
Study location	Five hospitals in Belgium: University Hospitals of Leuven, Antwerp University Hospital, Saint-Pierre University Hospital in Brussels, Ghent University Hospital, and General Hospital Groeninge in Kortrijk
Study setting	Participants recruited from the five hospitals and treated in an outpatient setting
Study dates	Recruitment from February 2016 to September 2019
Sources of funding	Agency for Innovation by Science and Technology (Applied Biomedical Research) (IWT 60519)
Inclusion criteria	Unilateral arm and/or hand lymphoedema after breast cancer treatment Chronic lymphoedema stage I to IIb for >3 months ≥5% excess volume between arms and/or hands
Exclusion criteria	Age <18 years Upper limb oedema from non-breast cancer cause Inability to participate for full study period Mental/physical inability to participate Allergy to indocyanine green, iodine or sodium iodide Increased thyroid activity or benign thyroid tumours Previous lymph node transplant or lymph venous shunt Bilateral axillary lymph node dissection
Intervention(s)	Fluoroscopy-guided MLD group (n=65): MLD tailored based on baseline lymphofluoroscopy Traditional MLD group (n=64): MLD based on normal lymphatic anatomy
Comparator	Placebo MLD group (n=65):
Number of participants	194 participants randomized (fluoroscopy-guided MLD n=65, traditional MLD n=64, placebo MLD n=65) 190 included in intention-to-treat analysis
Duration of follow-up	Participants were followed for 6 months after the end of the 6-month maintenance treatment phase (total 12 months)
Loss to follow-up	Four participants withdrew and were not included in the analysis (2.1% attrition)

Methods of analysis	Intention-to-treat analysis

Study arms
Fluoroscopy-guided MLD group (N = 65)

Traditional MLD group (N = 64)

Placebo MLD group (N = 65)

Characteristics
Study-level characteristics

Characteristic	Study (N = 194)
% Female Sample size	n = 193 ; % = 99
Mean age (SD) Custom value	61 (10) years
Lymphoedema stage / severity Custom value	Stage I: 17% Stage IIa: 56% overall Stage IIb: 27%
Location of lymphoedema Custom value	Arm: 95% Hand: 5%

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Dhar, 2022

Bibliographic Reference	Dhar, Anita; Srivastava, Anurag; Pandey, Ravindra M; Shrestha, Prasanna; Villet, Stephanie; Gogia, Arun Rekha; Safety and Efficacy of a Mobiderm Compression Bandage During Intensive Phase of Decongestive Therapy in Patients with Breast Cancer-Related Lymphoedema: A Randomized Controlled Trial.; Lymphatic research and biology; 2023; vol. 21 (no. 1); 52-59

Study details

Study type	Randomised controlled trial (RCT)
Study location	India
Study setting	Institute of Medical Sciences

Study dates	July 2015 to December 2017
Sources of funding	This study and the costs associated with the development of this article were supported by THUASNE.
Inclusion criteria	Women aged from 18 to 60 years, with established secondary upper limb lymphoedema after breast cancer surgery, considered suitable for intensive phase decongestive lymphoedema therapy
Exclusion criteria	Primary lymphoedema, co-existing cardiac or arterial disease, involvement in any other clinical study within the previous 3 months, and the inability to provide informed consent
Intervention(s)	In the Mobiderm group, participants received a multi-layer bandage composed of: an inner layer of cotton band (Bande Coton; THUASNE); an intermediate layer (Mobiderm band; THUASNE); and an external layer of elastic short-stretch bandage (Biflexideal®; THUASNE).
Comparator	In the conventional multilayered bandages group, the intermediate layer comprised an ortho cotton wool soft pad (as used in current treatment in India), whereas the internal and external layers were the same as used in the Mobiderm group.
Outcome measures	Lymphoedema Volume reductions in the affected limb (Upper limb volume [in mL] was measured by using the volume displacement method, the gold standard, which involves immersing the entire upper limb in a large container, with the volume of water displaced assessed by using a large measuring cylinder) Pain/heaviness Symptoms of pain were measured using the visual analogue scale (VAS) in which 0 indicates 'no pain' and 10 indicates the 'worst possible pain'
Number of participants	49 participants
Duration of follow-up	15 days after compression bandaging
Methods of analysis	Per protocol analysis. Continuous variables were expressed as mean – standard deviation or standard error; categorical variables were expressed as counts and percentage as appropriate (with percentage calculated on the basis of the per-protocol population). Changes in volume were expressed as means and associated 95% confidence intervals. Percent reductions in limb volume were calculated by using the following formula: limb volume day 0 – limb volume day 15/limb volume day 0x100. For categorical data, differences were evaluated by using the Fisher exact test or the Chi-square test. Continuous variables were compared by using the independent t-

	test (for data following normal distribution) and the Wilcoxon ranksum test (for non-normally distributed data). Within- and between-group changes between days 0 and 15 were compared by using paired or independent t-tests or Wilcoxon rank-sum test as appropriate; repeated-measures analysis of covariance (ANCOVA) was used to adjust for differences in baseline values. For all comparisons, a p-value of <0.05 was considered statistically significant.
Additional comments	In both groups, the compression bandages were initially applied by Certified Lymphoedema Therapist in the AIIMS hospital team, and then reapplied three times during the first week and once during the second week by the same clinical team All patients were provided with clear detailed instructions on relevant exercises, skin care, and hygiene associated with intensive phase decongestive therapy To reduce the risk of dermatolymphangioadenitis, all patients received a course of Benzathine penicillin G (1.2 MU) via a deep intramuscular injection given once every 3 weeks There was no new episode of cellulitis during the study treatment period, and no patient discontinued treatment due to cellulitis. Both compression regimens were well tolerated

Study arms

Mobilising bandaging using Mobiderm (N = 25)

Conventional multilayered bandages (N = 24)

Characteristics

Arm-level characteristics

Characteristic	Mobilising bandaging using Mobiderm (N = 25)	Conventional multilayered bandages (N = 24)
Mean age (SD) Mean (SD)	50.8 (10.2)	54.9 (11.1)
BMI (kg/m²) Mean (SD)	30 (2.2)	31.5 (1.5)
Diabetes No of events	n = 1 ; % = 4	n = 7 ; % = 29.2
Radical mastectomy with axillary lymph node dissection No of events	n = 25 ; % = 100	n = 24 ; % = 100
Preoperative chemotherapy	n = 15 ; % = 60	n = 15 ; % = 62.5

Characteristic	Mobilising bandaging using Mobiderm (N = 25)	Conventional multilayered bandages (N = 24)
No of events		
Postoperative radiotherapy No of events	n = 20 ; % = 80	n = 21 ; % = 87.5
Affected upper limb volume (mL) Mean (SD)	3096 (900.2)	3025 (710.3)
Contralateral upper limb volume (mL) Mean (SD)	2036 (561)	2125 (515)
Excess volume in affected upper limb (mL) SD was not reported Mean (SD)	1060 (*NR*)	900 *(NR)*

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. Per protocol analysis. No information about participants' adherence to interventions. Pre-specified analysis plan was not available. Protocol was not registered.)*
Overall bias and Directness	Overall Directness	Directly applicable

Duygu-Yildiz, 2023

Bibliographic Reference	Duygu-Yildiz, Elif; Bakar, Yesim; Hizal, Mustafa; The effect of complex decongestive physiotherapy applied with different compression pressures on skin and subcutaneous tissue thickness in individuals with breast cancer-related lymphoedema : a double-blinded randomized comparison trial.; Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer; 2023; vol. 31 (no. 7); 383

Study details

Trial registration number and/or trial name	NCT05660590, 12/26/2022 retrospectively registered.
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Department of Physiotherapy and Rehabilitation
Study dates	June 2019 and March 2022
Sources of funding	Not reported
Inclusion criteria	Stage 2 unilateral breast cancer-related lymphoedema according to International Society of Lymphology, involving whole extremity, and to be volunteer
Exclusion criteria	Acute deep vein thrombosis, acute soft tissue infection, peripheral artery disease in upper extremity, systemic diseases with peripheral oedema (kidney, hearth insufficiency, etc.), allergy to materials used for treatment, mental diseases affecting cooperation, sensory loss, and open wound in the upper limb
Intervention(s)	In the low-pressure bandage group, compression bandage was applied at 20–30 mmHg pressure. Determination of the pressure groups was based on Damstra et al. (2009)'s study. Four to five short stretch bandages were used until the desired pressure was achieved according to the sensor of Kikuhime. The compression bandage application was repeated if the desired pressure could not be achieved. Palpation was used to ensure that the pressure was decreasing upwards. When the compression bandage was finished, the sensor was removed by pulling the cable to which it was attached. The compression bandage stayed on the individual’s arm for approximately 23 h.
Comparator	In the high-pressure bandage group compression bandage was applied at 45–55 mmHg pressure. Determination of the pressure groups was based on Damstra et al. (2009)'s study. Four to five short stretch bandages were used until the desired pressure was achieved according to the sensor of Kikuhime. The compression bandage application was repeated if the desired pressure could not be achieved. Palpation was used to ensure that the pressure was decreasing upwards. When the compression bandage was finished, the sensor was removed by pulling the cable to which it was attached. The compression bandage stayed on the individual’s arm for approximately 23 h.
Outcome measures	Lymphoedema

	Extremity volume was determined by the overflowing water method and calculated in percent with the formula [(affected extremity volume-unaffected extremity volume)/ unaffected extremity volume] × 100). Changes in tissue / skin condition Evaluation of skin and subcutaneous tissue thickness via ultrasound was performed by a radiologist using a 6–15 MHz linear probe with a LOGIQ US system (GE Healthcare, USA) device. Ultrasound evaluations were performed bilaterally from six reference points: hand dorsum, volar side of wrist joint, 5 cm below the elbow joint (forearm volar) and 7 cm above (arm volar), 7 cm below the olecranon (forearm dorsum), and 7 cm above olecranon (arm dorsum). The volumetric vessel was filled with tap water up to the overflow point of the vessel. Subjects were asked to lean forward and slowly dip their arms into the water until the bar at the base of the volumetric cup snapped between the 2nd and 3rd fingers. During immersion, individuals were asked to avoid movements that could increase the transport of water. The overflow water was calculated by transferring it to the measuring cups and recorded in millilitre. Measurements were made bilaterally. The volumetric measuring cup was emptied and disinfected for the subsequent measurement.
Number of participants	21 participants
Duration of follow-up	3 months
Loss to follow-up	**NR**
Methods of analysis	For descriptive statistics, mean and standard deviation or median and minimum–maximum values were given in numerical variables. Categorical variables were defined by number and percentage. The assumption of normality was analyzed using the Shapiro-Wilks test and graphs (histogram, QQ plot, etc.). In comparing the two groups, the t-test was used for independent groups when the assumptions were met, and the Mann–Whitney U test was used when the assumptions were not met. Considering the small number of individuals in the groups, non-parametric tests were preferred for in-group comparisons. Wilcoxon's test or Friedman's test was used to examine the time change. Paired comparison (post-hoc) tests were used to determine the group that made the difference. Chi-square tests were used to examine whether there was a significant difference between categorical variables. There are no post-power calculation methods in the programs for non-parametric methods; the calculations were obtained by parametric test methods according to the subcutaneous thickness values of the forearm

	volar. When the alpha margin of error was accepted as 5%, the post hoc power of the study was 88.3%.
Additional comments	Participants were administered complex decongestive physiotherapy (CDP), which consisted of manual lymph drainage, skin care, compression bandage, and exercise. The CDP application took about an hour a day. The treatment was planned for 20 sessions for four weeks, five days a week.

Study arms

Low bandage pressure (N = 11)

Secondary publication of another included study- see primary study for details	None
Loss to follow-up	5 participants

High bandage pressure (N = 10)

Loss to follow-up	4 participants

Characteristics

Arm-level characteristics

Characteristic	Low bandage pressure (N = 11)	High bandage pressure (N = 10)
Mean age (SD) Mean (SD)	61.18 (8.87)	66.3 (12.16)
BMI (kg/m²) Mean (SD)	28.07 (3.65)	31.66 (3.65)
Modified radical mastectomy No of events	n = 7 ; % = 63.6	n = 6 ; % = 60
Lumpectomy No of events	n = 4 ; % = 36.4	n = 4 ; % = 40
Lymph node excision - axillar lymph node dissection No of events	n = 8 ; % = 72.7	n = 10 ; % = 100
Lymph node excision - sentinel lymph node biopsy	n = 3 ; % = 27.3	n = 0 ; % = 0

Characteristic	Low bandage pressure (N = 11)	High bandage pressure (N = 10)
No of events		
Radiotherapy No of events	n = 9 ; % = 81.8	n = 6 ; % = 60
Chemotherapy No of events	n = 11 ; % = 100	n = 7 ; % = 70
Affected extremity - Right No of events	n = 4 ; % = 36.4	n = 4 ; % = 40
Affected extremity - Left No of events	n = 7 ; % = 63.6	n = 6 ; % = 60

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Per protocol analysis. Nearly half of the participants from each group were lost to follow-up [The study coincided with the COVID-19 pandemic period, participants avoided attending the follow-up evaluations at 3 months]. No information about participants' adherence to interventions. Trial was registered retrospectively.)*
Overall bias and Directness	Overall Directness	Directly applicable

Ergin, 2019

Bibliographic Reference	Ergin, Gulbin; Sahinoglu, Ertan; Karadibak, Didem; Yavuzsen, Tugba; Effectiveness of Kinesio Taping on Anastomotic Regions in Patients with Breast Cancer-Related Lymphoedema: A Randomized Controlled Pilot Study.; Lymphatic research and biology; 2019; vol. 17 (no. 6); 655-660

Study details

Trial registration number and/or trial name	NCT03765996
Study location	Turkey
Study setting	Hospital/Outpatient

Study dates	Between 2012 - 2014
Sources of funding	**NR**
Inclusion criteria	Patients with unilateral BCRL; >18 years old; with significant/marked/severe lymphoedema
Exclusion criteria	Patients with paralysis on part of the affected arm; who had undergone CDP more than once within 6 months; with an active infection/skin disease
Intervention(s)	Complete Decongestive Therapy (includes short-stretch bandages, MLD, lymph-reducing exercises, skin care) for 1 hour a day, 5 days a week for 4 weeks
Comparator	Complete Decongestive Therapy (includes short-stretch bandages, MLD, lymph-reducing exercises, skin care) and kinesiotaping for 1 hour a day, 5 days a week for 4 weeks
Outcome measures	Lymphoedema Limb volume
Number of participants	32 patients
Duration of follow-up	4 weeks
Loss to follow-up	4 patients not completed treatment
Methods of analysis	Data were analysed using the SPSS 20.0 program. Whether the data had normal distribution was determined with the use of Shapiro–Wilk test. As the ‘‘p’’ values acquired from the Shapiro–Wilk test was <0.05, it was determined that there was no normal distribution. Thus, nonparametric hypothesis tests were used in the study. Mean and standard deviation were analysed using descriptive analyses, and the data were determined by the number, presented as the number and percentage. The characteristics of the groups were categoric, and were analysed using the chi-square test; however, some cells did not obey the rule that the ‘‘observational number must not be below five.’’ For this reason, the Fischer’s exact test was used in 2 tables. Not all characteristics could be analysed statistically. Differences between the before and after treatment results within groups were analysed using the Wilcoxon rank-sum test. The Mann–Whitney U-test was used to determine the differences in volume reduction between the two groups. The significance level was set at 0.05.

Study arms

CDT (N = 14)

CDT + KT (N = 18)

Characteristics

Arm-level characteristics

Characteristic	CDT (N = 14)	CDT + KT (N = 18)
Mean age (SD) Mean (SD)	53.42 (7.68)	58.44 (10.12)
BMI (kg/m2) Mean (SD)	28.95 (5.7)	30.25 (6.16)
Radiotherapy + chemotherapy No of events	% = 14.3	% = 16.7
Radiotherapy + chemotherapy + medical therapy No of events	% = 57.1	% = 50
Radiotherapy + chemotherapy + hormone replacement therapy No of events	% = 14.3	% = 22.2
Chemotherapy + medical therapy No of events	% = 7.1	% = 5.6
Radiotherapy + chemotherapy + hormone replacement therapy + medical therapy No of events	% = 7.1	% = 5.6
Significant No of events	% = 14.3	% = 22.2
Marked No of events	% = 28.6	% = 22.2
Severe No of events	% = 57.1	% = 55.6
Right arm No of events	n = 5 ; % = 35.7	n = 7 ; % = 38.9
Left arm No of events	n = 9 ; % = 64.3	n = 11 ; % = 61.1

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. Study reports "slightly significant difference" between BMI in both groups.)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Jonis, 2024

Bibliographic Reference	Jonis, Y M J; Wolfs, J A G N; Hummelink, S; Tielemans, H J P; Keuter, X H A; van Kuijk, S; Ulrich, D J O; van der Hulst, R R W J; Qiu, S S; The 6 month interim analysis of a randomized controlled trial assessing the quality of life in patients with breast cancer related lymphoedema undergoing lymphaticovenous anastomosis vs. conservative therapy.; Scientific reports; 2024; vol. 14 (no. 1); 2238

Study details

Trial registration number and/or trial name	NCT02790021
Study type	Randomised controlled trial (RCT)
Study location	The Netherlands
Study setting	Hospital
Study dates	Between 2018 - 2022
Sources of funding	ZonMw grant and Academic Hospital of Maastricht
Inclusion criteria	Women over 18 years; treated for breast cancer with SLNB, ALND or axillary radiotherapy; early stage lymphoedema of the arm (stage 1-2A ISL); viable lymphatic vessels (stage <=3); at least 3 months conservative therapy; primary breast cancer; unilateral disease and treatment
Exclusion criteria	History of earlier lymph reconstruction efforts; recurrent breast cancer; distant breast cancer metastases; bilateral lymphoedema; primary congenital lymphoedema
Intervention(s)	Lymphaticovenous anastamosis (LVA) + Complete Decongestive Therapy (3 months)
Comparator	CDT
Outcome measures	Lymphoedema Excess lymph volume Quality of life Adverse events

Number of participants	92 patients
Duration of follow-up	12 months follow-up post intervention 24 months follow-up post informed consent/intervention
Loss to follow-up	1 patient at 6 months
Methods of analysis	To examine the effect of LVA, the paired-samples t-test was used to evaluate the changes between baseline, 3 and 6 months within the groups for the Lymph ICF questionnaire, the relative volume difference measured by water displacement and the UEL index. To measure the effect of the LVA between groups the independent-samples t-test was performed for the above-mentioned variables. Furthermore, a linear regression was used to determine the relationship between the number of LVAs, follow-up months, lymphoedema onset, BMI and ICG stage and for the HrQoL and volume reduction (measured by volume displacement). Results were expressed as regression coefficient with a 95% confidence interval (CI). The use of compression garments, adverse and serious adverse events were reported as frequency. All analysis were performed with IBM SPSS version 25 (IBM Corp., Armonk, N.Y).
Additional comments	6 months interim analysis

Study arms

LVA (N = 46)

CDT (N = 46)

Characteristics

Arm-level characteristics

Characteristic	**LVA (N = 46)**	**CDT (N = 46)**
BMI (kg/m²) Mean (SD)	26 (3.55)	27 (5.11)
Radiotherapy No of events	n = 41 ; % = 89	n = 42 ; % = 90
Radiotherapy in the armpit No of events	n = 24 ; % = 52.2	n = 21 ; % = 44.7
Sentinel node procedure No of events	n = 40 ; % = 87	n = 40 ; % = 87
Axillary lymph node dissection No of events	n = 43 ; % = 94	n = 41 ; % = 89

Characteristic	LVA (N = 46)	CDT (N = 46)
Chemotherapy No of events	n = 42 ; % = 90	n = 44 ; % = 96
Hormone therapy No of events	n = 33 ; % = 72	n = 32 ; % = 69
ISL stage I No of events	n = 0 ; % = 0	n = 2 ; % = 4
ISL stage II No of events	n = 46 ; % = 100	n = 44 ; % = 96
Left arm No of events	n = 26 ; % = 56	n = 27 ; % = 58
Right arm No of events	n = 20 ; % = 44	n = 19 ; % = 41
Smoking No of events	n = 2 ; % = 4	n = 1 ; % = 2

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Karafa, 2018

Bibliographic Reference	Karafa, M; Karafova, A; Szuba, A; The effect of different compression pressure in therapy of secondary upper extremity lymphoedema in women after breast cancer surgery.; Lymphology; 2018; vol. 51 (no. 1); 28-37

Study details

Study type	Randomised controlled trial (RCT)
Study location	Polyclinic evi-MED, Gdynia, Poland
Study setting	Outpatient clinic setting
Study dates	NR
Sources of funding	NR
Inclusion criteria	Women aged 35-74 years with unilateral breast cancer-related lymphoedema (stage II according to ISL criteria) after modified radical mastectomy

Exclusion criteria	Not reported
Intervention(s)	Group II A (n=32): Compression at 31-40 mmHg Group II B (n=32): Compression at 41-60 mmHg
Comparator	Control group (n=32):
Number of participants	96 women randomized (32 per group)
Duration of follow-up	Outcomes assessed at baseline, 24 hours, 7 days and 14 days of therapy (total 2 weeks)
Loss to follow-up	NR

Study arms
Control group (N = 32)

Group II A (N = 32)
Complete Decongestive Therapy Compression at 31-40 mmHg

Group II B (N = 32)
Compression at 41-60 mmHg

Characteristics
Study-level characteristics

Characteristic	Study (N = 96)
% Female Sample size	n = 96 ; % = 100
Mean age (SD) Range	35 to 74
Lymphoedema stage / severity Custom value	All participants had stage II unilateral lymphoedema according to ISL criteria
Location of lymphoedema Custom value	Unilateral upper limb

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. No information about participants' adherence to interventions. Pre-specified analysis plan was not available.)*
Overall bias and Directness	Overall Directness	Directly applicable

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4 **Kilbreath, 2020**

Bibliographic Reference	Kilbreath, S L; Ward, L C; Davis, G M; Degnim, A C; Hackett, D A; Skinner, T L; Black, D; Reduction of breast lymphoedema secondary to breast cancer: a randomised controlled exercise trial.; Breast cancer research and treatment; 2020; vol. 184 (no. 2); 459-467

5
6 **Study details**

Trial registration number and/or trial name	Australian Clinical Trials Registry: ACTRN12612000771853
Study type	Randomised controlled trial (RCT)
Study location	Australia
Study setting	Community
Study dates	Not reported
Sources of funding	National Health and Medical Research Grant (APP1021608)
Inclusion criteria	Women aged ≥18 years; had undergone surgery for breast cancer that included wide local excision and axillary surgery; reported having breast oedema for longer than 3 months in which the intensity of the breast-related symptoms such as heaviness and/or discomfort were ≥3 on a 10-cm visual analogue scale at enrolment into the study
Exclusion criteria	Women who had undergone intensive lymphoedema therapy (i.e. decongestive therapy); experienced infections in the lymphoedematous regions requiring antibiotic treatments; and/ or had experienced exacerbation that led to a change in their activities of daily living in the last 3 months

	Women who had a history of primary lymphoedema, were fitted with a pace maker, had undergone bilateral axillary dissections, engaged in regular moderate-to-high intensity exercise, or had any condition which excluded them from participating in exercise. Women who were pregnant or lactating
Intervention(s)	Exercise. 3 x 1hr sessions/week for 12 weeks. An Accredited Exercise Physiologist (AEP), trained by the study AEP with cancer care expertise, supervised each of the three exercise sessions in the first week and then once weekly thereafter for the duration of the intervention. Low intensity warm up, 30 mins muscular hypertrophy training using free weights and resistance machines, 2x10 minute blocks of aerobic training. The resistance exercises targeted upper and lower limb muscle groups as well as the abdominal, chest and back. Resistance was increased if the weight was able to be lifted >12 times. Every 4 weeks, the exercises changed to add variety and promote adherence. Training sessions were monitored and recorded to assess progression, compliance, and adherence.
Comparator	Control Women allocated to the Control were contacted weekly to monitor their general health and lymphoedema status, but no advice was provided about exercise.
Outcome measures	Lymphoedema -BIS measurement Patient-reported outcomes -breast score, arm symptom score (LSIDS) Quality of life EORTC BR-23 Changes in tissue / skin condition -dermal thickness Adverse events Function -upper limb strength
Number of participants	N=89 Exercise: 41 Control: 47
Duration of follow-up	12 weeks
Loss to follow-up	N=3/89 Exercise: 0/41 Control: 3/47
Methods of analysis	Intention to treat analysis.

	Non-parametric analyses of change scores (12 weeks—baseline) were undertaken, with the median and 25th and 75th quartiles reported unless otherwise specified. Where no significant differences were identified, post hoc analysis was undertaken to determine if the measurements for the combined groups changed over the 12-week intervention period.
Additional comments	Measurements were taken by a blinded research assistant. EORTC BR23 (breast module): Women rated the extent to which they experienced pain, swelling, oversensitivity, and skin problems in the affected breast over the previous week which were used to derive a breast score. Similarly, pain, swelling and difficulty raising their arm on the affected side in the past week were used to derive a score for arm symptoms Lymphoedema Symptom Intensity and Distress Survey (LSIDS): Patients asked about symptoms present in breast / chest wall. Required women to indicate the presence of a symptom, and if yes, to then rate its intensity and distress on separate 10-point numeric scales, with 1 representing ‘‘slight’’ and 10 representing ‘‘severe’’. Extracellular fluid in the breast measured using BIS: supine measurements. Electrodes fitted. For both breast and limb measurements, the data (resistance at zero frequency, R0) was reported as a ratio in which unaffected or non-dominant limb/breast was expressed relative to the affected or dominant limb. Dermal thickness: assessed using ultrasound. The skin was assessed at 4 locations on the breast. Three images of each measurement location were obtained.

Study arms

Exercise (N = 41)

Control (N = 47)

Characteristics

Arm-level characteristics

Characteristic	Exercise (N = 41)	Control (N = 47)
% Female No of events	n = 41 ; % = 100	n = 47 ; % = 100
Mean age (SD) Mean (SD)	53.7 (10.4)	59.5 (8)
BMI Mean (SD)	28.1 (5.5)	30.4 (5.9)
Type of cancer treatment - radiotherapy No of events	n = 41 ; % = 100	n = 46 ; % = 98

Characteristic	Exercise (N = 41)	Control (N = 47)
Type of cancer treatment - chemotherapy No of events	n = 29 ; % = 71	n = 29 ; % = 62
Type of cancer treatment - hormone therapy No of events	n = 30 ; % = 73	n = 33 ; % = 70
Time from surgery to diagnosis of breast lymphoedema (Months) Mean (SD)	8 (8)	7 (5)
Arm also affected No of events	n = 16 ; % = 39	n = 17 ; % = 36

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Overall at moderate risk of bias. Patient reported outcomes and BIS outcomes at high risk of bias, other outcomes at low risk of bias.)*
Overall bias and Directness	Overall Directness	Directly applicable.

Kizil, 2018

Bibliographic Reference	Kizil, Ramazan; Dilek, Banu; Sahin, Ebru; Engin, Onur; Soylu, Ali Can; Akalin, Elif; Alper, Serap; Is Continuous Passive Motion Effective in Patients with Lymphoedema? A Randomized Controlled Trial.; Lymphatic research and biology; 2018; vol. 16 (no. 3); 263-269

Study details

Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Outpatient clinic
Study dates	February 2014 to September 2015
Sources of funding	No funding reported. Authors report that they have no competing interests.

Inclusion criteria	Age 25 to 75 Presence of unilateral lymphoedema at least 6 months and up to 8 years after treatment of breast cancer At least 2cm difference at a point between affected and unaffected arm
Exclusion criteria	Prior treatment for lymphoedema over past year, local or distant cancer recurrence associated with breast cancer, active infection or deep venous occlusion, additional diseases or psychiatric disorders interrupting the follow-up schedule, history of bilateral mastectomy, and severe shoulder pain and frozen shoulder
Intervention(s)	Complete decongestive therapy plus continuous passive motion. 15 total sessions on 15 consecutive days. Self manual lymphatic drainage was taught and shown individually to each patient for 20 minutes. The patients were subjected to CPM (Kinetec Centura Shoulder CPM model Michigan St. NE) with third-level speed plus flexion-directed exercise up to approximately 90% of the shoulder joint ROM for 20 minutes in the first five sessions and for 30 minutes in the next ten sessions. A researcher conducted all these treatments.
Comparator	Complete decongestive therapy. 15 total sessions on 15 continuous days. CDT program (self-manual lymphatic drainage, multilayer short stretch compression bandage, instructions in self-care, therapeutic exercise (supervised range of movement and strengthening program were given by researcher), and meticulous education on skin and nail care).
Outcome measures	Lymphoedema -DASH scores and volumetric measurement Quality of life -FACT-B4 Mobility -Range of motion (flexion and abduction, internal rotation and external rotation)
Number of participants	N=32 CDT+CPM: 16 CDT only: 16
Duration of follow-up	15 days
Loss to follow-up	N = 2/32 CDT+CPM: 2/16 (travelling outside of city) CDT only: 0/16
Methods of analysis	Groups were compared for differences using the Mann–Whitney U test. All analyses were conducted on a per protocol basis.

Additional comments	Per protocol analysis only - 16 patients randomised to each arm, but 2 dropped out from the intervention arm. Characteristics and results presented for those who completed follow-up only (n=30 total). Study had small sample size and short-term follow up. Range of motion measures were not statistically significantly different between groups at baseline, however flexion and abduction were slightly more favourable in control group. DASH scores and FACT B-4 scores could not be extracted as reporting was unclear.

Study arms
CDT+CPM (N = 14)
Complete decongestive therapy + continuous passive motion

CDT (N = 16)
Complete decongestive therapy only

Characteristics
Arm-level characteristics

Characteristic	CDT+CPM (N = 14)	CDT (N = 16)
% Female No of events	n = 14 ; % = 100	n = 16 ; % = 100
Mean age (SD) Custom value	Median 55.5, range 40-73	Median 58, range 35-75
BMI Custom value	Median 30, range 24.2-40	Median 27.5, range 25.7-44
Lymphoedema stage 2 No of events	n = 6 ; % = 43	n = 5 ; % = 31
Lymphoedema stage 3 No of events	n = 8 ; % = 57	n = 11 ; % = 69
Duration of lymphoedema (year) Custom value	Median 2.25, range 0.5-8	Median 2.5, range 0.5-8

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. No information about participants' adherence to interventions.)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Lampinen, 2021

Bibliographic Reference	Lampinen, Riikka; Lee, Jeannette Q; Leano, Janella; Miaskowski, Christine; Mastick, Judy; Brinker, Lisa; Topp, Kimberly; Smoot, Betty; Treatment of Breast Cancer-Related Lymphoedema Using Negative Pressure Massage: A Pilot Randomized Controlled Trial.; Archives of physical medicine and rehabilitation; 2021; vol. 102 (no. 8); 1465-1472e2

Study details

Trial registration number and/or trial name	NCT03252145
Study type	Randomised controlled trial (RCT)
Study location	US
Study setting	Health sciences university
Study dates	Not reported
Sources of funding	Supported by a Magistro Family Foundation Research Grant from the Foundation for Physical Therapy Research.
Inclusion criteria	Women aged >18 years of age, had completed active treatment for breast cancer, were diagnosed with unilateral arm lymphoedema for ≥1 year, were not receiving lymphoedema care, and had stable (no change in the last 3mo) lymphoedema at the time of enrolment
Exclusion criteria	Current infection or lymphangitis in the affected arm; current reoccurrence of breast cancer; lymphoedema before cancer treatment; current venous thrombosis or use of anticoagulant therapy; or a condition that precluded the measurement of lymphoedema with bioelectrical impedance spectroscopy
Intervention(s)	Negative pressure massage treatment device (LymphaTouchb) is Food and Drug Administration approved as a therapeutic massage device in the US. This handheld device administers negative pressure in the range of 80-250 mmHg under the treatment head, which gently pulls the underlying tissue into the suction cup. All women were scheduled for 12 sessions provided at 2-3 times per week for 4-6 weeks. Over 4-6 weeks, the intervention group

	received twelve 60-minute sessions of negative pressure massage treatment using the LymphaTouch device.
Comparator	Manual lymphatic drainage treatment was given in twelve 60-minute sessions.
Outcome measures	Lymphoedema DASH scores range from 0-100, with higher scores indicating greater disability Total limb volume, quantified by measuring circumference and calculating volume. Circumferential measurements were done using a weighted-end, spring-loaded tape measure at 10 cm intervals from the ulnar styloid to 40 cm proximally. Circumferences were measured using the procedures outlined by Cornish et al (2001). Two measurements were averaged for each arm. Limb volume was calculated using the formula for the volume of a truncated cone [$V=1/12\pi\sum h\ (C12+C1C2+C22)$] Bioelectrical impedance spectroscopy measurements were taken using the L-Dex U400a. The L-Dex score was derived from the bioelectrical impedance ratio of unaffected to affected limb. Two L-Dex readings were averaged for each arm. Higher L-Dex values reflect greater extracellular fluid volume in the affected limb
Number of participants	28 participants
Duration of follow-up	At the end of the 4- to 6-week treatment
Methods of analysis	Descriptive statistics and frequency distributions were generated for demographic and clinical characteristics. Between-group differences at enrolment were evaluated with independent samples t-tests for continuous variables and chi-square or Fisher exact tests for categorical variables. For changes in interlimb volume difference, L-Dex, and DASH, the normality of data distributions was assessed and independent t tests or Mann-Whitney U tests were used for parametric and nonparametric data, respectively, with a statistical significance set at $P<.05$ to evaluate for between-group differences in pre- to posttreatment change. For this small exploratory study, the use $a=.05$ was purposefully chosen as the criterion for each hypothesis test; thus, post hoc multiple comparison corrections (eg, Bonferroni) were not made. However, the specific P values were presented for each so that the reader could draw a more conservative conclusion if desired. Effect sizes for between group differences were calculated using Cohen's d standardized mean difference (SMD) with pooled SD. Effect size was considered small (SMD=0.2), medium (SMD=0.4), and large SMD=0.8). Data analyses were conducted on an intention-to-treat basis.

Additional comments	Women who had received previous lymphoedema treatment were not excluded Both groups received the unilateral lymphoedema treatment sequence described by Vodder (http://www.archives-pmr.org/) Pressures for both interventions were determined by the study lymphoedema therapist based on patient comfort, tissue induration, and degree of swelling Higher pressures were used over more indurated areas After each treatment, participants donned their compression sleeve (provided if participant did not have one) and were advised to wear it for a minimum of 2 hours after the treatment Participants were advised to continue usual self-care (for example, night compression garment, skin protection, self-manual lymphatic drainage, activity). They were asked not to seek out additional clinician-delivered lymphoedema treatments during the study period.

Study arms

Negative pressure massage treatment (N = 15)

Loss to follow-up	2 participants

Manual lymphatic drainage (N = 13)

Loss to follow-up	2 participants

Characteristics

Arm-level characteristics

Characteristic	Negative pressure massage treatment (N = 15)	Manual lymphatic drainage (N = 13)
Mean age (SD) Mean (SD)	64.24 (13.69)	60.34 (10.65)
BMI (kg/m²) Mean (SD)	28.93 (5.44)	29.16 (13.12)
Type of breast cancer surgery - Mastectomy No of events	n = 10 ; % = 66.7	n = 9 ; % = 75
Type of breast cancer surgery - Breast conserving surgery No of events	n = 6 ; % = 33.3	n = 3 ; % = 25
Type of cancer treatment - Radiation therapy	n = 12 ; % = 80	n = 8 ; % = 66.7

Characteristic	Negative pressure massage treatment (N = 15)	Manual lymphatic drainage (N = 13)
No of events		
Type of cancer treatment - chemotherapy No of events	n = 15 ; % = 100	n = 12 ; % = 92.3
Lymphoedema severity - mild No of events	n = 5 ; % = 33.3	n = 8 ; % = 61.5
Lymphoedema severity - moderate No of events	n = 6 ; % = 40	n = 3 ; % = 23.1
Lymphoedema severity - severe No of events	n = 4 ; % = 26.7	n = 2 ; % = 15.4
Location of lymphoedema - right No of events	n = 5 ; % = 33.3	n = 6 ; % = 53.8
Location of lymphoedema - left No of events	n = 10 ; % = 66.7	n = 6 ; % = 46.2

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Potential bias in the randomisation process as the number of participants with lymphoedema for more than 5 years was significantly higher in the group receiving negative pressure massage treatment: n= 8 vs 1. No information about deviations from intended interventions but the total duration of garment use and the vigour of treatment was not controlled which could have led to potential between-group differences. There was no information about deviations from intended interventions but the total duration of garment use and the vigour of treatment was not controlled which could have led to potential between-group differences.)*
Overall bias and Directness	Overall Directness	Directly applicable

Ligabue, 2019

Bibliographic Reference	Ligabue, M B; Campanini, I; Veroni, P; Cepelli, A; Lusuardi, M; Merlo, A; Efficacy of self-administered complex decongestive therapy on breast cancer-related lymphoedema : a single-blind randomized controlled trial.; Breast cancer research and treatment; 2019; vol. 175 (no. 1); 191-201

Study details

Study type	Randomised controlled trial (RCT)
Study location	Italy
Study setting	Hospital
Study dates	Not reported
Sources of funding	None reported
Inclusion criteria	Women with lymphoedema secondary to breast cancer who received CDT treatment at the hospital over a 1-year period Who had mastectomy or quadrantectomy, removal of at least two axillary lymph nodes, concluded chemotherapy and radiotherapy, superior arm lymphoedema , CDT concluded within 6 months and at least 4 cm of difference between affected and unaffected arm total circumference
Exclusion criteria	Recurrent cancer, active infections, vascular damages (e.g., phlebitis)
Intervention(s)	Self-administered CDT: CDT followed by education on self-administered CDT. A trained physiotherapist held a ten-session course over a period of 4 weeks. Each meeting lasted about one and half hours. The program of each of the 10 meetings was standardised in terms of topics, practical demonstrations, trials, and discussion time with patients. The women were taught: manual lymphatic self-drainage, self-bandage, breathing exercises, mobilization exercises, muscle reinforcement exercises, muscle contracture management, and the understanding of the changes occurring after suffering from lymphoedema . The physiotherapist taught women until they were able to manage the whole treatment autonomously at home. Women were strongly encouraged to carry out all the saCDT protocol 6 days out of seven. The study physician offered medical expertise including lifestyle and nutritional recommendations aiming at preventing weight gain and promoting selfcare activities. All patients in both groups were asked to use the arm-guard.
Comparator	Usual care: CDT followed by usual care (educational leaflet). The usual care provided at discharge after CDT, including a point-by-point briefing and discussion of the leaflet which included

	descriptions of specifically designed exercises and behavioural and hygienic standards. Women were strongly encouraged to follow the recommendations contained in the leaflet.
Outcome measures	Lymphoedema Asymmetry - Excess Limb Volume (ELV) indicator (interlimb discrepancy). Computed for hand (handELV) and arm (armELV), using ELV = (Affected Side Volume−Unaffected Side Volume)/Unaffected Side Volume × 100. Pain/heaviness Pain - Numerical Pain Rating Scale
Number of participants	41
Duration of follow-up	6 months after enrolment (outcomes reported at 1 month and 6 months)
Methods of analysis	The Mann–Whitney test was used to verify the presence of group differences at each stage of the study. The Wilcoxon test was used to analyse variations with respect to the baseline values. Non-parametric tests were selected, based on a preliminary analysis of data (Lilliefors test). Data analysis was performed using Matlab and its statistical toolbox (The Mathworks inc., Thorofare, USA). Statistical significance was set at 5%.
Additional comments	Change from baseline data calculated by reviewer

Study arms

Self-administered CDT (N = 20)

Comparator	
Loss to follow-up	3

CDT followed by education on self-administered CDT

Usual care (N = 21)

Comparator	
Loss to follow-up	3

CDT followed by usual care (educational leaflet)

Characteristics

Arm-level characteristics

Characteristic	Self-administered CDT (N = 20)	Usual care (N = 21)
Mean age (SD) Mean (SD)	56.8 (8.8)	57.1 (9.8)
Mastectomy Nominal	8	3
Quadrantectomy Nominal	12	18

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low *(Low for objective outcome (asymmetry). Some concerns for patient-reported pain outcome as participants were not blinded to the intervention)*
Overall bias and Directness	Overall Directness	Directly applicable

Liu, 2023

Bibliographic Reference	Liu, Ying; Zhao, Xiaoyi; Song, Jian; Zhao, Wowa; Ge, Ying; Guan, Jinghong; The Effect of Manual Lymph Drainage and Compression Bandaging for Stage 2 Breast Cancer-Related Lymphoedema: A Randomized Controlled Trial.; Lymphatic research and biology; 2023; vol. 21 (no. 5); 479-484

Study details

Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	China
Study setting	Hospital
Study dates	Not reported
Inclusion criteria	Breast cancer survivors with a history of mastectomy who complained of swelling or heaviness in the affected side and diagnosed as lymphoedema stage 2 using the grading standard issued by the International Society of Lymphology in 2016 and willing to receive conservative treatment for breast cancer-related lymphoedema

Exclusion criteria	Survivors who had any evidence of cancer metastases or recurrences; acute inflammation; acute allergy; acute thrombosis; and cardiac decompensation
Intervention(s)	Manual lymph drainage (MDL) consisted of four basic techniques (stationary circle, rotary technique, pump technique, scoop technique) initiated from the unaffected trunk quadrants (neck and chest) and after preparation of these regions, the affected areas of the trunk were treated. Then manual lymph drainage was applied to the oedematous limb starting proximally at the shoulder, moving in segments progressively down the limb, using specific oedema techniques. Finally, the trunk was cleared, including the affected chest and back. Compression therapy (CB) was given to the patients in the CB group and the combined decongestive therapy (CDT) group by the certified doctors with short stretch bandages. CB was worn soon after MLD and was kept day and night in the combined decongestive therapy group. MLD and CB were performed once a day, five times a week during 2 weeks.
Comparator	Combined decongestive therapy included MDL and CB
Outcome measures	Lymphoedema Volume was calculated using circumferential measurements at every 4 cm from the styloid process to the shoulder Local tissue water and oedema of affected arms were measured in the ventral midpoint of the affected upper arm and forearm with moisture meter (Moisture Meter D Compact; Delfin Technologies LTD, Kuopio Finland). A probe with diameter of 23mm and detection depth of 2.5mm was selected in the study
Number of participants	60 participants
Duration of follow-up	After 2 weeks' treatment
Loss to follow-up	None
Methods of analysis	A matched t test was used to compare the volume and the TDC value before and after treatment. One-way ANOVA and S-N-K were used to determine the difference among three groups. Significant statistically difference is $p < 0.05$
Additional comments	Participants were female breast cancer survivors who underwent axillary lymph node dissection and radiotherapy, complained of swelling in the affected side, and were diagnosed as stage 2 breast cancer-related lymphoedema

Study arms

Manual lymph drainage (N = 20)

Secondary publication of another included study- see primary study for details		

Compression bandaging (N = 20)

Combined decongestive therapy (N = 20)

Characteristics

Arm-level characteristics

Characteristic	Manual lymph drainage (N = 20)	Compression bandaging (N = 20)	Combined decongestive therapy (N = 20)
Mean age (SD) Mean (SD)	54.5 (10.1)	57.3 (9.2)	51.4 (10.1)
BMI Mean (SD)	25.9 (3.9)	26 (3)	26.3 (1.8)

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Per protocol analysis. No information about awareness of intervention from participants and people delivering the interventions. No information about participants' adherence to interventions. Pre-specified analysis plan was not available. Protocol was not registered.)*
Overall bias and Directness	Overall Directness	Directly applicable

McNeely, 2022

Bibliographic Reference	McNeely, Margaret L; Dolgoy, Naomi D; Rafn, Bolette Skjodt; Ghosh, Sunita; Ospina, Paula A; Al Onazi, Mona M; Radke, Lori; Shular, Mara; Kuusk, Urve; Webster, Marc; Campbell, Kristin L;

Mackey, John R; Nighttime compression supports improved self-management of breast cancer-related lymphoedema : A multicenter randomized controlled trial.; Cancer; 2022; vol. 128 (no. 3); 587-596

Study details

Study type	Randomised controlled trial (RCT)
Study location	Three centers in Canada: Cross Cancer Institute in Edmonton, Tom Baker Cancer Centre in Calgary, and University of British Columbia/Mount St. Joseph's Hospital in Vancouver
Study setting	Outpatient cancer rehabilitation setting
Study dates	Recruitment between November 2014 and August 2017
Sources of funding	Alberta Cancer Foundation Investigator Initiated Trials Opportunity Canadian Institutes of Health Research
Inclusion criteria	Women with BCRL of ipsilateral arm ≥200 mL or 10% increase in arm volume vs unaffected arm ≥1 month post-completion of primary and adjuvant cancer treatments In lymphoedema maintenance phase Has own properly fitted compression sleeve for daytime use (≥12 hrs/day) Not using nighttime compression pre-study
Exclusion criteria	Evidence of active breast cancer (local or metastatic) Bilateral arm lymphoedema Serious non-malignant disease precluding daily treatment and follow-up Contraindications to compression therapy Inability to adhere to protocol due to mental/physical disorders or schedule conflicts
Intervention(s)	SC + nighttime compression bandaging (CB) group (n=44): SC + multilayered CB 8 hrs/night, ≥5 nights/week for 4 weeks, then ≥3 nights/week for 8 week SC + nighttime compression system garment (NCSG) group (n=37): SC + NCSG 8 hrs/night, ≥5 nights/week for 4 weeks, then ≥3 nights/week for 8 weeks
Comparator	Standard care (SC) group (n=39): Daytime compression sleeve (≥30 mmHg) ≥12 hrs/day, skin care, exercise, weight management advice
Number of participants	120 women enrolled and randomized (SC n=39, CB n=44, NCSG n=37)
Duration of follow-up	Primary endpoint at 12 weeks (end of RCT) Additional follow-up to 24 weeks
Loss to follow-up	118/120 (98%) completed 12-week RCT 114/120 (95%) completed 24-week follow-up

Methods of analysis	Intent-to-treat analysis

Study arms

standard care (SC) group (N = 39)

SC + nighttime compression bandaging (CB) group (N = 44)

SC + nighttime compression system garment (NCSG) group (N = 37)

Characteristics

Study-level characteristics

Characteristic	**Study (N = 120)**
Mean age (SD) Custom value	61 (11) years
Lymphoedema stage / severity Custom value	Mild lymphoedema : 57% overall Moderate lymphoedema : 43% overall
Location of lymphoedema Custom value	Unilateral arm lymphoedema on side of breast cancer surgery

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	**Question**	**Answer**
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Mestre, 2017

Bibliographic Reference	Mestre, S; Calais, C; Gaillard, G; Nou, M; Pasqualini, M; Ben Amor, C; Quere, I; Interest of an auto-adjustable nighttime compression sleeve (MOBIDERM R Autofit) in maintenance phase of upper limb lymphoedema : the MARILYN pilot RCT.; Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer; 2017; vol. 25 (no. 8); 2455-2462

Study details

Trial registration number and/or trial name	MARILYN pilot RCT. Trial number not outlined in study. Search of clinical trial register potentially identifies it but the record does not refer to it as a 'pilot' trial (NCT02253186).

Study type	Randomised controlled trial (RCT)
Study location	France
Study setting	Hospital
Study dates	September 2014 to February 2015
Sources of funding	Not outlined in study. Search of clinical trial register potentially identifies it as Thuasne (a medical technologies manufacturer) who manufacture both MOBIDERM and the THUASNE lymphology hosiery used in the study.
Inclusion criteria	women aged ≥18 years, with unilateral secondary upper limb lymphoedema of stage II or III according to the ISL classification, with evident pitting sign (assessed as ++ or +++) Patients had to have undergone an intensive phase treatment with a decrease of lymphoedema volume at least of 10% prior to study entry
Exclusion criteria	active cellulitis, lymphoedema associated with active cancer requiring chemotherapy, motor and/or sensitive neurological deficiency, postoperative oedema (i.e., acute edema occurring in the days following breast cancer-related surgery), active skin lesions on the arm, and pregnant or breastfeeding female
Intervention(s)	Post intensive phase of decongestive lymphoedema therapy (DLT) those randomised to the night-use group (Group I) were fitted with MOBIDERM® Autofit device additionally to their daytime elastic hosiery (circular made to measure knitted garment applying a level of pressure of 15–20 mmHg (French class 2) or 20–36 mmHg (French class 3) from THUASNE company (THUASNE Lymphology®) for 90 days.
Comparator	Post intensive phase of decongestive lymphoedema therapy (DLT) those randomised to the no night-use group (Group II) were fitted only with the day time elastic hosiery - circular made to measure knitted garment applying a level of pressure of 15–20 mmHg (French class 2) or 20–36 mmHg (French class 3) from THUASNE company (THUASNE Lymphology®) for the first 30 days. From Day 31 to Day 90 they were fitted with MOBIDERM® Autofit device for night-use.
Outcome measures	Patient-reported outcomes Quality of life Function Lymphoedema volume variation (volume excess variation) Treatment compliance
Number of participants	40

Duration of follow-up	90 days
Loss to follow-up	n=0 (ITT undertaken). n=5 (Per protocol)
Methods of analysis	Lymphoedema volume variation (volume excess variation) - bilateral Wilcoxon-Mann-Whitney test on the ITT population. All secondary endpoints and PP analysis were provided descriptively: (functional symptoms at Day 30 and Day 90 vs. baseline, QOL based on LYMQOL ARM questionnaire at each study visits and patient's satisfaction with self-reported questionnaires, compliance of treatment evaluated by patient diary between Day 0 and Day 30 and by questioning the patients at Day 90 regarding the study period between Day 30 and Day 90.
Additional comments	N/A

Study arms

MOBIDERM Autofit (Compression) (N = 20)

Comparator	Post intensive phase of decongestive lymphoedema therapy (DLT) those randomised to the no night-use group (Group II) were fitted only with the day time elastic hosiery - circular made to measure knitted garment applying a level of pressure of 15–20 mmHg (French class 2) or 20–36 mmHg (French class 3) from THUASNE company (THUASNE Lymphology®) for the first 30 days. From Day 31 to Day 90 they were fitted with MOBIDERM® Autofit device for night-use.
Number of participants	20

A standard lowstretch garment designed to apply a pressure of 15 mmHg and is an auto-adjustable semi-open sleeve

Elastic hosiery (compression) (N = 20)

Comparator	Post intensive phase of decongestive lymphoedema therapy (DLT) those randomised to the no night-use group (Group II) were fitted only with the day time elastic hosiery - circular made to measure knitted garment applying a level of pressure of 15–20 mmHg (French class 2) or 20–36 mmHg (French class 3) from THUASNE company (THUASNE Lymphology®) for the first 30 days. From Day 31 to Day 90 they were fitted with MOBIDERM® Autofit device for night-use.
Number of participants	20

Loss to follow-up	n=0 (ITT undertaken). n=4 (Per protocol)

A circular made to measure knitted garment applying a level of pressure of 15–20 mmHg (French class 2) or 20– 36 mmHg (French class 3) from THUASNE company (THUASNE Lymphology®).

Characteristics

Arm-level characteristics

Characteristic	MOBIDERM Autofit (Compression) (N = 20)	Elastic hosiery (compression) (N = 20)
% Female Nominal	100	100
Mean age (SD) Mean (SD)	65.11 (8.62)	68.87 (11.79)
BMI Mean (SD)	27.44 (4.54)	29.63 (6.53)
Radiotherapy Number of participants Nominal	20	20
Hormone therapy Number of participants Nominal	7	7
Chemotherapy Number of participants Nominal	12	12
Surgery Number of participants Nominal	20	20
Stage 2 Participant numbers Nominal	20	17
Stage 3 Participant numbers Nominal	0	3

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Pilot study. Randomisation process described as 1:1 post 'intensive phase' but a lack of detail regarding this. Patient demographic table (table 1) indicates differences between study arms for certain characteristics that may impact the efficacy of compression intervention but no statistical analysis for differences between arms post randomisation has been undertaken to assess this and its impact. Unclear if blinding occurred or mitigations put in place to address this and the impact of randomisation. Blinding might not be a major issue given the nature of the intervention. ITT undertaken and data for all participants randomised (n=40) is outlined. 5 participants excluded for deviation from protocol (intervention adherence) but 87.5% of participants completed the study as specified. ITT analysis undertaken. Deviations from the protocols occurred - Five patients were excluded from the protocol (PP) population due to lack of adherence to intervention protocol. ITT undertaken.)*
Overall bias and Directness	Overall Directness	Directly applicable *(French study in a hospital setting focused on compression on lymphoedema volume.)*

Ochalek, 2023

Bibliographic Reference	Ochalek, Katarzyna; Kurpiewska, Joanna; Gradalski, Tomasz; Adjustable Compression Wraps (ACW) vs. Compression Bandaging (CB) in the Acute Phase of Breast Cancer-Related Arm Lymphoedema Management-A Prospective Randomized Study.; Biology; 2023; vol. 12 (no. 4)

Study details

Study type	Randomised controlled trial (RCT)
Study location	Krakow, Poland
Study setting	Lymphoedema Clinic, St. Lazarus Hospice,
Study dates	Recruitment between January and November 2022
Sources of funding	Project financed by the Ministry of Science and Higher Education under Regional Initiative of Excellence program, project number 022/RID/2018/19
Inclusion criteria	Stage II lymphoedema (per ISL criteria) ≥20% excess limb volume Positive pitting sign No signs of active cancer, venous thrombosis, or previous compression

Exclusion criteria	Not reported
Intervention(s)	ACW group (n=18): Adjustable compression garments (circaid juxtafit essentials arm sleeve and glove) worn 24 hrs/day for 2 weeks Pressure 20-30 mmHg
Comparator	Multi-layer short-stretch bandaging worn 24 hrs/day for 2 weeks Pressure 20-30 mmHg Education in self-bandaging during 1st week Both groups performed upper limb exercises 15 min/day
Number of participants	36 women randomized (ACW n=18, CB n=18)
Duration of follow-up	Outcomes assessed at baseline, 1 week, and 2 weeks (end of intervention)
Loss to follow-up	N/A
Methods of analysis	Mann-Whitney test for between-group differences Wilcoxon signed rank test or Friedman test for within-group changes

Study arms

ACW group (N = 18)
Adjustable compression garments (circaid juxtafit essentials arm sleeve and glove) worn 24 hrs/day for 2 weeks Pressure 20-30 mmHg Education in self-application during 1st week

CB group (N = 18)
Multi-layer short-stretch bandaging worn 24 hrs/day for 2 weeks Pressure 20-30 mmHg Education in self-bandaging during 1st week Both groups performed upper limb exercises 15 min/day

Characteristics

Study-level characteristics

Characteristic	Study (N = 36)
% Female Sample size	n = 36 ; % = 100
Mean age (SD) Custom value	ACW group: 62.3 (9.4) years CB group: 69.6 (9.5) years
Lymphoedema stage / severity Custom value	All participants had Stage II lymphoedema per ISL criteria ≥20% excess limb volume

Characteristic	Study (N = 36)
Location of lymphoedema Custom value	Unilateral upper limb

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. No information about participants' adherence to interventions. Poor reporting of baseline characteristics)*
Overall bias and Directness	Overall Directness	Directly applicable

Omar, 2020

Bibliographic Reference	Omar, Mohammed T A; Gwada, Rehab F M; Omar, Ghada S M; El-Sabagh, Rokia M; Mersal, Abd-El Aziz E; Low-Intensity Resistance Training and Compression Garment in the Management of Breast Cancer-Related Lymphoedema: Single-Blinded Randomized Controlled Trial.; Journal of cancer education : the official journal of the American Association for Cancer Education; 2020; vol. 35 (no. 6); 1101-1110

Study details

Study location	Cairo, Egypt
Study setting	Outpatient clinics at the National Cancer Institute and El-Mattaria Teaching Hospital
Study dates	not reported
Sources of funding	not reported
Inclusion criteria	Women ≥18 years old Unilateral BCRL ≥5% inter-limb volume or circumference differences
Exclusion criteria	Bilateral BCRL Current metastases, continuing radiotherapy, cellulitis, venous thrombosis, infection, congestive heart failure Paralysis, severe trauma Previous lymphoedema therapy within last 3 months Medication affecting body fluid/electrolyte balance Participation in exercise program in last month (≥1 hr moderate intensity 3x/week)
Intervention(s)	Rex-Comp group (n=30):

	Low-intensity resistance training 3x/week for 8 weeks
Comparator	Rex group (n=30): Low-intensity resistance training 3x/week for 8 weeks Both groups: 10-12 reps at 50-60% 1RM, 2 sets of 7 upper body exercises
Number of participants	60 women completed the study and were analysed (Rex-Comp n=30, Rex n=30) 70 were randomized (number per group not provided)
Duration of follow-up	Outcomes assessed at baseline, 8 weeks (end of intervention), and 12 weeks (4 weeks post-intervention)
Loss to follow-up	10 participants withdrawn after randomization

Study arms

Rex-Comp group (N = 30)
Exercise and Movement + Complete Decongestive Therapy Low-intensity resistance training 3x/week for 8 weeks Instructed to wear compression garment during exercise

Rex group (N = 30)
Low-intensity resistance training 3x/week for 8 weeks Both groups: 10-12 reps at 50-60% 1RM, 2 sets of 7 upper body exercises

Characteristics

Study-level characteristics

Characteristic	**Study (N = 60)**
% Female Sample size	n = 60 ; % = 100
Mean age (SD) Custom value	Rex-Comp group: 53.78 (2.99) years Rex group: 52.62 (2.92) years
Lymphoedema stage / severity Custom value	Mild severity: Rex-Comp 66.67%, Rex 60% Moderate severity: Rex-Comp 33.33%, Rex 40%
Location of lymphoedema Custom value	Unilateral upper limb

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. No information about participants' adherence to interventions.)*
Overall bias and Directness	Overall Directness	Directly applicable

Omidi, 2020

Bibliographic Reference	Omidi, Zahra; Kheirkhah, Masoomeh; Abolghasemi, Jamileh; Haghighat, Shahpar; Effect of lymphoedema self-management group-based education compared with social network-based education on quality of life and fear of cancer recurrence in women with breast cancer: a randomized controlled clinical trial.; Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation; 2020; vol. 29 (no. 7); 1789-1800

Study details

Trial registration number and/or trial name	IRCT2017052834176N1
Study type	Randomised controlled trial (RCT)
Study location	Tehran, Iran
Study setting	Rehabilitation centre
Study dates	September 2017 - June 2018
Sources of funding	Iran University of medical sciences, Grant/Award Numbers: IR.IUMS.REC1396-01–28-9411373002
Inclusion criteria	A history of confirmed breast cancer (stages 0 to IV), lymphoedema established by a physician in the past year, aged 18–65 years old, completion of primary cancer treatments, ability to read and write and work with the Telegram™ messenger, no post-cancer psychiatric disorders requiring drug therapy, and access to the Internet through cell phones or computers.
Exclusion criteria	failure to attend in the third and fourth sessions of in-person education as the key sessions, failure to approve delivery of messages in the Telegram™ in the SNE group, detection of cancer recurrence during the study, and unwillingness to continue the intervention

Intervention(s)	1. Group-based education: 5 sessions of 60 to 90 min twice a week, held in the form of face-to-face group discussions and Q&A in groups of 5 in a quiet room in the clinic. After the end of the sessions, a CD of the educational content was provided. 2. Social network-based education: A channel was created in the Telegram™ messenger called “Lymphoedema Self-Management Education,” and then all SNE group participants were invited to the channel by the researcher. Educational content was uploaded on the channel twice a week for three weeks. It was presented to the channel as 20 audio and photo messages at different times of the day.
Comparator	Control: No education intervention
Outcome measures	Quality of life Measured using Persian version of the Lymphoedema Life Impact Scale (LLIS)
Number of participants	105
Duration of follow-up	3 months (outcomes reported immediately after intervention and at 3 months)
Methods of analysis	Chi-square and one-way ANOVA tests assessed the difference in demographic and clinical variables’ frequency between three groups. Kolmogorov–Smirnov test confirmed the normal distribution of QoL and FCR variables, so parametric tests were used. Mixed-model ANOVA was applied to study the main effect of time and groups and interaction of them on outcomes after checking its assumptions in data. The difference of outcomes at the end of the study was compared by ANCOVA test and adjusting the baseline values and group effect. The statistical significance was set as $P < 0.05$.
Additional comments	Also reported fear of cancer recurrence, but outcome not relevant to this review. Change from baseline data calculated by reviewer

Study arms

Group-based education (N = 35)

Duration of follow-up		
Loss to follow-up	3	3

5 sessions of 60 to 90 min twice a week, held in the form of face-to-face group discussions and Q&A in groups of 5 in a quiet room in the clinic. After the end of the sessions, a CD of the educational content was provided.

Social network-based education (N = 35)

Loss to follow-up	1	1
Methods of analysis		

A channel was created in the Telegram™ messenger called “Lymphoedema Self-Management Education,” and then all SNE group participants were invited to the channel by the researcher. Educational content was uploaded on the channel twice a week for three weeks. It was presented to the channel as 20 audio and photo messages at different times of the day.

Control (N = 35)

Loss to follow-up	4	4

No education (an educational CD was provided after the study)

Characteristics

Arm-level characteristics

Characteristic	Group-based education (N = 35)	Social network-based education (N = 35)	Control (N = 35)
Mean age (SD) (years) Mean (SD)	52.47 (10.62)	50.44 (8.81)	50.23 (8.9)
BMI (years) Mean (SD)	28.04 (5.07)	28.41 (5.1)	28.35 (4.52)
Grade I Custom value	33.3%	33.3%	33.3%
grade II Custom value	26.8%	39.3%	33.9%
Grade III/IV Custom value	46.9%	29.4%	32.3%
stage I Custom value	12.5%	23.5%	25.8%
Stage II/III Custom value	87.5%	76.5%	74.2%
Duration of lymphoedema (Months) Mean (SD)	6.22 (3.86)	7.5 (3.51)	7.26 (3.34)

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(No information about allocation concealment. Participants could not be blinded to their allocation and this could have affected the outcome (patient-reported quality of life). Methods of statistical analysis and results are not particularly clear)*
Overall bias and Directness	Overall Directness	Directly applicable

Ozsoy-Unubol, 2019

Bibliographic Reference	Ozsoy-Unubol, T; Sanal-Toprak, C; Bahar-Ozdemir, Y; Akyuz, G; Efficacy of kinesio taping in early stage breast cancer associated lymphoedema : A randomized single blinded study.; Lymphology; 2019; vol. 52 (no. 4); 166-176

Study details

Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Hospital/Outpatient
Study dates	
Sources of funding	
Inclusion criteria	Participants between 18-70 years old, with unilateral stage 1 BCAL (ISL), undergone at least 3 months of follow-up post breast surgery, did not receive lymphoedema treatment
Exclusion criteria	People with skin disease, infections, thrombophlebitis, pregnancy, metastases in the lymph nodes, uncontrolled psychiatric and systemic diseases, sensorial or language problems, cognitive disorders or were undergoing diuretic therapy.
Intervention(s)	Usual care and Kinesiotape applied in three-four day intervals for four weeks and compression garments after 4 weeks.
Comparator	Usual care. Skin and nail care education, preventive measures (limb elevation, maintenance of ideal body weight, and avoidance of infection, injury, tight fitting clothing, blood pressure cuffing) and exercises that included upper extremity ranges of motion, muscle pumping and abdominal breathing.

Outcome measures	Lymphoedema Circumference differences Mobility Pain/heaviness Using VAS
Number of participants	35 participants
Duration of follow-up	3 months
Loss to follow-up	3 in intervention arm 1 in usual care arm
Methods of analysis	Statistical analysis was performed with SPSS 22.0 statistical package program. In addition to descriptive statistical methods (mean, frequency, percentage, and standard deviation), the Shapiro-Wilk test was used to examine normal distribution parameters. Pearson's chi-squared test and Fisher's exact test were used to compare the qualitative data. The student's t-test and the Mann-Whitney U test were used to compare the intergroup parameters. The Friedman test was used for repeated comparisons, and the Wilcoxon signed-rank test was performed in the Bonferroni correction for pairwise comparisons. The results were evaluated at a 95% confidence interval and a significance level of $p<0.05$.

Study arms

KT (N = 16)

Usual care (N = 19)

Characteristics

Arm-level characteristics

Characteristic	KT (N = 16)	Usual care (N = 19)
Mean age (SD) Mean (SD)	50.56 (6.45)	54.57 (7.49)
BMI (kg/m2) Mean (SD)	29.58 (6.29)	29.28 (4.46)
Chemotherapy No of events	n = 14 ; % = 78	n = 17 ; % = 90
Radiotherapy No of events	n = 13 ; % = 81	n = 15 ; % = 79
Axillary lymph node dissection No of events	n = 16 ; % = 100	n = 19 ; % = 100

Characteristic	KT (N = 16)	Usual care (N = 19)
Right arm No of events	n = 8 ; % = 50	n = 11 ; % = 58
Left arm No of events	n = 8 ; % = 50	n = 8 ; % = 42
Modified radical mastectomy No of events	n = 12 ; % = 75	n = 16 ; % = 84.2
Breast-conserving surgery No of events	n = 4 ; % = 25	n = 3 ; % = 15.8

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Park, 2023

Bibliographic Reference	Park, Yun-Jin; Na, Song-Ju; Kim, Myung-Ki; Effect of progressive resistance exercise using Thera-band on edema volume, upper limb function, and quality of life in patients with breast cancer-related lymphoedema .; Journal of exercise rehabilitation; 2023; vol. 19 (no. 2); 105-113

Study details

Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Korea
Study setting	Complex decongestive physical therapy: likely outpatient setting Progressive resistive exercise intervention (PRE): likely outpatient setting Self-home resistance exercise (SRE): home-based
Study dates	Not reported
Sources of funding	College of Culture and Sports at Korea University

Inclusion criteria	Individuals diagnosed with lymphoedema after mastectomy, those who completed their courses of chemotherapy or had the plan to receive chemotherapy, those with current or completed radiotherapy after anti-cancer treatment, those who could perform exercise according to the therapist's instructions, those who did not have a problem in cognitive functions, and those without abnormal findings on physical and neurological examinations.
Exclusion criteria	Current administration of chemotherapy, metastatic cancer, serious problems in the cardiopulmonary system, and orthopaedic or neurological problems.
Intervention(s)	Complex decongestive physical therapy (CDPT): both groups had 3 sessions/week for 6 weeks: 15 minutes of manual lymphatic drainage, 5 minutes of low elastic compression bandages, and 15 minutes of intermittent pneumatic compression therapy. Progressive resistive exercise intervention: After CDPT completed, 50 minutes of resistance exercise, 3 sessions/week for 6 weeks. Using Thera-band of progressive tension, changing every 2 weeks. Exercises focussed on stretching, stabilising scapula and strengthening upper limb muscles. The role of the physiotherapist in the progressive resistance exercise is not clear.
Comparator	Complex decongestive physical therapy: As for intervention group. Self-home resistance exercise: home-based: After CDPT completed, 50 minutes of "self-home resistive exercise" using Thera-band, 3 sessions/week for 6 weeks. Exercises are the same as for the intervention group, but no progression in Thera-band tension. The role of the physiotherapist in the self-home resistance exercise is unclear.
Outcome measures	Lymphoedema Oedema volume, grip strength, K-DASH questionnaire
Number of participants	N=20 PRE: 10 SRE: 20
Duration of follow-up	Not reported. Likely that outcomes were measured soon after 12-week intervention concluded.
Loss to follow-up	N=4/20 (20%) PRE: 2/10 SRE: 2/10
Methods of analysis	To compare pre- and post-exercise variations, the paired t-test and Wilcoxon signed-rank test were used. The independent t-test and Mann–Whitney test was used to compare the intergroup variations in the dependent variables.

Additional comments	Limitations: Follow-up duration not specified, small sample size, reasons for drop outs (4/20) not specified. Same practitioner completed CDPT for both groups, but information on blinding not reported. Outcome measures: Arm circumference: The arm circumference measurement method was used to measure the circumference of upper the extremity BCRL. Using a tape measure, the length between each marked point at 4-cm intervals from the ulnar styloid to the axillary on the affected upper limb was measured (12 parts in total), and the volume was calculated using the cone formula. Grip strength: Digital dynamometer used. Using the standardized method suggested by the American Society of Hand Therapists, the patients were instructed to pull the handle of the dynamometer with maximum strength in a sitting posture. The mean of triplicate measurements was estimated for both hands. K-DASH: The Korean version of the disability of the arm, shoulder and hand scale. Self-reported. 30 items including pain, effects of disability on society, sleep, and psychological effects. Score 1-100, increasing severity with increasing score. Sex of participants not specified

Study arms

Progressive resistance exercise (N = 10)

Self directed resistance exercise (N = 10)

Characteristics

Arm-level characteristics

Characteristic	Progressive resistance exercise (N = 10)	Self directed resistance exercise (N = 10)
Mean age (SD) Mean (SD)	58.86 (3.28)	60.29 (5.09)
Weight Kg Mean (SD)	61.22 (2.99)	58.32 (4.87)

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. Poor reporting of baseline characteristics, weight between both groups not balanced.)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Pujol-Blaya, 2019

Bibliographic Reference	Pujol-Blaya, Vicenta; Salinas-Huertas, Sira; Catasus, M Luisa; Pascual, Teresa; Belmonte, Roser; Effectiveness of a precast adjustable compression system compared to multilayered compression bandages in the treatment of breast cancer-related lymphoedema: a randomized, single-blind clinical trial.; Clinical rehabilitation; 2019; vol. 33 (no. 4); 631-641

Study details

Study location	Four hospitals in the metropolitan area of Barcelona, Spain participated (Hospital Universitari Bellvitge, Hospital Universitari Germans Trias i Pujol, Hospital Mar-Esperança Parc de Salut Mar, Hospital Universitari Vall d'Hebron).
Study setting	The rehabilitation services of the four general university hospitals.
Study dates	Patients were recruited between November 2014 and October 2015, and follow-up was completed in January 2016.
Sources of funding	Not reported.
Inclusion criteria	Older than 18 years Female Upper limb lymphoedema after axillary lymph node dissection for breast cancer Lymphoedema affecting at least arm or forearm Lymphoedema volume excess ≥10% Lymphoedema not previously treated or without treatment for last 12 months
Exclusion criteria	Bilateral upper limb lymphoedema Cognitive or sensorial impairments interfering with collaboration Plexus injury after radiotherapy Disease progression Pregnancy or breastfeeding
Intervention(s)	Manual lymphatic drainage followed by precast adjustable compression system
Comparator	Manual lymphatic drainage followed by multilayered compression bandages
Number of participants	48 patients were randomized, 42 (89.4%) were analyzed (22 in precast adjustable compression system group, 20 in multilayered compression bandages group).
Duration of follow-up	3 months

Loss to follow-up	6 patients (12.5%) were lost to follow-up
Methods of analysis	Intention-to-treat

Study arms

MLD + precast adjustable compression system (N = 24)
Manual lymphatic drainage followed by precast adjustable compression system

MLD + multilayered compression bandages (N = 24)

Characteristics

Study-level characteristics

Characteristic	Study (N = 100)
% Female Sample size	n = 48 ; % = 100
Mean age (SD) Custom value	59.4 (12.0) years
Lymphoedema stage / severity Custom value	33.3% mild, 35.7% moderate, 31.0% severe (based on excess limb volume)
Location of lymphoedema Custom value	Upper limb breast cancer-related lymphoedema

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Ridner, 2020

Bibliographic Reference	Ridner, Sheila H; Dietrich, Mary S; Davis, Amanda J; Sinclair, Vaughn; A Randomized Clinical Trial Comparing the Impact of a Web-Based Multimedia Intervention Versus an Educational Pamphlet on Patient Outcomes in Breast Cancer Survivors with Chronic Secondary Lymphoedema.; Journal of women's health (2002); 2020; vol. 29 (no. 5); 734-744

Study details

Study type	Randomised controlled trial (RCT)
Study location	US

Study setting	Vanderbilt Medical Center, Nashville, US
Study dates	Not reported
Sources of funding	Research Scholar Grant, RSG-13-022-01-CPPB from the American Cancer Society
Inclusion criteria	People with a history of breast cancer, a diagnosis of Stage II lymphoedema based on the International Society of Lymphoedema, aged 18 or older, and able to see and read printed documents in English.
Exclusion criteria	People undergoing chemotherapy or radiation, or receiving hospice care
Intervention(s)	Web-based multimedia intervention: 12 sessions of videos, each 20–45 minutes long, that featured narration, reflective questions, and interviews with patients sharing stories about living with lymphoedema . The 12 sessions covered basic physiology of lymphoedema and self-care, goal setting and self-reward, diet and exercise strategies, methods of dealing with negative emotions and stress, body image changes, uncertainty, and enhancing emotional and instrumental social support. The last session discussed looking at life from a different perspective and finding a new identity.
Comparator	Educational pamphlet: A hard copy of an educational pamphlet titled, ‘‘Guide to Understanding Lymphoedema’’. Pamphlet topics included lymphoedema risk reduction, early warning signs, advice regarding lymphoedema treatment, emotions and lymphoedema , and paying for treatment.
Outcome measures	Patient-reported outcomes Symptom burden, measured using the Lymphoedema Symptom Intensity and Distress Scale–Arm (LSIDS-A) Function Measured using the 11-item Quick-Disabilities of Arm, Shoulder, and Hand (QuickDASH) tool
Number of participants	160
Duration of follow-up	12 months (outcomes reported at 1 month and 12 months post-intervention)
Methods of analysis	Nominal and ordinal variables were summarised by using frequency distributions. If normally distributed, continuous variables were summarized by using mean and standard deviation (SD); if skewed, median and interquartile range were used. Differences between the groups in demographic and clinical characteristics were conducted by using Chi-Square Tests of Independence (nominal, ordinal) or Mann–Whitney (continuous) tests.

	Generalized linear models that controlled for the baseline values were used to assess differences between groups in the amount of change between baseline and end of study in the study outcome variables. Cohen's d effect size indices were used to quantify the effects of the WBMI on those outcomes.
Additional comments	Relevant outcomes reported to be skewed and reported as median (IQR). Results therefore reported but not included in meta-analysis.

Study arms

Web-based multimedia intervention (N = 80)

Number of participants	80
Loss to follow-up	33 (41.2%)

Videos with reflective questions and interviews with patients. 12 sessions covered basic physiology of lymphoedema and self-care, goal setting and self-reward, diet and exercise strategies, methods of dealing with negative emotions and stress, body image changes, uncertainty, and enhancing emotional and instrumental social support.

Educational pamphlet (N = 80)

Outcome measures	Patient-reported outcomes Symptom burden, measured using the Lymphoedema Symptom Intensity and Distress Scale–Arm (LSIDS-A)
Number of participants	80
Loss to follow-up	38 (22.5%)

A hard copy of an educational pamphlet titled, ''Guide to Understanding Lymphoedema''. Pamphlet topics included lymphoedema risk reduction, early warning signs, advice regarding lymphoedema treatment, emotions and lymphoedema , and paying for treatment.

Characteristics

Arm-level characteristics

Characteristic	Web-based multimedia intervention (N = 80)	Educational pamphlet (N = 80)
Age (years) Mean (SD)	59.8 (8.6)	56 (9.2)

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(A high percentage of people did not complete the trial, and loss to follow-up was higher in the intervention (44.2%) than control group (22.5%). Patient-reported outcomes with no information about blinding, so could have been affected by knowledge of the intervention received)*
Overall bias and Directness	Overall Directness	Directly applicable

Rockson, 2022

Bibliographic Reference	Rockson, Stanley G; Whitworth, Pat W; Cooper, Andrea; Kania, Sarah; Karnofel, Heidi; Nguyen, Michelle; Shadduck, Kristin; Gingerich, Phyllis; Armer, Jane; Safety and effectiveness of a novel nonpneumatic active compression device for treating breast cancer-related lymphoedema : A multicenter randomized, crossover trial (NILE).; Journal of vascular surgery. Venous and lymphatic disorders; 2022; vol. 10 (no. 6); 1359-1366e1

Study details

Study type	Cross-over RCT
Study location	Multicenter trial across 5 sites in the United States (3 in California, 1 in Ohio, 1 in Tennessee)
Study setting	Private lymphoedema clinics associated with cancer care centers
Study dates	Recruitment began in January 2021
Sources of funding	Not reported
Inclusion criteria	Adults aged >18 years Diagnosis of unilateral upper limb lymphoedema (primary or secondary)
Exclusion criteria	Systemic disorders contraindicating compression therapy Active cellulitis or open/partially healed wounds Lipedema Active or recent cancer (<3 months since treatment) Recent infection (<4 weeks) or venous thromboembolism (<6 months) Pulmonary edema, uncontrolled heart failure, renal failure Seizure disorder, uncontrolled asthma, conditions where increased venous/lymph return is undesirable Pregnancy, nursing Participation in another clinical trial within 30 days Cognitive or physical impairment interfering with device use
Intervention(s)	Novel nonpneumatic compression device (NPCD) used daily for 60 minutes

Comparator	Advanced pneumatic compression device (APCD, Flexitouch model) used daily for 60 minutes
Number of participants	52 enrolled, 50 included in analysis
Duration of follow-up	28 days with each compression device, with a 4-week washout period between devices
Loss to follow-up	2 participants lost to follow-up
Methods of analysis	Paired t-tests

Study arms

Novel nonpneumatic compression device (NPCD) (N = 23)

Advanced pneumatic compression device (APCD) (N = 27)

Characteristics

Study-level characteristics

Characteristic	Study (N = 50)
% Female Sample size	n = 50 ; % = 100
Mean age (SD) Custom value	60 ± 10.8 years
Lymphoedema stage / severity Custom value	All had unilateral breast cancer-related (secondary) lymphoedema , stage not specified
Location of lymphoedema Custom value	Upper limb lymphoedema

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Some concerns with assessment of outcomes due to allocation concealment.)*
Overall bias and Directness	Overall Directness	Directly applicable

Sanal-Toprak, 2019

Bibliographic Reference	Sanal-Toprak, C; Ozsoy-Unubol, T; Bahar-Ozdemir, Y; Akyuz, G; The efficacy of intermittent pneumatic compression as a substitute for manual lymphatic drainage in complete decongestive therapy in the treatment of breast cancer related lymphoedema .; Lymphology; 2019; vol. 52 (no. 2); 82-91

Study details

Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	University
Study dates	March 2014 to March 2015
Sources of funding	Not reported
Inclusion criteria	Patients with stages 2-3 lymphoedema who agreed to participate in the study, aged between 18 to 70 years, and were at least 3 months past breast surgery
Exclusion criteria	People with signs of cellulitis, lymphangitis, fungal infection, metastases to the lymph nodes, and uncontrolled psychiatric or systemic diseases
Intervention(s)	Intermittent pneumatic compression (IPC) plus compression bandage: treatment with IPC (30 min), compressive bandages, and home exercise program. A total of 15 sessions (5 weeks) were applied 3 times per week, and after each session, the compressive bandage was repeated. A 12-chamber sequential gradient compression pump was used for the IPC treatment. Inflation pressures ranged from 50 to 80 mmHg, and the garment was inflated fully from distal to proximal. Inflation time lasted for 60 seconds. Once the entire garment reached full inflation, it was deflated and the cycle repeated. Deflation time lasted for 25 seconds.
Comparator	Manual lymphatic drainage (MLD) plus compression bandage: treatment with MDL (30 min), compressive bandages, and home exercise program. A total of 15 sessions (5 weeks) were applied 3 times per week, and after each session, the compressive bandage was repeated. MDL was performed by an expert massage therapist. During application, a pressure of approximately 30-45 mmHg was applied with the hands and fingers.

Outcome measures	Lymphoedema Circumference differences were evaluated between the 2 arms with a nonelastic tape measure at five levels: metacarpophalangeal joints, wrists, 15 cm distally from the medial epicondyle, medial epicondyle, and 15 cm proximally from the medial epicondyle Goniometric measurements of shoulder range of motion (abduction, adduction, flexion, extension, internal rotation, external rotation) Pain/heaviness Shoulder pain and sensations of heaviness were also evaluated with a 100 mm horizontal visual analogue scale (VAS) ranging from '0 mm' (no discomfort) to '100 mm' (worst imaginable)
Number of participants	46 participants
Duration of follow-up	3 months
Loss to follow-up	None
Methods of analysis	In addition to descriptive statistical methods (mean, frequency, percentage and standard deviation), the Kolmogorov-Smirnov distribution test was used for examination of normal distribution parameters. Pearson's Chi-square test and Fisher's exact test were used for comparison of the qualitative data. The Mann-Whitney U test was used for comparison of the intergroup parameters. Friedman test was used for repeated comparisons and Wilcoxon signed-rank test was performed with a Bonferroni correction for pairwise comparisons. Results were evaluated at a 95% confidence intervals and a significant level of $p<0.05$.
Additional comments	For both groups: Ladder, pendulum, and range of motion exercises were given for affected upper extremities and organised for the home exercise programs At the end of the 5th week, patients in both groups were treated with a daily 23-hour compression garment and home exercise routines

Study arms

Intermittent pneumatic compression (N = 22)

Manual lymphatic drainage (N = 24)

Characteristics

Arm-level characteristics

Characteristic	Intermittent pneumatic compression (N = 22)	Manual lymphatic drainage (N = 24)
Mean age (SD) Mean (SD)	55.36 (10.3)	59.04 (2.83)
BMI Mean (SD)	30.23 (6.21)	30.9 (4.96)
Radiotherapy No of events	n = 20 ; % = 90.9	n = 24 ; % = 100
Chemotherapy No of events	n = 19 ; % = 86.4	n = 22 ; % = 91.7
Surgery method - modified radical mastectomy No of events	n = 19 ; % = 86.4	n = 14 ; % = 58.3
Surgery method - breast-conserving surgery No of events	n = 3 ; % = 13.6	n = 10 ; % = 41.7
Axillary lymph node dissection No of events	n = 22 ; % = 100	n = 24 ; % = 100
Lymphoedema stage 2 No of events	n = 19 ; % = 86.4	n = 15 ; % = 62.5
Lymphoedema stage 3 No of events	n = 3 ; % = 13.6	n = 9 ; % = 37.5
Lymphoedema side - right No of events	n = 12 ; % = 54.5	n = 13 ; % = 54.2
Lymphoedema side - left No of events	n = 10 ; % = 45.5	n = 11 ; % = 45.8

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(No information on whether allocation sequence was concealed until participants were enrolled and assigned to interventions. Per protocol analysis. No information about deviations from intended interventions. Higher number of participants in the intermittent pneumatic compression had modified radical mastectomy. Researchers mentioned that they could not be sure of the patients' compliance to the interventions completely.*

Section	Question	Answer
		Pre-specified analysis plan was not available. Protocol was not registered.)
Overall bias and Directness	Overall Directness	Directly applicable

Selcuk Yilmaz, 2023

Bibliographic Reference	Selcuk Yilmaz, Sedef; Ayhan, Fikriye Figen; The Randomized Controlled Study of Low-Level Laser Therapy, Kinesio-Taping and Manual Lymphatic Drainage in Patients With Stage II Breast Cancer-Related Lymphoedema.; European journal of breast health; 2023; vol. 19 (no. 1); 34-44

Study details

Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Hospital/outpatient
Study dates	Not reported
Sources of funding	
Inclusion criteria	People with unilateral, stage I-III BC, stage II arm lymphoedema and arm volume difference 5-20% on the affected side after BC surgery.
Exclusion criteria	People with stage IV BC; bilateral BC; bilateral lymphoedema; stage I (spontaneous reversible), late stage II (spontaneous irreversible with fibrotic changes) or stage III lymphoedema; skin infection or lesion in the arms; diseases of the cardiovascular, pulmonary, renal, hepatic, other skin and allergic diseases; and patients who had received lymphoedema treatment in the last six months
Intervention(s)	Kinesiotaping
Comparator	MLD
Outcome measures	Lymphoedema Circumferential measurement and volume calculation Quality of life LymQoL Pain/heaviness Function Range of motion

Number of participants	45 participants
Duration of follow-up	12 weeks
Loss to follow-up	3 from KT due to skin allergy
Methods of analysis	The data collected from the patients were entered into the SPSS 21.0 package program (IBM Inc., Armonk, NY, USA), a data set was created and statistical analysis was performed. Descriptive statistics [frequency, percentages, means ± standard deviations, median (range between quarters)] of the variables were indicated with tables. Conformity to normal distribution was determined by Kolmogorov–Smirnov and Shapiro–Wilk tests in order to determine whether the variables met the parametric test assumptions. After determining that the variables fit the normal distribution, for pairs Student's t–test and ANOVA test were used for more than two groups. ANOVA test if the difference between the groups was found to be significant after the post-hoc comparisons were made in order to determine that it originated from the group Bonferoni paired comparison test was continued. Repeated measures ANOVA test was performed for repeated measures for parametric variables. If significance was found after performing the ANOVA test in repeated measurements Bonferoni to determine at what time the difference is due to the measurement corrected Bonferoni corrected paired Sample t–test was performed. After determining that the variables do not fit the normal distribution binary groups the Mann–Whitney U test was used for each group, and the Kruskal–Wallis H test for more than two groups. If the difference between the groups was found to be significant after the Kruskal– Wallis H test, Pairwise comparisons were made to determine which group the difference originated from. Dunn–Bonferoni pairwise comparison test was used. Friedman test was used for non-parametric repeated variables. Significance after Friedman test determined, to determine at what time the difference was due to measurement. Wilcoxon test with Bonferoni correction was performed. The chi-square test was used for the comparison of categorical variables. A p value of <0.05 was considered statistically significant.
Additional comments	Study included 3 arms, only KT and MLD arms extracted for analysis. Third arm on low level laser therapy is not relevant intervention. All patients prescribed compression garments for maintenance phase, distribution of BMI difference p=0.043

Study arms
MLD (N = 15)

KT (N = 15)

Characteristics

Arm-level characteristics

Characteristic	MLD (N = 15)	KT (N = 15)
Mean age (SD) Mean (SD)	57.6 (9.5)	51.4 (10.7)
BMI (kg/cm2) Mean (SD)	31.5 (4.1)	28 (4.2)
Radiation therapy No of events	n = 15 ; % = 100	n = 13 ; % = 86.7
Modified radical mastectomy No of events	n = 12 ; % = 80	n = 6 ; % = 40
Breast conserving surgery No of events	n = 3 ; % = 20	n = 9 ; % = 60
Chemotherapy No of events	n = 13 ; % = 86.7	n = 14 ; % = 93.3
Neo-adjuvant chemotherapy No of events	n = 13 ; % = 86.7	n = 14 ; % = 93.3
Endocrine therapy No of events	n = 10 ; % = 66.7	n = 9 ; % = 60
Stage 1 No of events	n = 1 ; % = 6.7	n = 2 ; % = 13.3
Stage 2 No of events	n = 10 ; % = 66.7	n = 8 ; % = 53.3
Stage 3 No of events	n = 4 ; % = 26.7	n = 5 ; % = 33.3
Right arm No of events	n = 6 ; % = 40	n = 7 ; % = 46.7
Left arm No of events	n = 9 ; % = 60	n = 8 ; % = 53.3

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Imbalance in baseline BMI distribution between groups, suggests an impact on interventions. Unclear how this was mitigated in study.)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Sen, 2021

Bibliographic Reference	Sen, Ekin Ilke; Arman, Sina; Zure, Mert; Yavuz, Hadi; Sindel, Dilsad; Oral, Aydan; Manual Lymphatic Drainage May Not Have an Additional Effect on the Intensive Phase of Breast Cancer-Related Lymphoedema: A Randomized Controlled Trial.; Lymphatic research and biology; 2021; vol. 19 (no. 2); 141-150

Study details

Study type	Randomised controlled trial (RCT)
Study location	Istanbul, Turkey.
Study setting	The study was conducted at the Department of Physical Medicine and Rehabilitation, Istanbul University Istanbul Faculty of Medicine
Study dates	NR
Sources of funding	The authors didn't receive any funding for this work
Inclusion criteria	Unilateral BCRL with 3-8 cm circumference difference between healthy and affected extremity at any reference point Completed chemotherapy and/or radiotherapy in the 6 months before study start No previous surgery involving other major node-bearing areas that may affect lymphatic flow
Exclusion criteria	Stage 0-1 lymphoedema Lymphoedema with papilloma, hyperkeratosis, or elephantiasis History of contralateral breast cancer Uncontrolled hypertension, pulmonary oedema or severe cardiovascular disease Clinical or radiologic evidence of active cancer or metastases Active infection
Intervention(s)	Complex decongestive therapy (CDT) group 15 sessions (every weekday for 3 weeks) of manual lymphatic drainage (MLD), compressive multilayer bandaging and exercise training. Both groups received educational program on lymphoedema
Comparator	Standard therapy (ST) group 15 sessions (every weekday for 3 weeks) of compressive multilayer bandaging and exercise training. Both groups received educational program on lymphoedema
Number of participants	54 women met the inclusion and were randomized to the CDT group (n=27) or ST group (n=27).

Duration of follow-up	Arm circumference measurements were performed at baseline and at the end of the 3 weeks following completion of treatment sessions. Feelings of heaviness, swelling, functional status, and health-related quality of life were assessed at baseline and 1 week after the end of treatment, considering the difficulties of compression treatment.
Loss to follow-up	4 participants withdrew due to personal reasons, attendance failure, and insufficient follow-up. The dropout rate was 7.4% (4 out of 54 participants).
Methods of analysis	Within-group changes from baseline to post-intervention were compared using Wilcoxon signed-rank test. Between-group differences in changes were compared using Mann-Whitney U test.

Study arms

Complex decongestive therapy (CDT) group (N = 27)
15 sessions (every weekday for 3 weeks) of manual lymphatic drainage (MLD), compressive multilayer bandaging and exercise training

Standard therapy (ST) group (N = 27)
15 sessions (every weekday for 3 weeks) of compressive multilayer bandaging and exercise training

Characteristics

Study-level characteristics

Characteristic	**Study (N = 50)**
% Female Sample size	n = 50 ; % = 100
Mean age (SD) Mean (SD)	56 (13.7)
Lymphoedema stage / severity Custom value	Stage II: CDT group: 16 (64%) ST group: 20 (80%) Stage III: CDT group: 9 (36%) ST group: 5 (20%)
Location of lymphoedema Custom value	Unilateral upper extremity lymphoedema

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	**Question**	**Answer**
Overall bias and Directness	Risk of bias judgement	Low

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Sener, 2017

Bibliographic Reference	Sener, Hulya Ozlem; Malkoc, Mehtap; Ergin, Gulbin; Karadibak, Didem; Yavuzsen, Tugba; Effects of Clinical Pilates Exercises on Patients Developing Lymphoedema after Breast Cancer Treatment: A Randomized Clinical Trial.; The journal of breast health; 2017; vol. 13 (no. 1); 16-22

Study details

Trial registration number and/or trial name	Not reported
Study type	Randomised controlled trial (RCT)
Study location	Turkey
Study setting	Community
Study dates	Not reported
Sources of funding	No funding received
Exclusion criteria	Presence of metastatic cancer, diagnosis of severe heart failure and/or arrhythmia, infection in the affected limb, severe psychological disorders, severe pain of unknown cause in the axillary region, musculoskeletal problems in the upper extremity before treatment for breast cancer, presence of other health problems that would prevent participation in the evaluation and treatment program
Intervention(s)	Clinical pilates exercise Exercises performed in groups of 5-8 people 3 times/week for 8 weeks. Supervised by physiotherapists. Focus on spinal stabilisation, and hand-arm-shoulder movements in all positions and pumping activities (opening and closing of fingers), aiming to accelerate the lymphatic flow. After 4 weeks, a resistance band exercises were added. Training on Pilates exercises and postures delivered prior to starting. The patients in the clinical Pilates exercise group, which was supervised by physiotherapists, were also asked to practice a home program every day that included manual lymphatic drainage training, wall extension, and Wand exercises used to improve shoulder flexibility and skin care training.

Comparator	Control group Participants were taught lumbopelvic stability (core stabilization) and how to protect core stabilization while performing activities of daily living. They were also taught how to conduct manual lymphatic drainage included in the complex decongestive therapy method, skincare, and shoulder exercises, and were instructed to perform each exercise every day. To increase their shoulder function and to reduce joint limitations, the participants were taught wall extension and Wand exercises, head and neck exercises, and exercises to improve shoulder girdle stability. In addition they were recommended to perform pumping activities and breathing exercises. The participants were given a brochure that described these exercises and were recommended to repeat these exercises at least 10 times. They were also advised to pay attention to skin care and to walk 1 hour every day. The participants were followed up through telephone calls.
Outcome measures	Patient-reported outcomes -pain, social appearance anxiety (SAA) Quality of life -with the European Organization for Research and Treatment of Cancer (EORTC) quality of life questionnaire (QLQ-BR23) Mobility -grip strength, shoulder flexion, abduction and external rotation,
Number of participants	N=60 Pilates: 30 Control: 30
Duration of follow-up	8 weeks from baseline
Loss to follow-up	0 loss to follow-up
Methods of analysis	To compare the difference between the two groups, the independent samples t-test was used. For the analysis of survey results calculated at certain periods and rates, the Wilcoxon test was used, which is the non-parametric counterpart of the t-test.
Additional comments	Outcome scores presented at baseline and follow up with means and SDs. Mean differences and SDs not presented. Follow-up means and SDs extracted. Grip strength: measured with Jamar hand dynamometer. Highest of three measurements taken, while patient standing with arm close to body and elbow at 90 degrees. Range of motion measurements performed using goniometer with patient in supine position.

	Social Appearance Anxiety was assessed using the Social Appearance Anxiety (SAA) Scale. The scale was developed as a self-report scale to measure a patient's cognitive, behavioural and emotional anxieties. The SAA Scale is a 16-item, 5-point Likert-type scale. High scores indicated poor performance. The European Organization for Research and Treatment Quality of Life Questionnaire – Breast Cancer Module (EORTC QLQ-BR23) was developed to assess challenges of daily life faced by patients with breast cancer and was used to assess the Quality of Life of the participants. It is a 4-point Likert scale ranging from 1 (not at all) to 4 (very much). To assess the functional level of upper limbs, the 30-item DASH questionnaire was administered. The measurements were compared after all the items were given scores ranging from 0 (no disability) to 100 (the most severe disability). A lower score indicated an improvement in functional status.

Study arms

Clinical pilates (N = 30)

Control (N = 30)

Characteristics

Arm-level characteristics

Characteristic	Clinical pilates (N = 30)	Control (N = 30)
% Female No of events	n = 30 ; % = 100	n = 30 ; % = 100
Mean age (SD) Mean (SD)	53.17 (7.66)	54.03 (12.57)
BMI Mean (SD)	28.53 (4.51)	30.35 (4.99)
Lymphoedema development time In years Mean (SD)	5 (3.57)	4.95 (4.87)

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate *(Some concerns with blinding and selective reporting)*
Overall bias and Directness	Overall Directness	Directly applicable

Singh, 2016

Bibliographic Reference	Singh, Ben; Buchan, Jena; Box, Robyn; Janda, Monika; Peake, Jonathan; Purcell, Amanda; Reul-Hirche, Hildegard; Hayes, Sandra C; Compression use during an exercise intervention and associated changes in breast cancer-related lymphoedema .; Asia-Pacific journal of clinical oncology; 2016; vol. 12 (no. 3); 216-24

Study details

Study type	Randomised controlled trial (RCT)
Study location	Greater Brisbane area, Australia
Study setting	home
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Aged 18+ years History of primary breast cancer Currently cancer-free and completed active treatment (excluding hormone therapy) Clinical diagnosis of unilateral breast cancer-related lymphoedema Stable lymphoedema (no exacerbation/infection in previous 3 months)
Exclusion criteria	Currently undertaking >75 min/week of moderate exercise Musculoskeletal, cardiovascular or neurological disorders limiting ability to exercise safely
Intervention(s)	Aerobic exercise: 12 weeks of home-based aerobic exercise progressing from moderate to high intensity
Comparator	Resistance exercise: 12 weeks of home-based resistance training progressing in intensity
Duration of follow-up	12 weeks
Loss to follow-up	2 participants withdrew prior to 12-week follow-up
Methods of analysis	Descriptive statistics, ANOVA to assess group x time interactions

Study arms

Home-based aerobic exercise program (N = 21)

Home-based resistance exercise program (N = 20)

Characteristics

Study-level characteristics

Characteristic	Study (N = 41)
% Female Sample size	n = 41 ; % = 100
Mean age (SD) Custom value	not reported
Lymphoedema stage / severity Custom value	Unilateral breast cancer-related lymphoedema, 40% had stage I, 60% had stage II in compression group
Location of lymphoedema Custom value	oedema: Upper limb breast cancer-related lymphoedema Copy Retry Claude can make mistakes. Please

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Moderate (*Some concerns with selective reporting, only reports data for those who wore compression bandaging vs not, doesn't categorise data as per original analysis plan)*
Overall bias and Directness	Overall Directness	Directly applicable

Tantawy, 2019

Bibliographic Reference	Tantawy, Sayed A; Abdelbasset, Walid K; Nambi, Gopal; Kamel, Dalia M; Comparative Study Between the Effects of Kinesio Taping and Pressure Garment on Secondary Upper Extremity Lymphoedema and Quality of Life Following Mastectomy: A Randomized Controlled Trial.; Integrative cancer therapies; 2019; vol. 18; 1534735419847276

Study details

Study type	Randomised controlled trial (RCT)
Study location	Cairo, Egypt
Study setting	outpatient/clinic setting
Study dates	between February and November 2017
Sources of funding	Not reported
Inclusion criteria	Women with unilateral upper extremity lymphoedema stages II and III following breast cancer Lymphoedema present for at least 6 months Completed phase 1 of complex decongestive therapy

Exclusion criteria	Active disease causing swelling Medications like diuretics Allergy or infection Pregnancy Heart or kidney disease Bilateral lymphoedema Skin diseases or cellulitis
Intervention(s)	Kinesio taping (KT) applied twice per week for 3 weeks
Comparator	Pressure garment (20-60 mmHg) worn 15-18 hours per day for 3 weeks
Number of participants	66 randomized (33 in KT group, 33 in pressure garment group). 59 completed the study.
Duration of follow-up	3 weeks
Loss to follow-up	7 participants (3 from KT group, 4 from pressure garment group)
Methods of analysis	Kolmogorov-Smirnov test

Study arms

Kinesio taping (KT) (N = 33)

pressure garment (PG) group (N = 33)

Characteristics

Study-level characteristics

Characteristic	**Study (N = 66)**
% Female Sample size	n = 66 ; % = 100
Mean age (SD) Custom value	54.3 (4.16) years in KT group, 55.15 (3.27) years in pressure garment group
Lymphoedema stage / severity Custom value	70% had stage II, 30% had stage III in KT group. 62.1% had stage II, 37.9% had stage III in pressur
Location of lymphoedema Custom value	Upper extremity lymphoedema following breast cancer treatment

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	**Question**	**Answer**
Overall bias and Directness	Risk of bias judgement	Moderate *(some concerns with reporting of baseline characteristics, as well as selective reporting of some outcomes. Assessors not blinded)*

Section	Question	Answer
Overall bias and Directness	Overall Directness	Directly applicable

Torres-Lacomba, 2020

Bibliographic Reference	Torres-Lacomba, Maria; Navarro-Brazalez, Beatriz; Prieto-Gomez, Virginia; Ferrandez, Jean Claude; Bouchet, Jean Yves; Romay-Barrero, Helena; Effectiveness of four types of bandages and kinesio-tape for treating breast-cancer-related lymphoedema: a randomized, single-blind, clinical trial.; Clinical rehabilitation; 2020; vol. 34 (no. 9); 1230-1241

Study details

Trial registration number and/or trial name	NCT03250364
Study type	Randomised controlled trial (RCT)
Study location	Spain
Study setting	Physiotherapy in Women's Health Research Group
Study dates	October 2014 to January 2020
Sources of funding	The author(s) received no financial support for the research, authorship and/or publication of this article.
Inclusion criteria	Older than 20 years of age; showing clinical stage I and II breast cancer-related lymphoedema according to the International Society of Lymphology based on a diagnostic criterion of ⩾2 cm difference in at least two consecutive perimeters of the affected upper limb compared to the contralateral limb for at least six months; lymphoedema onset at least six months after surgery or radiation therapy; lymphoedema has not been previously treated
Exclusion criteria	Women who had bilateral axillary lymph node dissection; women with only hand lymphoedema; women with erysipelas or other active skin infection; women with loco-regional cancer recurrence; women with primary or metastatic lymphoedema; women with allergy or intolerance to kinesiotape (tested by previously applying 1 cm2 of kinesiotape to the non-affected arm); women unable to adhere to interventions guidelines due to cognitive impairment and visual impairment for reading; and women who were taking medication that could cause fluid retention
Intervention(s)	Multilayer bandage: Multiple layers were applied on cleaned and dried skin. The first one was a 100% cotton tubular bandage

	directly placed on the skin to prevent any injury (Tubinylex™). The second one was a soft foam (Emulsified Latex Foam™ 8 mm, Thuasne, France) with the purpose of unify and increase pressure; and the third layer of inelastic bandages (6, 8 and/or 10 cm Rosidal K Short Stretch Bandage, Germany) was sequentially applied in a spiral method around the limb, with the smallest bandage starting at the hand and a layer overlap of 50%, so that the greatest compression was located at the distal points, gradually decreasing towards the proximal shoulder part. The inelastic bandages were applied at full stretch. Simplified multilayer bandage: Two layers were applied on cleaned and dried skin combining inelastic and elastic bandages. The first one was an inelastic (rigid) cotton bandage (11 cm Bande coton short stretch; Thuasne, France) and the second one was an elastic bandage (Biflex™ 16 light; Thuasne, France). The inelastic bandage 'contains' oedema and the elastic bandage 'compress' oedema increasing pressure at rest which limits capillary filtration and favours reabsorption due to increased tissue pressure. Both were applied in a spiral method around the limb, starting at the hand and a layer overlap of 50%, so that the greatest compression was located at the distal points, gradually decreasing towards the proximal shoulder part. The first one was applied at full stretch, and the second one at 30% stretch. Cohesive bandage: Cohesive bandage is a self-adherent lightweight bandage, made of a porous nonwoven polyester material. A single self-adherent inelastic (short stretch) bandage was directly applied at full stretch on cleaned and dried skin (10 cm 3M Coban™ Minnesota Mining and Manufacturing Co., United States) in a spiral method around the limb, starting at the hand and a layer overlap of 50%, so that the greatest compression was located at the distal points, gradually decreasing towards the proximal shoulder part. Cohesive latex-free bandages were available for those allergic women. This bandage was reused twice in the same subject. Adhesive bandage: Adhesive bandage is an inelastic bandage. An inelastic (short stretch) bandage (10 cm Biplast™ Thuasne, France) over a stretchy thin foam protection bandage (7 cm Foam protection™ Thuasne, France) was applied at full stretch on cleaned and dried skin in a spiral method around the limb, starting at the hand and a layer overlap of 50%, so that the greatest compression was located at the distal points, gradually decreasing towards the proximal shoulder part. In each physiotherapy session, the bandage had to be replaced with a new one. Kinesiotaping: Kinesio-tape is made of 100% cotton, 100% acrylic, latex-free and heat-activated and it is more elastic than the conventional rigid tape by 120% to 140%. It pulls the upper layers of the skin allowing space between the dermis and the muscles

	relieving pressure on the lymphatic and blood vessels and improving lymphatic drainage of the area. Kinesio-tape (5 cm K-Active Tape©, Japan) was applied on cleaned and dried skin. The kinesio-tape was changed every treatment session for a new one. The women were asked by the physiotherapist about continuing to wear the bandage or kinesio-tape until the next treatment session, even during the weekend (Saturday and Sunday).
Outcome measures	Lymphoedema Percentage reduction in the excess volume of the lymphoedema: To assess the volume of the limb a perimeter measurement was used. Arm perimeters were measured using a standard 1 cm wide, retractable, fiberglass tailor's tape measure (Babel, Spain). With the participant in an upright sitting position with both arms on a table, shoulders in neutral rotation and flexion of 45° and forearms at maximum supination, we measured the circumference at 5 cm intervals along both arms, using the elbow fold as the landmark starting point. To calculate the volume, we considered each segment as a truncated cone and we calculated the segmental volume of each truncated cone using the formula described for it. Total limb volume for the segment between the wrist and the upper boundary was obtained by adding the volumes of the truncated cones between these points. The severity of lymphoedema was defined as the excess lymphoedema volume relative to the healthy arm expressed in millilitre and in percentage as follows: percentage of excess volume = ((volume of lymphoedema arm − volume of healthy arm)/(volume of healthy arm)) × 100%. The volume and percentage reduction in the excess volume was obtained as follows: 100% × ((pretreatment volume of lymphoedema arm − post treatment volume of lymphoedema arm)/pretreatment excess volume). Adverse events Adverse events were documented, including their description, date of onset and their relation to the bandaging.
Number of participants	146 participants
Duration of follow-up	Post-treatment
Methods of analysis	Categorical variables were summarised with proportions and continuous variables with means and standard deviations or median and interquartile interval. The distribution was verified by the Shapiro–Wilk statistical test. To analyze the effectiveness of the excess volume, the difference of the two moments in absolute and percentage values, and the perceived bandage/kinesio-tape comfort were calculated, and the non-parametric Kruskal–Wallis H test was used to study the differences between the five

	bandage/kinesio-taping groups. Post-hoc contrasts were performed on those variables where statistically significant differences were found between the bandage/kinesio-taping groups by applying the Bonferroni correction to the level of significance. If significant differences were found, the Cuzick non-parametric test was used, which contrasted the existence of a trend with the effectiveness according to the type of bandage/kinesio-tape. Regarding the effectiveness of heaviness and tightness, the chisquare test or Fisher's exact test were used for each type of bandage/kinesio-tape. Values of <0.05 were considered significant. Regarding the effectiveness of heaviness and tightness, the chi-square test or Fisher's exact test were used for each type of bandage/kinesio-tape. Values of <0.05 were considered significant.
Additional comments	All the interventions lasted three weeks and were carried out in the intensive phase of complex decongestive physiotherapy A two-week period with each week running from Monday to Friday, followed by a week comprising three alternate days until the patient received a tailored compression garment The same physiotherapist who had more than 10 years' experience in the physiotherapy management of breast cancer related lymphoedema, including bandaging, carried out all the interventions All the women received manual lymph drainage using a modification of the strokes described by Leduc. It included resorption manoeuvre in the oedematous areas of the affected limb, in a cranial- to-caudal direction, once the physiotherapist saw a change in the tissue qualities of the oedema. Then, women received 30 minutes of five-chamber intermittent pneumatic compression (Eureduc™) with a pressure of 40 mm Hg and a therapeutic educational strategy comprising instruction about lymphatic system anatomy and pathophysiology, the prevention and identification of possible lymphoedema risk factors, complications or infection, how to protect their skin, how to use and exercise this arm, how to deal with trauma, injury, an excess of heat and arm constriction. For every session treatment, before removing the bandage or kinesio-tape, active functional exercises were encouraged for 15 minutes to improve mobility and enhance lymphatic flow.

Study arms

Multilayer bandage (N = 28)

Loss to follow-up	2 participants: Discomfort (n=1) Irregular attendance (n=1)	2 participants: Discomfort (n=1) Irregular attendance (n=1)	2 participants: Discomfort (n=1) Irregular attendance (n=1)	2 participants: Discomfort (n=1) Irregular attendance (n=1)

Simplified multilayer bandage (N = 30)

Loss to follow-up	None	None	None	None

Cohesive bandage (N = 29)

Loss to follow-up	1 participant (discomfort)	1 participant (discomfort)	1 participant (discomfort)	1 participant (discomfort)

Adhesive bandage (N = 30)

Loss to follow-up	None	None	None	None

Kinesiotaping (N = 29)

Loss to follow-up	1 participant (skin irritation)	1 participant (skin irritation)	1 participant (skin irritation)	1 participant (skin irritation)

Characteristics

Arm-level characteristics

Characteristic	Multilayer bandage (N = 28)	Simplified multilayer bandage (N = 30)	Cohesive bandage (N = 29)	Adhesive bandage (N = 30)	Kinesiotaping (N = 29)
Mean age (SD) Mean (SD)	58 (11.4)	56.2 (11.5)	58 (13.8)	59.8 (9.4)	59.6 (10.6)
BMI Mean (SD)	29.7 (5.9)	29.1 (5.8)	29.2 (5.5)	30.8 (6.3)	27 (7.6)
Type of surgery - Modified mastectomy No of events	n = 10 ; % = 36	n = 12 ; % = 40	n = 11 ; % = 38	n = 10 ; % = 33	n = 11 ; % = 38
Type of surgery - Quadrantectomy No of events	n = 10 ; % = 36	n = 10 ; % = 33	n = 9 ; % = 31	n = 10 ; % = 33	n = 10 ; % = 34
Type of surgery - Lumpectomy No of events	n = 8 ; % = 28	n = 8 ; % = 27	n = 9 ; % = 31	n = 10 ; % = 33	n = 8 ; % = 28
Adjuvant therapy - Radiotherapy No of events	n = 24 ; % = 86	n = 27 ; % = 90	n = 26 ; % = 89.65	n = 27 ; % = 90	n = 25 ; % = 86
Adjuvant therapy - Chemotherapy No of events	n = 27 ; % = 96	n = 28 ; % = 93	n = 28 ; % = 96.55	n = 29 ; % = 97	n = 27 ; % = 93

Characteristic	Multilayer bandage (N = 28)	Simplified multilayer bandage (N = 30)	Cohesive bandage (N = 29)	Adhesive bandage (N = 30)	Kinesiotaping (N = 29)
Adjuvant therapy - Hormonotherapy No of events	n = 17 ; % = 61	n = 18 ; % = 60	n = 16 ; % = 55.17	n = 17 ; % = 57	n = 15 ; % = 52
Lymphoedema stage I No of events	n = 22 ; % = 78	n = 23 ; % = 77	n = 23 ; % = 79	n = 23 ; % = 77	n = 24 ; % = 83
Lymphoedema stage II No of events	n = 6 ; % = 22	n = 7 ; % = 23	n = 6 ; % = 21	n = 7 ; % = 23	n = 5 ; % = 17
Lymphoedema severity - mild No of events	n = 7 ; % = 25	n = 6 ; % = 20	n = 7 ; % = 24	n = 7 ; % = 23	n = 7 ; % = 24
Lymphoedema severity - moderate No of events	n = 17 ; % = 61	n = 19 ; % = 66	n = 18 ; % = 62	n = 19 ; % = 63	n = 19 ; % = 66
Lymphoedema severity - severe No of events	n = 4 ; % = 14	n = 5 ; % = 14	n = 4 ; % = 14	n = 4 ; % = 14	n = 3 ; % = 10
Lymphoedema location - proximal No of events	n = 4 ; % = 14	n = 4 ; % = 13	n = 5 ; % = 17	n = 5 ; % = 17	n = 4 ; % = 14
Lymphoedema location - distal No of events	n = 11 ; % = 39	n = 12 ; % = 40	n = 11 ; % = 38	n = 11 ; % = 36	n = 12 ; % = 41
Lymphoedema location - complete No of events	n = 13 ; % = 46	n = 14 ; % = 47	n = 13 ; % = 45	n = 14 ; % = 47	n = 13 ; % = 45
Affected upper limb - dominant No of events	n = 8 ; % = 29	n = 10 ; % = 33	n = 6 ; % = 21	n = 10 ; % = 33	n = 5 ; % = 17
Affected upper limb - non-dominant No of events	n = 20 ; % = 71	n = 20 ; % = 67	n = 23 ; % = 79.31	n = 20 ; % = 67	n = 24 ; % = 83

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High *(Per protocol analysis. No information about deviations from intended interventions. No information about participants' adherence to interventions. Trial was registered but pre-specified analysis plan was not available.)*
Overall bias and Directness	Overall Directness	Directly applicable

Uzkeser, 2013

Bibliographic Reference	Uzkeser, H; Karatay, S; Intermittent pneumatic compression pump in upper extremity impairments of breast cancer-related lymphoedema ; Turkish journal of medical sciences; 2013; vol. 43 (no. 1); 99-103

Study details

Study type	Randomised controlled trial (RCT)
Study location	Erzurum, Turkey (at Atatürk University Faculty of Medicine and Erzurum Research and Training Hospital)
Study setting	Physical Medicine and Rehabilitation Department
Study dates	Not reported
Sources of funding	Not reported
Inclusion criteria	Unilateral upper extremity lymphoedema following mastectomy Lymphoedema for at least 3 months No prior physical therapy
Exclusion criteria	Bilateral lymphoedema Current metastases or ongoing radiotherapy Elephantiasis, infection, lymphangiosis, cellulitis, venous thrombosis, heart failure Medications affecting fluid/electrolyte balance
Intervention(s)	IPC combined with manual lymph drainage, compression bandages, exercises for 3 weeks
Comparator	Manual lymph drainage, compression bandages, exercises for 3 weeks (control group)
Number of participants	25 randomized (12 in IPC group, 13 in control group)

Duration of follow-up	1 month after completing 3-week treatment
Loss to follow-up	No loss to follow-up reported

Study arms
IPC combined with manual lymph drainage, compression bandages, exercises (N = 12)
3 weeks

control (N = 13)
Manual lymph drainage, compression bandages, exercises for 3 weeks (control group)

Characteristics
Study-level characteristics

Characteristic	Study (N = 25)
% Female Sample size	n = 25 ; % = 100
Mean age (SD) Custom value	not reported
Lymphoedema stage / severity Custom value	Not reported
Location of lymphoedema Custom value	Upper extremity lymphoedema following mastectomy for breast cancer

Critical appraisal - RQ2AB - RCT RoB STUDY LEVEL

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E – Forest plots

No meta-analyses of data were conducted; therefore no forest plots were produced.

Appendix F – GRADE tables

Complete decongestive therapy

Table 57 Manual lymphatic drainage vs Compression bandaging

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Tissue dielectric constant value in forearm +- MID -2.02 to 2.02 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	not serious	none	20	20	-	MD **4.61 lower** (6.48 lower to 2.74 lower)	Very low	IMPORTANT
Arm volume change (cm^3) +- MID -39 to 39 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	20	20	-	MD **2 lower** (40.18 lower to 36.18 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Liu 2023
b. Study at high risk of bias. Downgraded twice for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.

Table 58: Manual lymphatic drainage + compression bandaging + exercise vs Compression bandaging + exercise

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume (ml) +- MID -192.62 to 192.62 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **121 lower** (423.84 lower to 181.84 higher)	Low	CRITICAL
Excess arm volume (%) +- MID -7.17 to 7.17 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious [b]	not serious	serious[c]	none	25	25	-	MD **1.9 lower** (10.06 lower to 6.26 higher)	Low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Patient reported outcomes												
Arm swelling (Visual analogue scale) +- MID -1.22 to 1.22 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **1.1 lower** (2.33 lower to 0.13 higher)	Low	IMPORTANT
Discomfort (Visual analogue scale) +- MID -1.32 to 1.32 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **1.8 lower** (3.18 lower to 0.42 lower)	Low	IMPORTANT
Arm heaviness (Visual analogue scale) +- MID -1.18 to 1.18 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **1.6 lower** (2.93 lower to 0.27 lower)	Low	IMPORTANT
Arm function (Quick-DASH) +- MID -8 to 8 (follow-up: 4 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	25	25	-	MD **1.9 lower** (6.61 lower to 2.81 higher)	Moderate	IMPORTANT
Quality of life												
Quality of life-physical (Lymph-ICF) +- MID -10.67 to 10.67 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	25	25	-	MD **30.9 lower** (41.49 lower to 20.31 lower)	Moderate	IMPORTANT
Quality of life-mental (Lymph-ICF) +- MID -12.35 to 12.35 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **12.5 lower** (26.35 lower to 1.35 higher)	Low	IMPORTANT
Quality of life-household activities (Lymph-ICF) +- MID -11.33 to 11.33 (follow-up: 4 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **2.8 higher** (9.9 lower to 15.5 higher)	Low	IMPORTANT
Quality of life-mobility (Lymph-ICF) +- MID -8.2 to 8.2 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **0.8 higher** (7.04 lower to 8.64 higher)	Low	IMPORTANT
Quality of life-life and social activities (Lymph-ICF) +- MID -12.14 to 12.14 (follow-up: 4 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **5.9 lower** (18.81 lower to 7.01 higher)	Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Sen 2021.

b. Single study. Downgraded once for inconsistency.
c.. 95%CI crosses MID once. Downgraded once for imprecision.

Table 59: Fluoroscopy guided-manual lymphatic drainage vs manual lymphatic drainage

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Excess arm volume (%) +- MID -7.66 to 7.66 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	65	64	-	MD **1.6 lower** (6.84 lower to 3.64 higher)	Moderate	CRITICAL
Quality of life												
Quality of life-overall (Lymph-ICF) +- MID -9.83 to 9.83 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	65	64	-	MD **3.3 lower** (10.12 lower to 3.52 higher)	Low	IMPORTANT
Quality of life (McGill) +- MID -0.93 to 0.93 (follow-up: 6 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	65	64	-	MD **0.46 higher** (0.18 lower to 1.1 higher)	Low	IMPORTANT
Skin changes												
Trunk skin elasticity (induration force interlimb ratio) +- MID -0.21 to 0.21 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	65	64	-	MD **0.06 higher** (0.09 lower to 0.21 higher)	Low	IMPORTANT
Trunk skin thickness (interlimb ratio) +- MID -0.14 to 0.14 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	65	64	-	MD **0.01 lower** (0.11 lower to 0.09 higher)	Moderate	IMPORTANT
Arm skin elasticity (induration force interlimb ratio) +- MID -0.16 to 0.16 (follow-up: 6 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	65	64	-	MD **0.01 higher** (0.1 lower to 0.12 higher)	Moderate	IMPORTANT
Arm skin thickness (interlimb ratio) +- MID -0.20 to 0.20 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	65	64	-	MD **0.13 lower** (0.26 lower to 0)	Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a.. De Vrieze 2022
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID once. Downgraded once for imprecision.

Table 60: Self-lymphatic drainage + compression bandaging vs Compression bandaging

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume (ml) +- MID -52.87 to 52.87 (follow-up: 6 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **12.9 lower** (80.19 lower to 54.39 higher)	Very low	CRITICAL
Arm volume (ml) +- MID -51.6 to 51.6 (follow-up: 6 months)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **11.5 lower** (78.97 lower to 55.97 higher)	Very low	CRITICAL
Arm function												
Arm function (Quick-DASH) +- MID -8 to 8 (follow-up: 6 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **2.2 lower** (16.2 lower to 11.8 higher)	Very low	CRITICAL
Arm function (Quick-DASH) +- MID -8 to 8 (follow-up: 6 months)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **0.4 lower** (13.07 lower to 12.27 higher)	Very low	CRITICAL
Quality of life												
Quality of life-physical (SF-36) +- MID -5.41 to 5.41 (follow-up: 6 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **0.7 lower** (9.23 lower to 7.83 higher)	Very low	IMPORTANT
Quality of life-physical (SF-36) +- MID -6.59 to 6.59 (follow-up: 6 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[e]	none	10	14	-	MD **11.9 higher** (0.12 higher to 23.68 higher)	Very low	IMPORTANT
Quality of life-mental (SF-36) +- MID -6.22 to 6.22 (follow-up: 6 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[e]	none	10	14	-	MD **10.6 lower** (19.66 lower to 1.54 lower)	Very low	IMPORTANT
Quality of life-mental (SF-36) +- MID -5.78 to 5.78 (follow-up: 6 months)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **1.1 lower** (11.36 lower to 9.16 higher)	Very low	IMPORTANT
Patient reported outcomes												
Anxiety (HADS-A) +- MID -2.06 to 2.06 (follow-up: 6 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **0.8 higher** (2.28 lower to 3.88 higher)	Very low	IMPORTANT
Anxiety (HADS-A) +- MID -2.04 to 2.04 (follow-up: 6 months)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **0.1 lower** (2.95 lower to 2.75 higher)	Very low	IMPORTANT
Depression (HADS-D) +- MID -1.55 to 1.55 (follow-up: 6 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **0.3 higher** (3.04 lower to 3.64 higher)	Very low	IMPORTANT
Depression (HADS-D) +- MID -1.52 to 1.52 (follow-up: 6 months)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	10	14	-	MD **0.7 lower** (3.68 lower to 2.28 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Bahtiyarca 2019
b. Study at high risk of bias. Downgraded twice for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID twice. Downgraded twice for imprecision.
e. 95%CI crosses MID once. Downgraded once for imprecision.

Table 61: Compression garment vs No compression garment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Progression of lymphoedema relative volume ≥2% +- MID 0.8 to 1.25 (follow-up: 6 months)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	4/32 (12.5%)	17/37 (45.9%)	**RR 0.27** (0.10 to 0.73)	**335 fewer per 1,000** (from 414 fewer to 124 fewer)	Low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Progression of lymphoedema relative volume ≥10% +- MID 0.8 to 1.25 (follow-up: 6 months)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	very serious[d]	none	1/32 (3.1%)	4/32 (12.5%)	**RR 0.29** (0.03 to 2.46)	**89 fewer per 1,000** (from 121 fewer to 183 more)	Very low	CRITICAL
Lymphoedema relative volume (%) +- MID -1.41 to 1.41 (follow-up: 6 months)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	30	22	-	MD **3.9 lower** (5.58 lower to 2.22 lower)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference**; RR:** risk ratio

Explanations

a. Blom 2022
b. Study at moderate risk of bias. Downgraded once for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID twice. Downgraded twice for imprecision.
.

Table 62: Mobilising bandaging using Mobiderm vs Conventional multilayered bandages

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume reduction (ml) +- MID -272.77 to 272.77 (follow-up: 15 days)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	25	24	-	MD **285 lower** (591.89 lower to 21.89 higher)	Very low	CRITICAL
Patient reported outcomes												
Pain (Visual analogue scale) +- MID -1.12 to 1.12 (follow-up: 15 days)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	25	24	-	MD **1.01 lower** (2.26 lower to 0.24 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Dhar 2023
b. study at high risk of bias. Downgraded twice for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.

Table 63: Compression garment (night and day for 90 days) vs compression garment (daytime for 30 days, then night and day for 60 days)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm lymphoedema volume variation (ml) +- MID -98.39 to 98.39 (follow-up: 30 days)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	20	20	-	MD **46.2 lower** (142.74 lower to 50.34 higher)	Very low	CRITICAL
Patient reported outcomes												
Arm functional symptoms (heaviness and/or pain) +- MID 0.8 to 1.25 (follow-up: 30 days)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	3/20 (15.0%)	12/20 (60.0%)	**RR 0.25** (0.08 to 0.75)	**450 fewer per 1,000** (from 552 fewer to 150 fewer)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference**; RR:** risk ratio

Explanations

a. Mestre 2017
b. Study at moderate risk of bias. Downgraded once for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.

Table 64: Combined decongestive therapy vs Manual lymphatic drainage

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume change (cm^3) +- MID -19.4 to 19.4 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	20	20	-	MD **0.5 higher** (23.03 lower to 24.03 higher)	Very low	CRITICAL
Tissue dielectric constant value in upper arm +- MID -0.31 to 0.31 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	not serious	none	20	20	-	MD **1.57 higher** (0.8 higher to 2.34 higher)	Very low	CRITICAL
Tissue dielectric constant value in forearm +- MID -0.67 to 0.67 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[e]	none	20	20	-	MD **1.37 higher** (0.39 higher to 2.35 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Liu 2023
b. Study at high risk of bias. Downgraded twice for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.
e. 95%CI crosses MID twice. Downgraded twice for imprecision.

Table 65: Combined decongestive therapy vs Compression bandaging

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume change (cm^3) +- MID -39 to 39 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	20	20	-	MD **1.5 lower** (39.35 lower to 36.35 higher)	Very low	CRITICAL
Tissue dielectric constant value in upper arm +- MID -2.37 to 2.37 (follow-up: 2 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	20	20	-	MD **3.23 lower** (5.43 lower to 1.03 lower)	Very low	CRITICAL
Tissue dielectric constant value in forearm +- MID -2.02 to 2.02 (follow-up: 2 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	20	20	-	MD **3.24 lower** (5.17 lower to 1.31 lower)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Liu 2023
b. Study at high risk of bias. Downgraded twice for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.

Table 66: Negative pressure massage treatment vs Manual lymphatic drainage

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
L-Dex score (bioelectrical impedance ratio of unaffected to affected limb) +- MID -2.25 to 2.25 (follow-up: 5 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	very serious[d]	none	15	13	-	MD **7.28 lower** (11.85 lower to 2.71 lower)	Very low	CRITICAL
Interlimb volume difference (ml) +- MID -37.05 to 37.05 (follow-up: 5 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[e]	none	15	13	-	MD **78.53 lower** (147.09 lower to 9.97 lower)	Very low	CRITICAL
Shoulder, arm function												
DASH score change +-MID -7 to 7 (follow-up: 5 weeks)												
1[a]	randomised trials	very serious[b]	serious[c]	not serious	Serious[e]	none	15	13	-	MD **2.63 lower** (9.62 lower to 4.36 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Lampinen 2021
b. Study at high risk of bias. Downgraded twice for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID twice. Downgraded twice for imprecision.
e. 95%CI crosses MID once. Downgraded once for imprecision.

Table 67: Manual lymphatic drainage vs control

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume (ml) +- MID -0.5 to 0.5 (follow-up: range 1 months to 3 months)												
7[a]	randomised trials	serious[e]	not serious	not serious	not serious	none	188	182	-	SMD **0 SD** (0.2 lower to 0.21 higher)	Moderate	CRITICAL
Patient reported outcomes												
Pain (visual analogue scale) +- MID -0.5 to 0.5 (follow-up: 1 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
3[b]	randomised trials	serious[e]	not serious	not serious	serious[c]	none	89	84	-	SMD **0.72 SD lower** (1.34 lower to 0.09 lower)	Low	IMPORTANT
Quality of life												
Quality of life (range of QoL tools used) +- MID -0.5 to 0.5 (follow-up: range 1 months to 3 months)												
4[d]	randomised trials	serious[e]	not serious	not serious	serious[c]	none	114	109	-	SMD **0.26 SD higher** (0.01 lower to 0.52 higher)	Low	IMPORTANT

CI: confidence interval; **MID:** minimal important difference; **SD:** standard deviation; **SMD:** standardised mean difference

Explanations

a. Lin 2022 [Andersen 2000, Cho 2016, Gol 2020, Gradalski 2015, McNeely 2004, Sen 2020, Tambour 2018]
b. Lin 2022 [Cho 2016, Gol 2020, Tambour 2018]
c. 95%CI crosses MID once. Downgraded once for imprecision.
d. Lin 2022 [Cho 2016, Gradalski 2015, Sen 2020, Tambour 2018]
e. More than 33% of studies at moderate risk of bias. Downgraded once for risk of bias

Table 68: Manual lymphatic drainage vs control

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Upper limb volume change by number of manual lymphatic drainage (<20 sessions) +-MID 0.5 (follow-up: range 24 days to 7 months												
5[b]	randomised trials	serious[c]	not serious	not serious	serious[a]	none	125	119	-	SMD **0.82 SD higher** (0.17 lower to 1.82 higher)	Low	CRITICAL
Upper limb volume change by number of manual lymphatic drainage (>20 sessions) +-MID 0.5 (follow-up: range 24 days to 7 months)												
3[d]	randomised trials	serious[c]	not serious	not serious	serious[a]	none	111	102	-	SMD **0.31 SD higher** (0.03 higher to 0.58 higher)	Low	CRITICAL
Upper limb volume change by number of manual lymphatic drainage (<2 weeks treatment) +-MID 0.5 (follow-up: range 24 days to 7 months)												
3[e]	randomised trials	serious[c]	not serious	not serious	serious[a]	none	58	52	-	SMD **2.03 SD higher** (0.39 lower to 4.44 higher)	Low	CRITICAL
Upper limb volume change by number of manual lymphatic drainage (>2 weeks treatment) +-MID 0.5 (follow-up: range 24 days to 7 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	complete decongestive therapy	usual care/control	Relative (95% CI)	Absolute (95% CI)		
5[f]	randomised trials	serious[c]	not serious	not serious	not serious	none	178	169	-	SMD **0.23 SD higher** (0.02 higher to 0.44 higher)	Moderate	CRITICAL
Patient reported outcomes												
Pain (visual analogue scale) +- MID -0.5 to 0.5 (follow-up: range 24 days to 7 months)												
2[g]	randomised trials	serious[c]	not serious	not serious	not serious	none	67	66	-	SMD **0.09 SD lower** (0.43 lower to 0.25 higher)	Moderate	IMPORTANT

CI: confidence interval; **MID:** minimal important difference; **SD:** standard deviation; **SMD:** standardised mean difference

Explanations

a. 95% CI crosses MID once. Downgraded once for imprecision.
b. Qiao 2023 [Andersen 2000, Bermann 2014, Johansson 1999, Sitzia 2002, Tambour 2018]
c. More than 33% of studies at moderate risk of bias. Downgraded once for risk of bias.
d. Qiao 2023 [Dayes 2013, McNeely 2004, Williams 2002]
e. Qiao 2023 [Andersen 2000, Johansson 1999, Sitzia 2002]
f. Qiao 2023 [Bergmann 2014. Dayes 2013, McNeely 2004, Tambour 2018, Williams 2002]
g. Qiao 2023 [Bergmann 2014, Tambour 2018]

Exercise and movement

Table 69: Resistance exercise vs standard care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema (limb volume)												
Lymphoedema volume change +-MID 0.5												
3[d]	randomised trials	very serious[h]	not serious	not serious	not serious	none	NR	NR	-	SMD **0.01 SD higher** (0.48 lower to 0.5 higher)	Low	CRITICAL
Lymphoedema (arm function)												
Shoulder function DASH score +-MID 0.5												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[e]	randomised trials	very serious[h]	serious[b]	not serious	very serious[c]	none			-	SMD **2.49 SD higher** (1.79 higher to 3.19 higher)	Very low	CRITICAL
Quality of life												
Quality of life FACTB+4 +-MID 0.5												
1[f]	randomised trials	very serious[h]	serious[b]	not serious	serious[a]	none			-	SMD **0.31 SD higher** (0.23 lower to 0.86 higher)	Very low	IMPORTANT
Patient-reported outcomes (pain)												
Pain - BDI +-MID 0.5												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[f]	randomised trials	very serious[h]	serious[b]	not serious	serious[a]	none			-	SMD **1 SD higher** (1.57 lower to 0.43 lower)	Very low	IMPORTANT
Symptom severity scale +-MID 0.5												
1[g]	randomised trials	very serious[h]	serious[b]	not serious	serious[a]	none			-	SMD **0.38 SD lower** (0.72 lower to 0.05 lower)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations
a. 95%CI crosses MID once. Downgraded once for imprecision.
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID twice. Downgraded twice for imprecision.
d. Lytvyn 2020 [Cormie 2013, Jeffs &Wiseman 2013, Schmitz 2009]
e. Lytvyn 2020 [Cormie 2013]
f. Lytvyn 2020 [Cormie 2013]

g. Lytvyn 2020 [Schmitz 2009]
h. More than 33% of studies at high risk of bias

Table 70: Aerobic + resistance exercise vs standard care/CDT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
[Aerobic + resistance exercise vs standard care, Lytvyn 2020] Lymphoedema volume change +-MID 0.5												
3[d]	randomised trials	very serious[g]	not serious	not serious	serious[a]	none			-	SMD **0.19 SD higher** (0.34 lower to 0.72 higher)	Very low	CRITICAL
Shoulder function												
Shoulder abduction DASH scores +-MID 0.5												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[e]	randomised trials	very serious[g]	serious[b]	not serious	very serious[c]	none			-	SMD **1.87 SD higher** (1.27 higher to 2.46 higher)	Very low	CRITICAL
Patient reported outcomes												
Pain VAS +-MID 0.5												
1[e]	randomised trials	very serious[g]	serious[b]	not serious	very serious[c]	none			-	SMD **2.02 SD lower** (2.63 lower to 1.41 lower)	Very low	IMPORTANT
Lymphoedema swelling and symptoms (self-report score) +-MID 0.5												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[f]	randomised trials	very serious[g]	serious[b]	not serious	serious[a]	none			-	SMD **0.38 SD lower** (0.72 lower to 0.06 lower)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations
a. 95%CI crosses MID once. Downgraded once for imprecision.
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID twice. Downgraded twice for imprecision.
d. Lytvyn 2020 [Hayes 2009, McKenzie & Kalda 2003, Schmitz 2019]
e. Lytvyn 2020 [Park 2017]
f. Lytvyn 2020 [Schmitz 2019]
g. More than 33% of studies at high risk of bias

Table 71: Water-based and yoga exercise vs standard care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema (limb volume)												
Lymphoedema volume change +-MID 0.5												
5[d]	randomised trials	very serious[j]	not serious	not serious	serious[a]	none			-	SMD **0.29 SD lower** (0.77 lower to 0.19 higher)	Very low	CRITICAL
Lymphoedema (arm function)												
Shoulder function DASH score +-MID 0.5												
4[e]	randomised trials	very serious[j]	not serious	not serious	serious[a]	none			-	SMD **0.18 SD higher** (0.39 lower to 0.74 higher)	Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of life EORTC-QLQ-C30/BDI/FACTB/LYMQOL +-MID 0.5												
4[f]	randomised trials	very serious[j]	not serious	not serious	serious[a]	none			-	SMD **0.21 SD higher** (0.42 lower to 0.84 higher)	Very low	IMPORTANT
Patient-reported outcomes												
Pain - EORTC-QLQ-C30/VAS/MPQ +-MID 0.5												
3[g]	randomised trials	very serious[j]	not serious	not serious	serious[a]	none			-	SMD **0.58 SD lower** (1.07 lower to 0.09 lower)	Very low	IMPORTANT
Fatigue EORTC-QLQ-C30/VAS +-MID 0.5												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
2[h]	randomised trials	very serious[j]	not serious	not serious	not serious	none			-	SMD **0.39 SD lower** (0.099 lower to 0.2 higher)	Moderate	IMPORTANT
Sensations - VAS +-MID 0.5												
1[i]	randomised trials	very serious[j]	serious[b]	not serious	very serious[c]	none			-	SMD **0.07 SD lower** (0.88 lower to 0.75 higher)	Very low	IMPORTANT

a. 95%CI crosses MID once. Downgraded once for imprecision.
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID twice. Downgraded twice for imprecision.
d. Lytvyn 2020 [Johansson 2013, Letellier 2014; Loudon, 2014; McClure 2010, Pasyar et al., 2019]
e. Lytvyn 2020 [Johansson 2013, Letellier 2014, Loudon 2014, McClure 2010]
f. Lytvyn 2020 [Letellier 2014; Loudon, 2014; McClure 2010, Pasyar et al., 2019]
g. Lytvyn 2020 [Letellier 2014; Loudon, 2014, Pasyar et al., 2019]
h. Lytvyn 2020 [Loudon, 2014, Pasyar et al., 2019]
i. Lytvyn 2020 [Loudon, 2014 2019]
j. More than 33% of studies at high risk of bias

Table 72: CDT + resistance exercise vs standard care/CDT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Shoulder function												
Shoulder abduction DASH score +-MID 0.5												
2[d]	randomised trials	very serious[f]	not serious	not serious	serious[a]	none			-	SMD **0.33 SD lower** (0.75 lower to 0.1 higher)	Very low	CRITICAL
Quality of life												
Quality of life EORTC-QLQ-C30 +-MID 0.5												
1[e]	randomised trials	very serious[f]	serious[b]	not serious	very serious[c]	none			-	SMD **0.03 SD higher** (0.56 lower to 0.62 higher)	Very low	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Patient reported outcomes												
[CDT vs CDT + resistance exercise, Lytvyn 2020] Pain EORTC-QLQ-C30 +-MID 0.5												
1[e]	randomised trials	very serious[f]	serious[b]	not serious	very serious[c]	none			-	SMD **0.05 SD higher** (0.54 lower to 0.65 higher)	Very low	IMPORTANT
[CDT vs CDT + resistance exercise, Lytvyn 2020] Fatigue EORTC-QLQ-C30 +-MID 0.5												
1[e]	randomised trials	very serious[f]	not serious	not serious	serious[a]	none			-	SMD **0.13 SD higher** (0.46 lower to 0.72 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations
a. 95%CI crosses MID once. Downgraded once for imprecision.
b. Single study. Downgraded once for inconsistency.

c. 95%CI crosses MID twice. Downgraded twice for imprecision.
d. Lytvyn 2020 [Do 2015, Luz 2018]
e. Lytvyn [Do 2015]
f. More than 33% of studies at high risk of bias

Table 73 CDT + compression pump + resistance exercise vs CDT + compression pump

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of life EORTC-QLQ-C30 +-MID 0.5												
1[c]	randomised trials	not serious	serious[b]	not serious	serious[a]	none			-	SMD **0.27 SD higher** (0.35 lower to 0.89 higher)	Low	IMPORTANT
Patient reported outcomes												
Fatigue EORTC-QLQ-C30 +-MID 0.5												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[c]	randomised trials	not serious	not serious	not serious	serious[a]	none			-	SMD **0.53 SD lower** (1.17 lower to 0.1 higher)	Moderate	IMPORTANT
Pain EORTC-QLQ-C30 +-MID 0.5												
1[c]	randomised trials	not serious	serious[b]	not serious	serious[a]	none			-	SMD **0.21 SD lower** (0.83 lower to 0.41 higher)	Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations
a. 95%CI crosses MID once. Downgraded once for imprecision.
b. Single study. Downgraded once for inconsistency.
c. Lytvyn 2020 [Do 2017]

Table 74 Complex physical therapy vs multimodal approaches

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Reducing total volume of upper limb (immediate) +- MID 0.5 SD (follow-up: 1 months)												
1[d]	randomised trials	very serious[a]	serious[c]	not serious	serious[b]	none	30	30	-	SMD **0.12 SD lower** (0.62 higher to 0.39 higher)	Very low	CRITICAL
Reducing total volume of upper limb (short term) +-MID 0.5 (follow-up: range 1 months to 3 months)												
7[e]	randomised trials	very serious[a]	not serious	not serious	not serious	none	30	30	-	SMD **0.2 SD lower** (0.44 lower to 0.04 higher)	Low	CRITICAL
Reducing total volume of upper limb (long term) +-MID 0.5 (follow-up: range 6 months to 12 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
2[f]	randomised trials	very serious[a]	not serious	not serious	not serious	none	30	30	-	SMD **0.15 SD lower** (0.5 lower to 0.21 higher)	Low	CRITICAL
Patient reported outcomes												
Pain reduction of upper limb (immediate) +-MID 0.5 (follow-up: 1 months)												
4[g]	randomised trials	very serious[a]	not serious	not serious	not serious	none	129	130	-	SMD **0.1 SD higher** (0.17 lower to 0.37 higher)	Low	IMPORTANT
Pain reduction of upper limb (short term) +-MID 0.5 (follow-up: range 1 months to 3 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
7[h]	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	260	257	-	SMD **0.61 SD lower** (1.19 lower to 0.02 lower)	Very low	IMPORTANT
Pain reduction of upper limb (long term) +-MID 0.5 (follow-up: range 6 months to 12 months)												
1[i]	randomised trials	serious[a]	serious[c]	not serious	serious[b]	none	38	35	-	SMD **0.33 SD lower** (0.79 lower to 0.13 higher)	Very low	IMPORTANT
Physical function of upper limb (immediate) +-MID 0.5 (follow-up: 1 months)												
1[j]	randomised trials	very serious[a]	serious[b]	not serious	serious[b]	none	55	35	-	SMD **0.14 SD higher** (0.28 lower to 0.57 higher)	Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Physical function of upper limb (short term) +-MID 0.5 (follow-up: range 1 months to 3 months)												
4[k]	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	221	188	-	SMD **0.67 SD lower** (1.6 lower to 0.26 higher)	Very low	CRITICAL
Physical function of upper limb (long term) +-MID 0.5 (follow-up: range 6 months to 12 months)												
1[j]	randomised trials	very serious[a]	not serious	not serious	not serious	none	91	62	-	SMD **0.1 SD lower** (0.42 lower to 0.23 higher)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations
a. More than 33% of studies at high risk of bias. Downgraded twice for risk of bias.
b. 95%CI crosses MID once. Downgraded once for imprecision.
c. Single study. Downgraded once for inconsistency.
d. Rangon 2022 [Gradalski 2015]
e. Rangon 2022 [Burgadda 2015, Dayes 2013, Didem 2015, Ergin 2019, Gradalski 2015, Kim 2010, Tambour 2018]

f. Rangon 2022 [Gradalski 2015, Tambour 2018]
g. Rangon 2022 [Bergmann 2014, Haghigat 2010, Pekyavas 2014, Uzkeser 2015]
h. Rangon 2022[Burgadda 2015, Gradalski 2015, Haghigat 2010, Pekyavas 2014, Tambour 2018, Tastaban 2020. Uzkeser 2015]
i. Rangon 2022 [Tambour 2018]
j. Rangon 2022 [Dayes, 2013]
k. Rangon 2022 [Burgadda 2015, Dayes 2013, Do 2015, Tastaban 2020]

Table 75 Aquatic therapy vs standard care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm lymphoedema relative volume [(vol. affected arm - vol. control arm) x 100/vol. control arm]+- MID -0.5 to 0.5 (follow-up: 3 months)												
2[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	26	40	-	SMD **0.14 SD higher** (0.37 lower to 0.64 higher)	Low	CRITICAL
Arm function												
[Aqua lymphatic therapy vs Standard care, Yeung 2018] Arm physical function (range of tools used) +- MID -0.5 to 0.5 (follow-up: 3 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
2[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	26	40	-	SMD **0.27 SD lower** (0.78 lower to 0.23 higher)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations
a. Yeung 2018 [Letellier 2014, Tidhar 2010]
b. More than 33% of studies at moderate risk of bias. Downgraded once for risk of bias.
c. 95%CI crosses MID once. Downgraded once for imprecision.

Table 76: Aqua therapy exercise vs land-based exercise

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Arm volume (ml) +- MID -108.03 to 108.03 (follow-up: 8 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	25	25	-	MD **160.36 lower** (284.32 lower to 36.4 lower)	Low	CRITICAL
Range of motion												
Shoulder flexion (standard goniometry) +- MID -2.90 to 2.90 (follow-up: 8 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	25	25	-	MD **22.2 higher** (19.19 higher to 25.21 higher)	Moderate	CRITICAL
Shoulder abduction (standard goniometry) +- MID -2.19 to 2.19 (follow-up: 8 weeks)												
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	25	25	-	MD **19.8 higher** (17.58 higher to 22.02 higher)	Moderate	CRITICAL
Patient reported outcomes												
Pain (Visual analogue scale) +- MID -1.3 to 1.3 (follow-up: 8 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[a]	randomised trials	not serious	serious[b]	not serious	not serious	none	25	25	-	MD **2.32 lower** (2.83 lower to 1.81 lower)	Moderate	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Ali 2021
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID once. Downgraded once for imprecision.

Table 77: Continuous passive motion + complete decongestive therapy vs Complete decongestive therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume (ml) +- MID -459.08 to 459.08 (follow-up: 15 days)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[c]	randomised trials	serious[a]	serious[b]	not serious	very serious[d]	none	14	16	-	MD **62.81 lower** (658.21 lower to 532.59 higher)	Very low	CRITICAL
Range of motion												
Shoulder flexion (standard goniometry) +- MID -10.26 to 10.26 (follow-up: 15 days)												
1[c]	randomised trials	serious[a]	serious[b]	not serious	very serious[d]	none	14	16	-	MD **2.29 higher** (19.43 lower to 24.01 higher)	Very low	CRITICAL
Shoulder abduction (standard goniometry) +- MID -14.23 to 14.23 (follow-up: 15 days)												
1[c]	randomised trials	serious[a]	serious[b]	not serious	very serious[d]	none	14	16	-	MD **4.91 higher** (19.89 lower to 29.71 higher)	Very low	CRITICAL
Shoulder internal rotation (standard goniometry) +- MID -6.71 to 6.71 (follow-up: 15 days)												
1[c]	randomised trials	serious[a]	serious[b]	not serious	very serious[d]	none	14	16	-	MD **1.08 higher** (8 lower to 10.16 higher)	Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Shoulder external rotation (standard goniometry) +- MID -6.63 to 6.63 (follow-up: 15 days)												
1[c]	randomised trials	serious[a]	serious[b]	not serious	very serious[d]	none	14	16	-	MD **0.63 higher** (7.61 lower to 8.87 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Study at moderate risk of bias. Downgraded once for risk of bias.
b. Single study. Downgraded once for inconsistency.
c. Kizil 2018
d. 95%CI crosses MID twice. Downgraded twice for imprecision.

Table 78: Pilates vs Exercise + self-care education

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Arm function												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Grip strength (kg) +- MID -3.05 to 3.05 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **1.1 higher** (2.08 lower to 4.28 higher)	Very low	CRITICAL
Range of motion												
Shoulder flexion (standard goniometry) +- MID -6.13 to 6.13 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **9.01 higher** (0.54 higher to 17.48 higher)	Very low	CRITICAL
Shoulder abduction (standard goniometry) +- MID -11.36 to 11.36 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **11.84 higher** (2.39 lower to 26.07 higher)	Very low	CRITICAL
Shoulder external rotation (standard goniometry) +- MID -6.70 to 6.70 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **7.66 higher** (1.29 lower to 16.61 higher)	Very low	CRITICAL
Patient reported outcomes												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Body image (SAA score) +- MID -4.32 to 4.32 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **3.76 lower** (7.72 lower to 0.2 higher)	Very low	IMPORTANT
Arm Function												
Arm function (DASH score) +- MID -7 to 7 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **3.58 lower** (10.51 lower to 3.35 higher)	Very low	CRITICAL
Quality of life												
Quality of life (QLQ-BR23) +- MID -4.38 to 4.38 (follow-up: 8 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **1.8 higher** (2.82 lower to 6.42 higher)	Very low	IMPORTANT
Patient reported outcomes												
Pain (Visual analogue scale) +- MID -1.3 to 1.3 (follow-up: 8 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[d]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	30	30	-	MD **1.37 lower** (2.82 lower to 0.08 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Study at moderate risk of bias. Downgraded once for risk of bias.
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID once. Downgraded once for imprecision.
d. Sener 2017

Table 79: Exercise vs No exercise advice

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Adverse events												
Adverse events (musculoskeletal) +- MID 0.8 to 1.25 (follow-up: 12 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
1[d]	randomised trials	serious[a]	serious[b]	not serious	very serious[c]	none	2/40 (5.0%)	0/44 (0.0%)	**RR 5.49** (0.27 to 110.97)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	Very low	IMPORTANT
Arm function												
Arm strength (chest press, kg) +- MID -2 to 2 (follow-up: 12 weeks)												
1[d]	randomised trials	serious[a]	serious[b]	not serious	not serious	none	40	44	-	MD **4.1 higher** (2.41 higher to 5.79 higher)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference**; RR:** risk ratio

Explanations

a. Study at moderate risk of bias. Downgraded once for risk of bias.
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID twice. Downgraded twice for imprecision.
d. Kilbreath 2020

Table 80: Progressive resistance exercise vs Self-directed resistance exercise

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	exercise and movement	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Oedema volume (cm) +- MID -481.8 to 481.8												
1[e]	randomised trials	serious[a]	serious[b]	not serious	very serious[d]	none	8	8	-	MD **34.41 lower** (826.65 lower to 757.83 higher)	Very low	CRITICAL
Arm function												
Grip strength (kg) +- MID -2.05 to 2.05												
1[e]	randomised trials	serious[a]	serious[b]	not serious	serious[c]	none	8	8	-	MD **5.55 higher** (1.74 higher to 9.36 higher)	Very low	CRITICAL
K-DASH +- MID -7.35 to 7.35												
1[e]	randomised trials	serious[a]	serious[b]	not serious	not serious	none	8	8	-	MD **23.71 lower** (38.1 lower to 9.32 lower)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Study at moderate risk of bias. Downgraded once for risk of bias.
b. Single study. Downgraded once for inconsistency.
c. 95%CI crosses MID once. Downgraded once for imprecision.
d. 95%CI crosses MID twice. Downgraded twice for imprecision.
e. Park 2023

Skincare

No evidence was identified that met the criteria in the protocol for skincare interventions for managing breast cancer-related lymphoedema.

Lymphoedema education

Table 81: Education on lymphatic self-drainage and lifestyle recommendations vs Usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	lymphoedema education	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Excess arm volume [(vol. affected arm - vol. control arm) x 100/vol. control arm] +- MID -5.27 to 5.27 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	20	21	-	MD **6 lower** (14.34 lower to 2.34 higher)	Low	CRITICAL
Excess hand volume [(vol. affected hand - vol. control hand) x 100/vol. control hand] +- MID -7.09 to 7.09 (follow-up: 6 months)												
1[a]	randomised trials	not serious	serious[b]	not serious	serious[c]	none	20	21	-	MD **10 lower** (17.89 lower to 2.11 lower)	Low	CRITICAL
Patient reported outcomes												
Pain (NPRS) +- MID -1.54 to 1.54 (follow-up: 6 months)												
1[a]	randomised trials	serious[d]	serious[b]	not serious	serious[c]	none	20	21	-	MD **2.2 lower** (3.93 lower to 0.47 lower)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference; **NPRS:** numeric pain rating scale

Explanations

a. Ligabue 2019
b. Single study. Downgraded once for inconsistency,
c. 95%CI crosses MID once. Downgraded once for imprecision.
d. Study at moderate risk of bias. Downgraded once for risk of bias.

Table 82: Group education vs Control

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	lymphoedema education	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of life-psychosocial (LLIS) +- MID -0.15 to 0.15 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	32	35	-	MD **0.03 lower** (0.16 lower to 0.1 higher)	Very low	IMPORTANT
Quality of life-functional (LLIS) +- MID -0.14 to 0.14 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	32	35	-	MD **0.13 lower** (0.25 lower to 0.01 lower)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Single study. Downgraded once for inconsistency,

b. 95% CI crosses MID once. Downgraded once for imprecision.
c. Omidi 2020
d. Study at high risk of bias. Downgraded twice for risk of bias.

Table 83: Social network-based education vs Control

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	lymphoedema education	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of life-psychosocial (LLIS) +- MID -0.15 to 0.15 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	34	35	-	MD **0.05 higher** (0.08 lower to 0.18 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Single study. Downgraded once for inconsistency,
b. 95%CI crosses MID once. Downgraded once for imprecision.
c. Omidi 2020
d. Study at high risk of bias. Downgraded twice for risk of bias.

Table 84: Group education vs Social network-based education

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	lymphoedema education	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of life-psychosocial (LLIS) +- MID -0.13 to 0.13 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	32	34	-	MD **0.08 lower** (0.19 lower to 0.03 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Single study. Downgraded once for inconsistency,
b. 95%CI crosses MID once. Downgraded once for imprecision.
c. Omidi 2020
d. Study at high risk of bias. Downgraded twice for risk of bias.

Pneumatic compression devices

Table 85: Novel non-pneumatic compression device vs Traditional advanced pneumatic compression device

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pneumatic compression devices	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm oedema volume (%) +- MID -34.97 to 34.97 (follow-up: 28 days)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	23	27	-	MD **36.9 higher** (3.26 lower to 77.06 higher)	Very low	CRITICAL
Quality of life												
Quality of life (LYMQOL) +- MID -0.90 to 0.90 (follow-up: 28 days)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	23	27	-	MD **2.45 higher** (1.48 higher to 3.42 higher)	Low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Rockson 2022

b. Study at moderate risk of bias. Downgraded once for risk of bias.
c. Single study. Downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.

Table 86: Intermittent pneumatic compression + compression bandage vs Manual lymphatic drainage + compression bandage

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pneumatic compression devices	usual care	Relative (95% CI)	Absolute (95% CI)		
Range of motion												
Shoulder abduction (standard goniometry) +- MID -10.57 to 10.57 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	very serious[e]	none	22	24	-	MD **0.38 lower** (11.7 lower to 10.94 higher)	Very low	CRITICAL
Shoulder adduction (standard goniometry) +- MID -3.71 to 3.71 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	22	24	-	MD **1.85 lower** (5.91 lower to 2.21 higher)	Very low	CRITICAL
Shoulder flexion (standard goniometry) +- MID -9.96 to 9.96 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	22	24	-	MD **1.88 higher** (9.56 lower to 13.32 higher)	Very low	CRITICAL
Shoulder extension (standard goniometry) +- MID -4.75 to 4.75 (follow-up: 3 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pneumatic compression devices	usual care	Relative (95% CI)	Absolute (95% CI)		
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	22	24	-	MD **2.8 lower** (6.97 lower to 1.37 higher)	Very low	CRITICAL
Shoulder internal rotation (standard goniometry) +- MID -4.57 to 4.57 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	22	24	-	MD **1.12 lower** (5.21 lower to 2.97 higher)	Very low	CRITICAL
Shoulder external rotation (standard goniometry) +- MID -8.1 to 8.1 (follow-up: 3 months)												
1[c]	randomised trials	very serious[d]	serious[a]	not serious	serious[b]	none	22	24	-	MD **2.93 higher** (5.08 lower to 10.94 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Single study. Downgraded once for inconsistency.
b. 95%CI crosses MID once. Downgraded once for imprecision.
c. Sanal-Toprak 2018
d. Study at high risk of bias. Downgraded twice for risk of bias.
e. 95%CI crosses MID twice. Downgraded twice for imprecision.

Complementary therapy

Table 87: Moxibustion vs pneumatic circulation

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	acupuncture or moxibustion	any other treatment	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Mean arm circumference (assessed with: the average value of wrist crease, 10 cm proximal to the wrist crease, elbow crease, and 10 cm proximal to the elbow crease; cm) MID +-0.8												
2[a]	randomised trials	serious[b]	very serious[c]	not serious	very serious[d]	none	38	38	-	MD **0.66 cm lower** (2.63 lower to 1.31 higher)	Very low	CRITICAL
Circumference at wrist crease (cm) MID +-0.55												
2[e]	randomised trials	serious[b]	very serious[c]	not serious	very serious[d]	none	48	48	-	MD **0.2 cm lower** (1.25 lower to 0.85 higher)	Very low	CRITICAL
Circumference at proximal 10cm of wrist crease (cm) MID +-1.2												
2[e]	randomised trials	serious[b]	very serious[c]	not serious	very serious[d]	none	48	48	-	MD **0.17 cm lower** (2.13 lower to 1.78 higher)	Very low	CRITICAL
Circumference at proximal 10cm of elbow crease (cm) MID +-1.3												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	acupuncture or moxibustion	any other treatment	Relative (95% CI)	Absolute (95% CI)		
2[e]	randomised trials	very serious[b]	very serious[c]	not serious	very serious[d]	none	48	48	-	MD **0.48 cm lower** (5.07 lower to 4.12 higher)	Very low	CRITICAL
Circumference at elbow crease (cm) MID +-1.4												
2[e]	randomised trials	very serious[b]	very serious[c]	not serious	very serious[d]	none	48	48	-	MD **0.24 cm lower** (3.44 lower to 2.96 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference**;**
Explanations
a. Gao 2021 [Wang 2019, Zhang 2020]
b. More than 33% of studies at high risk of bias. Downgraded twice for risk of bias.
c. Downgraded twice as I^2 greater than 60%
d. Downgraded twice as crosses both MID
e. Gao 2021 [Shen 2019, Wang 2019]

Table 88: Acupuncture + moxibustion vs usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	acupuncture or moxibustion	any other treatment	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Circumference at elbow crease (cm) MID +-1.4												
2[b]	randomised trials	very serious[a]	not serious	not serious	not serious	none	61	61	-	MD **7.26 cm lower** (8.3 lower to 6.21 lower)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. More than 33% of studies at high risk of bias. Downgraded twice for risk of bias.

b. Gao 2021 [Zhao 2012, Jiao 2017]

Table 89: Acupuncture + moxibustion vs diosmin

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	acupuncture or moxibustion	any other treatment	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Effective index for upper limb lymphoedema (upper limb arm circumference before treatment−upper limb arm circumference after treatment/upper limb circumference of the affected arm before treatment−upper limb circumference of the unaffected arm before treatment; %) MID +-4												
2[b]	randomised trials	very serious[a]	not serious	not serious	not serious	none	45	45	-	MD **27.68 cm higher** (24.82 higher to 30.53 higher)	Low	CRITICAL

CI: confidence interval; **MD:** mean difference**; MID:** minimal important difference

Explanations
a. More than 33% of studies at high risk of bias. Downgraded twice for risk of bias.
b. Gao 2021 [Yao 2016, Liu 2019]

Psychological interventions

No evidence was identified that met the criteria in the protocol for psychological interventions for managing breast cancer-related lymphoedema.

Kinesiotaping

Table 90: Kinesiotaping vs Complete decongestive therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm circumference (cm) MID +/- 2.1 (follow-up: 1 months)												
1[c]	randomised trials	not serious	serious[a]	not serious	serious[b]	none	18	18	-	MD **1.3 higher** (0.81 higher to 3.41 higher)	Low	CRITICAL
Arm volume (ml) MID +/- 53.95 (follow-up: 1 months)												
1[c]	randomised trials	not serious	serious[a]	not serious	serious[b]	none	18	18	-	MD **1.58 lower** (213.14 higher to 103.46 lower)	Low	CRITICAL
Arm function												
Grip strength (kg) MID +/- 0.75 (follow-up: 1 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
1[c]	randomised trials	not serious	serious[a]	not serious	serious[b]	none	18	18	-	MD **0.4 lower** (1.15 lower to 0.35 higher)	Low	CRITICAL
Arm and shoulder function DASH scores MID +/- 2.85 (follow-up: 1 months)												
1[c]	randomised trials	not serious	serious[a]	not serious	very serious[d]	none	18	18	-	MD **2.1 lower** (8.05 lower to 3.85 higher)	Very low	CRITICAL
Quality of life												
Quality of Life FACT-B scores MID +/- 7 to 8 (follow-up: 1 months)												
1[c]	randomised trials	not serious	serious[a]	not serious	not serious	none	18	18	-	MD **1.8 lower** (6.66 lower to 3.06 higher)	Moderate	CRITICAL

1 **CI:** confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Single study. Study downgraded once for inconsistency.
b. 95%CI crosses MID once. Downgraded once for imprecision.
c. Basoglu 2021
d. 95%CI crosses MID twice. Downgraded twice for imprecision.

Table 91: Kinesiotaping vs Compression garment

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
Range of motion												
Shoulder abduction (standard goniometry) MID +/- 9.13 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	very serious[c]	none	16	19	-	MD **1.18 lower** (15.36 lower to 13 higher)	Very low	CRITICAL
Shoulder adduction (standard goniometry) MID +/- 3.51 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	serious[b]	none	16	19	-	MD **1.15 higher** (2.49 lower to 4.81 higher)	Low	CRITICAL
Shoulder flexion (standard goniometry) MID +/- 7.64 (follow-up: 3 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
1[d]	randomised trials	not serious	serious[a]	not serious	very serious[c]	none	16	19	-	MD **4.06 higher** (9.19 lower to 17.29 higher)	Very low	CRITICAL
Shoulder extension (standard goniometry) MID +/- 2.93 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	very serious[c]	none	16	19	-	MD **0.33 lower** (4.6 lower to 3.94 higher)	Very low	CRITICAL
Shoulder internal rotation (standard goniometry) MID +/- 7.04 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	serious[b]	none	16	19	-	MD **5.62 higher** (3.27 lower to 14.51 higher)	Low	CRITICAL
Shoulder external rotation (standard goniometry) MID +/- 2.85 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	very serious[c]	none	16	19	-	MD **1.54 higher** (5.49 lower to 8.57 higher)	Very low	CRITICAL
Patient reported outcomes												
Pain VAS MID +/- 0.57 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	very serious[c]	none	16	19	-	MD **0.23 higher** (0.61 lower to 1.07 higher)	Very low	IMPORTANT
Tightness VAS MID +/- 0.59 (follow-up: 3 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
1[d]	randomised trials	not serious	serious[a]	not serious	very serious[c]	none	16	19	-	MD **0.25 lower** (1.1 lower to 0.6 higher)	Very low	IMPORTANT
Heaviness VAS MID +/- 0.56 (follow-up: 3 months)												
1[d]	randomised trials	not serious	serious[a]	not serious	serious[b]	none	16	19	-	MD **0.25 lower** (0.49 lower to 0.6 higher)	Low	IMPORTANT
Lymphoedema												
Limb circumference (cm) MID +/- 8.06 (follow-up: 3 weeks)												
1[e]	randomised trials	serious[f]	serious[a]	not serious	serious[b]	none	30	29	-	MD **15.2 lower** (22.78 lower to 7.62 lower)	Very low	CRITICAL
Arm function												
Disability SPADI scores MID +/- 34.21 (follow-up: 3 weeks)												
1[e]	randomised trials	serious[f]	serious[a]	not serious	not serious	none	30	29	-	MD **82.19 lower** (107.33 lower to 57.05 lower)	Low	CRITICAL
Handgrip strength (kg) MID +/- 2.82 (follow-up: 3 weeks)												
1[e]	randomised trials	serious[f]	serious[a]	not serious	not serious	none	30	29	-	MD **21.25 higher** (14.87 higher to 27.63 higher)	Low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of Life EORTC-QLQC30 MID – 8 to 12 (follow-up: 3 weeks)												
1[e]	randomised trials	serious[f]	serious[a]	not serious	serious[b]	none	30	29	-	MD **10.6 higher** (2.39 higher to 18.81 higher)	Very low	IMPORTANT

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations
a. Single study. Study downgraded once for inconsistency.
b. 95%CI crosses MID once. Downgraded once for imprecision.
c. 95%CI crosses MID twice. Downgraded twice for imprecision.
d. Ozsoy-Unbol 2019
e. Tantawy 2019
f. Selective reporting of outcomes. Downgraded once for risk of bias.

Table 92: Kinesiotaping vs Manual lymphatic drainage

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Arm volume [(vol. affected arm - vol. control arm) x 100/vol. control arm] MID+/- 5.34 (follow-up: 3 months)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	15	15	-	MD **2.1 lower** (8.63 lower to 4.43 higher)	Very low	CRITICAL
Quality of life												
Quality of life scores LYMQoL MID+/- 3.85 (follow-up: 3 months)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	15	15	-	MD **3.97 lower** (11.26 lower to 3.32 higher)	Very low	IMPORTANT
Arm function												
Arm function Q-DASH MID+/- 8 (follow-up: 3 months)												
1[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	15	15	-	MD **8.13 lower** (22.84 lower to 6.58 higher)	Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference

Explanations

a. Selcuk-Yilmaz 2023
b. Imbalance in baseline characteristics. Study downgraded once for risk of bias.
c. Single study. Study downgraded once for inconsistency.
d. 95%CI crosses MID once. Downgraded once for imprecision.

Table 93: Kinesiotaping vs control

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	kinesiotaping	usual care	Relative (95% CI)	Absolute (95% CI)		
Lymphoedema												
Lymphoedema reduction* +-MID 0.5 (follow-up: range 4 weeks to 3 months)												
6[a]	randomised trials	serious[b]	not serious	not serious	not serious	none	96	100	-	SMD **0.04 SD higher** (0.24 lower to 0.33 higher)	Moderate	CRITICAL
Lymphoedema reduction* +- MID 0.5 (follow-up: range 4 weeks to 3 months)												
6[c]	randomised trials	serious[b]	not serious	not serious	not serious	none	96	103	-	SMD **0.12 SD higher** (0.16 lower to 0.41 higher)	Moderate	CRITICAL

* Note: The 2 meta-analyses are based on the same set of 6 studies. Three of the studies in the meta-analysis each had 3 treatment groups (2 of which were types of control), so 2 analyses were done to investigate the effect of including different types of control in the meta-analysis. See footnotes a and c for a description of which comparisons were examined in each meta-analysis.

CI: confidence interval; **MID:** minimal important difference**; SD:** standard deviation; **SMD:** standardised mean difference

Explanations
a. Kasawara 2018 [Malicka 2014, Melgaard 2016, Pekyavas 2014 (CDT + KT vs CDT + bandage), Smykla (KT vs quasi-KT) 2013, Taradaj 2016 (KT vs quasi-KT), Tsai 2009]
b. Nire than 33% of studies at moderate risk of bias. Downgraded once for risk of bias.
c. Kasawara 2018 [Malicka 2014, Melgaard 2016, Pekyavas 2014 (CDT + KT vs CDT + bandage + KT), Smykla (KT vs multilayered compression) 2013, Taradaj 2016 (KT vs bandage), Tsai 2009]

Wired vs non-wired bras, foam inserts, spaghetti foam

No evidence was identified that met the criteria in the protocol for bras, foam inserts or spaghetti foam for managing breast cancer-related lymphoedema.

Surgical interventions

Table 94: Lymphaticovenous anastomosis vs Complete decongestive therapy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	surgery	usual care	Relative (95% CI)	Absolute (95% CI)		
Quality of life												
Quality of life scores - Lymph-ICF +-MID - 9.1 to 9.1 (follow-up: 6 months)												
1[b]	randomised trials	not serious	serious[c]	not serious	serious[a]	none	46	46	-	MD **5.92 lower** (14.31 lower to 2.47 higher)	Low	IMPORTANT
Lymphoedema												
Volume reduction (ml) +-MID -94.99 to 94.99 (follow-up: 6)												
1[b]	randomised trials	not serious	serious[c]	not serious	not serious	none	46	46	-	MD **13.94 lower** (92.2 lower to 65.02 higher)	Moderate	CRITICAL
Limb circumference (upper extremity lymphoedema index) +-MID - 7.3 to 7.3 (follow-up: 6 months)												
1[b]	randomised trials	not serious	serious[c]	not serious	serious[a]	none	46	46	-	MD **2.68 SD higher** (3.29 lower to 8.65 higher)	Low	CRITICAL
Adverse events												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	surgery	usual care	Relative (95% CI)	Absolute (95% CI)		
Adverse events MID +/- 0.8 to 1.25 (follow-up: 6 months)												
1[b]	randomised trials	not serious	serious[c]	not serious	serious[a]	none	3/46 (6.5%)	5/46 (10.9%)	**RR 0.60** (0.15 to 2.37)	**43 fewer per 1,000** (from 92 fewer to 149 more)	Low	IMPORTANT
Serious Adverse events MID +/- 0.8 to 1.25 (follow-up: 6 months)												
1[b]	randomised trials	not serious	serious[c]	not serious	very serious[d]	none	1/46 (2.2%)	0/46 (0.0%)	**RR 3.07** (0.12 to 77.24)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	Very low	IMPORTANT

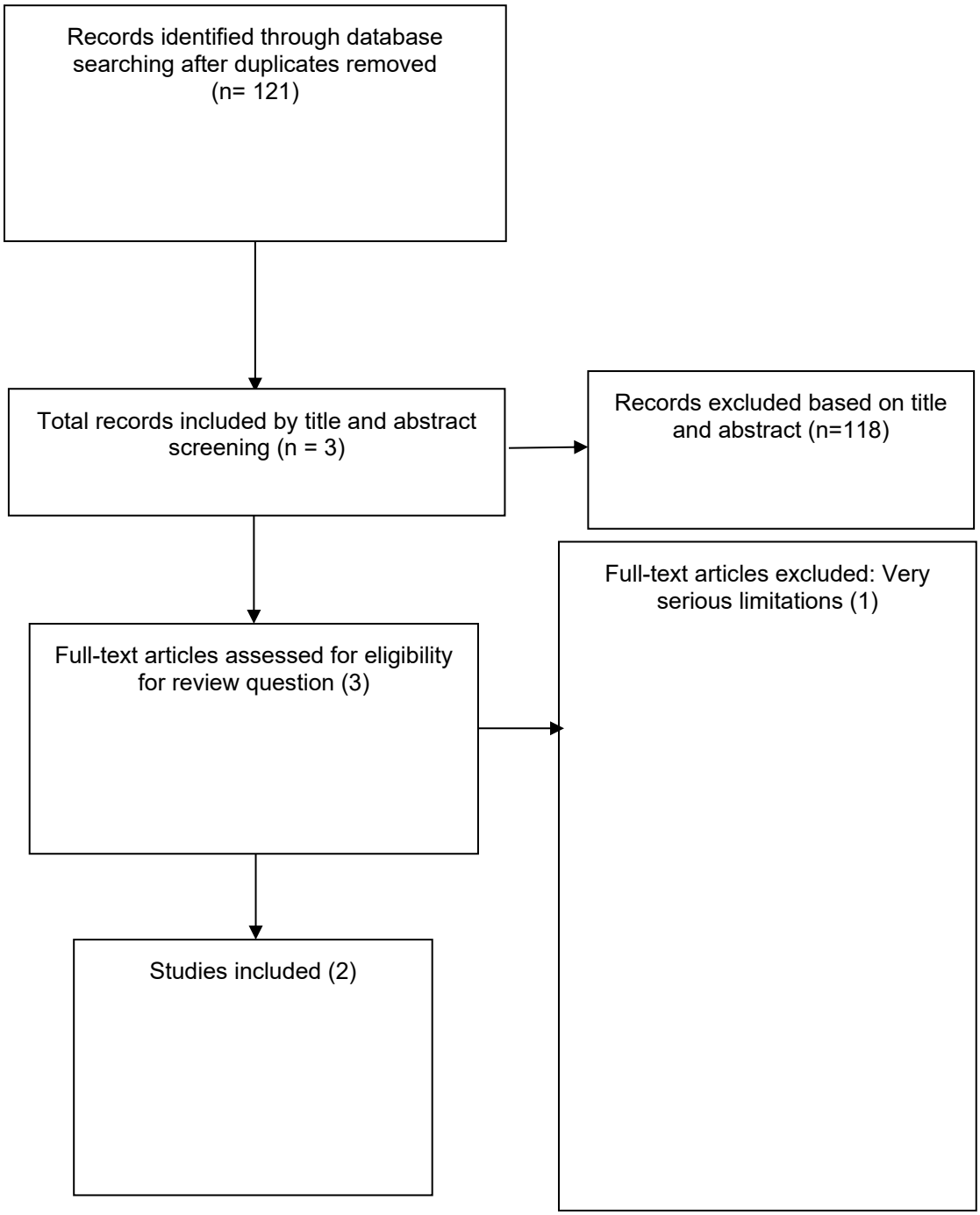
CI: confidence interval; **MD:** mean difference; **MID:** minimal important difference**; RR:** risk ratio

Explanations

a. 95%CI crosses MID once. Downgraded once for imprecision.
b. Jonis 2024
c. Single study. Study downgraded once for inconsistency.
d. 95%CI crosses MID twice. Downgraded twice for imprecision.

1

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

Study	Head, Momtazi (2019) Economics of Lymphovenous Bypass. Plastic and reconstructive surgery; 2019; vol. 144 (no. 5); 751e-759e			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
Economic analysis: Cost-comparison analysis (health outcome: none) **Study design:** Decision tree **Approach to analysis:** A Decision tree with 3 arms was used to estimate the costs associated with three strategies to manage lymphoedema. Lifetime costs were attached to each end node assuming a life expectancy of 15 years. The expected net present value for lymphovenous bypass was calculated using probabilities of no longer requiring complete decongestive therapy for each arm, provided by a meta-analysis (Basta 2014). **Perspective:** Canadian public healthcare provider and private health insurance **Time horizon:** 15 years **Discounting:** Costs: 5%	**Population:** People with stage II breast cancer-related lymphoedema **Cohort settings:** Start age: NR Male: NR **Interventions** 1. Complete decongestive therapy (CDT) 2. Lymphaticovenous Anastomosis bypass	**Total costs (mean per patient):** 1: £16,772 2: £14,786 Incremental (2-1): -£1,986 **Currency & cost year:** 2018/2019 Canadian dollars presented here as 2018/2019 UK pounds **Cost components incorporated:** Lymphoedema therapist session, compressive bandaging, daytime and night-time compression garments, perioperative and operative costs of microsurgery	NA participant, and total costs were then calculated	**Cost-effectiveness:** Lymphaticovenous Anastomosis bypass is cost-saving compared to CDT, due to reductions in requirement for CDT after surgery **Analysis of uncertainty:** Several one-way sensitivity and threshold analyses were conducted. In those, life expectancy, the number of lymphovenous bypass anastomoses and the likelihood of no longer requiring ongoing decongestive therapy after surgery were varied. Only in 37% of the simulated scenario complete decongestive therapy was cheaper than surgery. A probabilistic sensitivity was not conducted.
Data sources				

Study	Head, Momtazi (2019) Economics of Lymphovenous Bypass. Plastic and reconstructive surgery; 2019; vol. 144 (no. 5); 751e-759e			
Study details	**Population & interventions**	**Costs**	**Outcomes**	**Cost effectiveness**
Health outcomes: None. **Quality-of-life weights:** NA. **Cost sources:** Price lists for lymphoedema therapy were retrieved from professionals available in Ottawa (Ontario, Canada). Cost of compression bandaging and garments was retrieved from Ontario Medical Supply and CertiCare Medical Garments. Price lists for microsurgery were retrieved from the procurement office at The Ottawa Hospital. Surgical and anaesthesia professional fees were retrieved from the provincial physician fee schedule.				
Comments				
Source of funding: NR **Limitations:** The decision tree is simple but unable to capture events that occur over time, including adverse events of lymphoedema (skin and soft-tissue infections that could lead to hospitalisation). Therefore the analysis is expected to underestimate the real burden of lymphoedema. Discontinuation of decongestive therapy is assumed to either occur or not occur immediately after the surgery: this is a simplification as, in reality, this is a continuous process that may take time to occur even if the surgery is successful. Some important outcomes are not included in the analysis: adverse events of surgery, adverse events of lymphoedema and recurrence after surgery. The treatment effect is based on a meta-analysis (Basta 2014) that includes a few studies on congenital non-cancer-related lymphoedema. A probabilistic sensitivity analysis was not conducted. **Other:** Some costs borne by the individual or private insurance are included, as decongestive therapy and physiotherapy are not provided by Canadian public healthcare system.				
Overall applicability				
Partially applicable (Table 95)				
Overall quality				
Potentially serious limitations (Table 96)				

1

Study	Melgaard, Dorte (2016) What is the effect of treating secondary lymphoedema after breast cancer with complete decongestive physiotherapy when the bandage is replaced with Kinesio Textape? - A pilot study.; Physiotherapy theory and practice; 2016; vol. 32 (no. 6); 446-451			
Study details	**Population & interventions**	**Costs**	**Outcomes[(a)]**	**Cost effectiveness**
Economic analysis: Cost-consequence analysis (health outcomes: measurements of lymphoedema circumference) **Study design:** Within-trial analysis **Approach to analysis:**	**Population:** People with stage II breast cancer-related lymphoedema **Cohort settings:** Mean age: 62.5 (7.6) Female: 100%	**Total costs (mean per patient):** 1: £943 2: £385 Incremental (2-1): -£558 **Currency & cost year:**	**Metacorpophalangial joints (before-after reduction)** 1: 0.3 (-0.04 to 0.64) 2: 0.5 (0.06 to 0.94) Incremental (2-1): 0.2	**Cost-effectiveness:** CDT with Kinesio Textape is cost-saving compared to CDT with low-stretch bandages. **Analysis of uncertainty:** No sensitivity analysis was conducted.

Study	Melgaard, Dorte (2016) What is the effect of treating secondary lymphoedema after breast cancer with complete decongestive physiotherapy when the bandage is replaced with Kinesio Textape? - A pilot study.; Physiotherapy theory and practice; 2016; vol. 32 (no. 6); 446-451			
Study details	**Population & interventions**	**Costs**	**Outcomes[(a)]**	**Cost effectiveness**
A pilot randomised controlled trial was designed to compare clinical outcomes of Kinesio Textape compared with CDP. Costs of the two therapies were estimated and compared alongside the other outcomes. **Perspective:** Danish public healthcare system **Time horizon:** 4 weeks **Discounting:** NA	**Interventions** 1. Complete decongestive therapy (CDT) with low-stretch bandages 2. Complete decongestive therapy (CDT) with Kinesio Textape	2015/2016 Euros presented here as 2015/2016 UK pounds **Cost components Incorporated:** Lymphoedema therapist session, compressive bandaging, daytime and night-time compression garments, perioperative and operative costs of microsurgery	**Wrist (before-after reduction)** 1: 0.3 (-0.04 to 0.64) 2: 0.2 (-0.56 to 1.04) Incremental (2-1): -0.1 **Wrist + 8 cm (before-after reduction)** 1: 0.8 (-0.69 to 2.23) 2: -0.2 (-0.91 to 0.51) Incremental (2-1): -1 **Wrist + 15 cm (before-after reduction)** 1: 1.2 (-0.18 to 2.62) 2: -0.4 (-1.21 to 0.41) Incremental (2-1): -1.6 **Elbow (before-after reduction)** 1: 1.1 (-0.24 to 2.44) 2: 1 (-0.16 to 2.16) Incremental (2-1): -0.1 **Elbow + 10 cm (before-after reduction)** 1: 0.2 (-1.22 to 1.63)	

Study	Melgaard, Dorte (2016) What is the effect of treating secondary lymphoedema after breast cancer with complete decongestive physiotherapy when the bandage is replaced with Kinesio Textape? - A pilot study.; Physiotherapy theory and practice; 2016; vol. 32 (no. 6); 446-451			
Study details	**Population & interventions**	**Costs**	**Outcomes[(a)]**	**Cost effectiveness**
			2: 1.2 (0.07 to 2.32) Incremental (2-1): 1 **Deltoideus (before-after reduction)** 1: -0.1 (-1.29 to 1.09) 2: 0.9 (-1.17 to 2.98) Incremental (2-1): 1	
Data sources				
Health outcomes: Different measurements of lymphoedema circumference. **Quality-of-life weights:** NA. **Cost sources:** Not reported.				
Comments				
Source of funding: NR **Limitations:** The study has an extremely small sample size (10 people) that makes it very difficult to interpret difference in health outcomes. The sources of unit costs are not specified. The intervention is cost-saving by design: the authors assumed that people would need fewer physiotherapy sessions with Kinesio tape. This is not consistent with other studies on KT where prototol changed from 3 times a week for 3 weeks (9 sessions) (Pop et al., 2014) up to 5 times a week for 4 weeks (20 sessions) (Tsai et al., 2009, Kasawara 2018). The time horizon is too short to capture medium- or long-term outcomes **Other:**				
Overall applicability				
Partially applicable (Table 95)				
Overall quality				
Potentially serious limitations (Table 96)				

a) Only statistically significant different outcomes are reported

Table 95: Applicability checklist

Study	1.1 Is the study population appropriate for the review question?	1.2 Are the interventions appropriate for the review question?	1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?	1.4 Is the perspective for costs appropriate for the review question?	1.5 Is the perspective for outcomes appropriate for the review question?	1.6 Are all future costs and outcomes discounted appropriately?	1.7 Are QALYs derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome?	1.8 Overall judgement
Linden 2019	Yes	Yes	Partly (Canadian healthcare payer)	Yes	Yes	Partly – 5% discounting rate used	No – Cost only analysis. Measures of quality of life were not included.	Partially applicable
Melgaard 2016	Yes	Yes	Partly (Denmark)	Yes	Yes	NA – time horizon shorter than 1 year	No – cost only analysis. Measures of quality of life were not included.	Partially applicable

Table 96: Limitations checklist

Study	2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	2.3 Are all important and relevant outcomes included?	2.4 Are the estimates of baseline outcomes from the best available source?	2.5 Are the estimates of relative intervention effects from the best available source?	2.6 Are all important and relevant costs included?	2.7 Are the estimates of resource use from the best available source?	2.8 Are the unit costs of resources from the best available source?	2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	2.11 Has no potential financial conflict of interest been declared?	2.12 Overall assessment
Linden 2019	Partly – Decision tree model. Simple but unable to capture events that can occur over time such as adverse events of lymphoedema like skin and soft-tissue infections that can lead to hospital admission. Likewise, the discontinuation of decongestive therapy is treated as a binary variable (either occurs, or not occurs after surgery) whereas in reality, patients would need to receive therapy for a while before discontinuing.	Yes – 15 years	Partly – Missing outcomes: adverse events of surgery, adverse events of lymphoedema (including hospitalisations and infections), recurrence after surgery	Partly – Based on Basta 2014, a meta-analysis on a majority of studies on oncologic lymphoedema but including congenital	Partly – Based on Basta 2014, a meta-analysis on a majority of studies on oncologic lymphoedema but including congenital	Partly – Due to missing outcomes	Yes	Partly – Canadian healthcare service	No	Partly – Scenario analysis conducted but no PSA	Yes	Potentially serious limitations

Study	2.1 Does the model structure adequately reflect the nature of the topic under evaluation?	2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	2.3 Are all important and relevant outcomes included?	2.4 Are the estimates of baseline outcomes from the best available source?	2.5 Are the estimates of relative intervention effects from the best available source?	2.6 Are all important and relevant costs included?	2.7 Are the estimates of resource use from the best available source?	2.8 Are the unit costs of resources from the best available source?	2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?	2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	2.11 Has no potential financial conflict of interest been declared?	2.12 Overall assessment
Melgaard 2016	NA - Within trial analysis	Partly – 4 weeks to short to capture long-term outcomes	Partly – no medium- or long-term outcomes	Partly – within trial analysis (10 people)	Partly – within trial analysis (10 people)	Yes – cost of healthcare staff and consumables	Partly – designed by the authors	Unclear	Yes	No	Yes	Potentially serious limitations

1

Appendix J – Excluded studies

Randomised Controlled Trials

Study	Reason for exclusion
Abdelhalim, N.M. and Samhan, A.F. (2018) Comparison of extracorporeal shock waves therapy versus intermittent pneumatic compression therapy in breast cancer-related lymphoedema . International Journal of Cancer Research 14(2): 77-85	- Study does not contain a relevant intervention
Ammitzboll, Gunn, Hyldegaard, Ole, Forchhammer, Martin et al. (2023) Effects of an early intervention with Hyperbaric Oxygen Treatment on arm lymphoedema and quality of life after breast cancer-an explorative clinical trial. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 31(5): 313	- Study does not contain a relevant intervention
Argenbright, CA; Taylor-Piliae, RE; Loescher, LJ (2016) Bowenwork for symptom management of women breast cancer survivors with lymphoedema : A pilot study. Complementary Therapies in Clinical Practice 25: 142-9	- Not a relevant study design
Arinaga, Yoko, Piller, Neil, Sato, Fumiko et al. (2019) The 10-Min Holistic Self-Care for Patients with Breast Cancer-Related Lymphoedema: Pilot Randomized Controlled Study. The Tohoku journal of experimental medicine 247(2): 139-147	- Data not reported in an extractable format
Atef, Doaa, Elkeblawy, Mohmed Maher, El-Sebaie, Ashraf et al. (2020) A quasi-randomized clinical trial: virtual reality versus proprioceptive neuromuscular facilitation for postmastectomy lymphoedema . Journal of the Egyptian National Cancer Institute 32(1): 29	- Not a relevant study design
Aykac Cebicci, M and Dizdar, M (2021) A comparison of the effectiveness of complex decongestive therapy and extracorporeal shock wave therapy in the treatment of lymphoedema secondary to breast cancer. Indian journal of surgery 83(3): 749-753	- Study does not contain a relevant intervention
Bao, Ting, Iris Zhi, Wanqing, Vertosick, Emily A et al. (2018) Acupuncture for breast cancer-	- Study used as primary study in included systematic review

Study	Reason for exclusion
related lymphoedema : a randomized controlled trial. Breast cancer research and treatment 170(1): 77-87	*Used in Gao 2021*
Basha, Maged A, Aboelnour, Nancy H, Alsharidah, Ashwag S et al. (2022) Effect of exercise mode on physical function and quality of life in breast cancer-related lymphoedema : a randomized trial. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 30(3): 2101-2110	- Study does not contain a relevant intervention *Gaming / tech*
Bergmann, A, da Costa Leite Ferreira, M G, de Aguiar, S S et al. (2014) Physiotherapy in upper limb lymphoedema after breast cancer treatment: a randomized study. Lymphology 47(2): 82-91	- Not a relevant study design *Follow up timepoints dependent on treatment effect*
Bloomquist, Kira, Adamsen, Lis, Hayes, Sandra C et al. (2019) Heavy-load resistance exercise during chemotherapy in physically inactive breast cancer survivors at risk for lymphoedema : a randomized trial. Acta oncologica (Stockholm, Sweden) 58(12): 1667-1675	- Does not contain a population of people with lymphoedema
Bloomquist, Kira, Krustrup, Peter, Fristrup, Bjorn et al. (2021) Effects of football fitness training on lymphoedema and upper-extremity function in women after treatment for breast cancer: a randomized trial. Acta oncologica (Stockholm, Sweden) 60(3): 392-400	- Does not contain a population of people with lymphoedema *Contains people at risk of lymphoedema*
Bok, Soo-Kyung; Jeon, Yumi; Hwang, Pyoung-sik (2016) Ultrasonographic Evaluation of the Effects of Progressive Resistive Exercise in Breast Cancer-Related Lymphoedema. Lymphatic research and biology 14(1): 18-24	- Data not reported in an extractable format
Brown, Justin C and Schmitz, Kathryn H (2015) Weight Lifting and Physical Function Among Survivors of Breast Cancer: A Post Hoc Analysis of a Randomized Controlled Trial. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 33(19): 2184-9	- Data not reported in an extractable format
Brown, Justin C and Schmitz, Kathryn H (2015) Weight lifting and appendicular skeletal muscle mass among breast cancer survivors: a	- Data not reported in an extractable format

Study	Reason for exclusion
randomized controlled trial. Breast cancer research and treatment 151(2): 385-92	
Buragadda, S., Alhusaini, A.A., Melam, G.R. et al. (2015) Effect of complete decongestive therapy and a home program for patients with post mastectomy lymphoedema . Journal of Physical Therapy Science 27(9): 2743-2748	- Study used as primary study in included systematic review *Used in Rangon 2022*
Cai, HM, Wang, W, Wang, WJ et al. (2021) Kinesiology taping combined with manual lymph drainage reduces postoperative lymphoedema related to breast cancer. Chinese journal of tissue engineering research 25(14): 2247-2251	- Study not reported in English
Cho, Ho Soon Michelle, Davis, Gail C, Paek, Jae Eun et al. (2013) A randomised trial of nursing interventions supporting recovery of the postmastectomy patient. Journal of clinical nursing 22(78): 919-29	- Not a relevant study design
Collins, S., Bradley, N., Fitzgibbon, S. et al. (2018) Kinesiology taping for breast lymphoedema after breast cancer treatment: A feasibility randomised controlled trial. Physiotherapy Practice and Research 39(2): 107-116	- Insufficient information in the methods and results *Data not extractable .*
Cormie, Prue, Galvao, Daniel A, Spry, Nigel et al. (2013) Neither heavy nor light load resistance exercise acutely exacerbates lymphoedema in breast cancer survivor. Integrative cancer therapies 12(5): 423-32	- Data not reported in an extractable format *Small participant numbers, no pre-washout data reported*
Da Cuna-Carrera, Iria, Soto-Gonzalez, Mercedes, Abalo-Nunez, Rocio et al. (2024) Is the Absence of Manual Lymphatic Drainage-Based Treatment in Lymphoedema after Breast Cancer Harmful? A Randomized Crossover Study. Journal of clinical medicine 13(2)	- Data not reported in an extractable format
Dayes, Ian S, Whelan, Tim J, Julian, Jim A et al. (2013) Randomized trial of decongestive lymphatic therapy for the treatment of lymphoedema in women with breast cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 31(30): 3758-63	- Study used as primary study in included systematic review *Included in Jeffs 2022 and Qiao 2023*

Study	Reason for exclusion
De Groef, An, Van Kampen, Marijke, Verlvoesem, Nele et al. (2017) Effect of myofascial techniques for treatment of upper limb dysfunctions in breast cancer survivors: randomized controlled trial. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 25(7): 2119-2127	- Data not reported in an extractable format *Difficult to extract data for lymphoedema population*
Deacon, Rosalind, de Noronha, Marcos, Shanley, Leah et al. (2019) Does the speed of aquatic therapy exercise alter arm volume in women with breast cancer related lymphoedema? A cross-over randomized controlled trial. Brazilian journal of physical therapy 23(2): 140-147	- Data not reported in an extractable format
Dionyssiou, Dimitrios, Demiri, Efterpi, Tsimponis, Antonis et al. (2016) A randomized control study of treating secondary stage II breast cancer-related lymphoedema with free lymph node transfer. Breast cancer research and treatment 156(1): 73-9	- Study used as primary study in included systematic review *Used in Winters 2021*
Do, J H, Kim, W, Cho, Y K et al. (2015) EFFECTS OF RESISTANCE EXERCISES AND COMPLEX DECONGESTIVE THERAPY ON ARM FUNCTION AND MUSCULAR STRENGTH IN BREAST CANCER RELATED LYMPHOEDEMA. Lymphology 48(4): 184-96	- Study used as primary study in included systematic review *Used in Rangon 2022*
Esteban-Simon, A, Diez-Fernandez, DM, Rodriguez-Perez, MA et al. (2023) Does a resistance training program affect between-arms volume difference and shoulder-arm disabilities in female breast cancer survivors? The role of surgery type and treatments. Archives of physical medicine and rehabilitation	- Does not contain a population of people with lymphoedema
Esteban-Simon, Alba, Diez-Fernandez, David M, Rodriguez-Perez, Manuel A et al. (2023) Does a Resistance Training Program Affect Between-arms Volume Difference and Shoulder-arm Disabilities in Female Breast Cancer Survivors? The Role of Surgery Type and Treatments. Secondary Outcomes of the EFICAN Trial. Archives of physical medicine and rehabilitation	- Does not contain a population of people with lymphoedema

Study	Reason for exclusion
Fisher, MI, Donahoe-Fillmore, B, Leach, L et al. (2014) Effects of yoga on arm volume among women with breast cancer related lymphoedema : A pilot study. Journal of Bodywork and Movement Therapies 18(4): 559-65	- Not a relevant study design
Forner-Cordero, Isabel, Munoz-Langa, Jose, DeMiguel-Jimeno, Juan Maria et al. (2021) Physical therapies in the decongestive treatment of lymphoedema : A randomized, non-inferiority controlled study. Clinical rehabilitation 35(12): 1743-1756	- Data not reported in an extractable format *Study reports on upper limb, and lower limb lymphoedema no separate data on upper limb lymphoedema*
Friedman, Rosie, Johnson, Anna Rose, Shillue, Kathy et al. (2023) Acupuncture Treatment for Breast Cancer-Related Lymphoedema: A Randomized Pilot Study. Lymphatic research and biology 21(5): 488-494	- Not a relevant study design *Feasibility study - doesn't compare between trial arms; only reports means for LYMQOL no SD*
Fu, Mei Rosemary, Axelrod, Deborah, Guth, Amber A et al. (2022) A Web- and Mobile-Based Intervention for Women Treated for Breast Cancer to Manage Chronic Pain and Symptoms Related to Lymphoedema: Results of a Randomized Clinical Trial. JMIR cancer 8(1): e29485	- Does not contain a population of people with lymphoedema
Fu, Mei Rosemary, Du, Xinwen, Li, Yuan et al. (2023) Data on the effects of The-Optimal-Lymph-Flow program on lymphoedema symptoms in breast cancer survivors. Data in brief 48: 109278	- Study does not contain a relevant intervention
Guloren, Gulbala, Dogan, Yahya, Ozgul, Serap et al. (2023) Acute Effects of Remedial Exercises with and without Compression on Breast-Cancer-Related Lymphoedema. Healthcare (Basel, Switzerland) 11(22)	- Data not reported in an extractable format
Ha, K and Choi, S (2014) The effect of a PNF technique program after mastectomy on lymphoedema patients' depression and anxiety. Journal of Physical Therapy Science 26(7): 1065-7	- Not a relevant study design
Ha, Kyung-Jin, Lee, Sang-Yeol, Lee, Hojun et al. (2017) Synergistic Effects of Proprioceptive Neuromuscular Facilitation and Manual	- Study used as primary study in included systematic review *Used in Lin 2022*

Study	Reason for exclusion
Lymphatic Drainage in Patients with Mastectomy-Related Lymphoedema. Frontiers in physiology 8: 959	
Hansdorfer-Korzon, R., Teodorczyk, J., Gruszecka, A. et al. (2016) Relevance of low-pressure compression corsets in physiotherapeutic treatment of patients after mastectomy and lymphadenectomy. Patient Preference and Adherence 10: 1177-1187	- Does not contain a population of people with lymphoedema *Unclear which population had lymphoedema and were not at risk of lymphoedema.*
Hayes, SC, Rye, S, Disipio, T et al. (2013) Exercise for health: a randomized, controlled trial evaluating the impact of a pragmatic, translational exercise intervention on the quality of life, function and treatment-related side effects following breast cancer. Breast cancer research and treatment 137(1): 175-186	- Study used as primary study in included systematic review *Used in Yeung 2018*
Hemmati, Mahboobeh, Rojhani-Shirazi, Zahra, Zakeri, Zeinab Sadat et al. (2022) The effect of the combined use of complex decongestive therapy with electrotherapy modalities for the treatment of breast cancer-related lymphoedema : a randomized clinical trial. BMC musculoskeletal disorders 23(1): 837	- Study does not contain a relevant intervention *Faradic/ultrasound currently experimental therapies. Small participant numbers n=13 per each arm (n=39 total)*
Hughes, D, Hoffman, M, Gonzaba, J et al. (2021) Feasibility and Efficacy Exercises in Women With Lymphoedema Post Breast Cancer - A Pilot Study. Archives of Physical Medicine and Rehabilitation 102(10)	- Not a relevant study design
Jeffs, E and Wiseman, T (2013) Randomised controlled trial to determine the benefit of daily home-based exercise in addition to self-care in the management of breast cancer-related lymphoedema: a feasibility study. Supportive care in cancer 21(4): 1013-1023	- Data not reported in an extractable format
Jeong, Young Ju, Kwon, Hyo Jung, Park, Young Sun et al. (2015) Treatment of Lymphoedema with Saam Acupuncture in Patients with Breast Cancer: A Pilot Study. Medical acupuncture 27(3): 206-215	- Not a relevant study design
Johansson, K, Hayes, S, Speck, RM et al. (2013) Water-based exercise for patients with chronic arm lymphoedema : a randomized	- Study used as primary study in included systematic review *Used in Yeung 2018*

Study	Reason for exclusion
controlled pilot trial. American journal of physical medicine & rehabilitation 92(4): 312-319	
Johansson, K, Klernäs, P, Weibull, A et al. (2014) A home-based weight lifting program for patients with arm lymphoedema following breast cancer treatment: a pilot and feasibility study. Lymphology 47(2): 51-64	- Not a relevant study design
Johansson, Karin, Blom, Katarina, Nilsson-Wikmar, Lena et al. (2023) Early Intervention with a Compression Sleeve in Mild Breast Cancer-Related Arm Lymphoedema: A 12-Month Prospective Observational Study. Cancers 15(10)	- Not a relevant study design
Kheirkhah, M; Haghighat, S; Omidi, Z (2021) Comparing the effect of in-person and virtual lymphoedema self-management education on quality of life of women with breast cancer: a randomized clinical trial. Iranian journal of breast diseases 13(4): 8-22	- Study not reported in English
Kim, Yena; Park, Eun Y; Lee, Haneul (2023) The effect of myofascial release in patients with breast cancer-related lymphoedema : a cross-over randomized controlled trial. European journal of physical and rehabilitation medicine 59(1): 85-93	- Not a relevant study design *Cross-over trial that does not report results for each phase of the trial separately*
Koelmeyer, Louise A, Moloney, Emma, Boyages, John et al. (2021) Prospective surveillance model in the home for breast cancer-related lymphoedema: a feasibility study. Breast cancer research and treatment 185(2): 401-412	- Comparator in study does not match that specified in protocol
Letellier, M, Towers, A, Shimony, A et al. (2014) Breast Cancer-Related Lymphoedema. American journal of physical medicine & rehabilitation 93(9): 751-763	- Study used as primary study in included systematic review *Used in Yeung 2018*
Letellier, Marie-Eve, Towers, Anna, Shimony, Avi et al. (2014) Breast cancer-related lymphoedema : a randomized controlled pilot and feasibility study. American journal of physical medicine & rehabilitation 93(9): 751-1	- Study does not contain a relevant intervention
Li, Xiaonan, Fu, Haimei, Li, Panpan et al. (2022) Nano Carbon Tracing-based Treatment of	- Study does not contain a relevant intervention

Study	Reason for exclusion
Breast Cancer Lymphadenectomy and Nursing Intervention of Postoperative Lymphoedema. Cellular and molecular biology (Noisy-le-Grand, France) 68(3): 304-313	
Lin, Yawei, Wu, Chao, He, Chunyan et al. (2022) Effectiveness of three exercise programs and intensive follow-up in improving quality of life, pain, and lymphoedema among breast cancer survivors: a randomized, controlled 6-month trial. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 31(1): 9	- Does not contain a population of people with lymphoedema *Study indirectly looked at effect of exercise on lymphoedema incidence, did not contain population with lymphoedema/at risk of lymphoedema - only breast cancer survivors*
Lopez-Zamora, I., Campos-Varela, I., Munoz-Castro, S. et al. (2023) Effectiveness of aquatic multimodal physiotherapy through therapeutic exercise, manual self-drainage and self-care measures in upper limb lymphoedema in female breast cancer survivors. Randomized clinical trial. Fisioterapia 45(3): 145-155	- Study not reported in English
Malicka, I., Rosseger, A., Hanuszkiewicz, J. et al. (2014) Kinesiology Taping reduces lymphoedema of the upper extremity in women after breast cancer treatment: A pilot study. Przeglad Menopauzalny 13(4): 221-226	- Study used as primary study in included systematic review *Used in Kasawara*
McPherson, L. (2016) Research snapshot: Study to examine the role of acupuncture to reduce symptoms of lymphoedema after breast cancer: A randomised controlled trial. Australian Journal of Acupuncture and Chinese Medicine 10(1): 30-31	- Not a relevant study design
Melgaard, Dorte (2016) What is the effect of treating secondary lymphoedema after breast cancer with complete decongestive physiotherapy when the bandage is replaced with Kinesio Textape? - A pilot study. Physiotherapy theory and practice 32(6): 446-451	- Study used as primary study in included systematic review *Used in Kasawara 2018*
Mestre, Sandrine, Gaillard, Gessy, Benhamou, Murielle et al. (2017) An Auto-Adjustable Night Garment to Control Early Rebound Effect of Edema Volume After Intensive Phase of Decongestive Lymphoedema Therapy. Lymphatic research and biology 15(4): 364-370	- Secondary publication of an included study that does not provide any additional relevant information

Study	Reason for exclusion
Montag, Eduardo, Okada, Alberto Yoshikazu, Arruda, Eduardo Gustavo Pires et al. (2019) Influence of vascularized lymph node transfer (VLNT) flap positioning on the response to breast cancer-related lymphoedema treatment. Revista do Colegio Brasileiro de Cirurgioes 46(2): e2156	- Study used as primary study in included systematic review *Used in Winters 2021*
Munoz-Alcaraz, Maria Nieves, Jimenez-Vilchez, Antonio Jose, Santamaria-Pelaez, Mirian et al. (2022) Activity-Oriented Antiedema Proprioceptive Therapy (TAPA) for Shoulder Mobility Improvement in Women with Upper Limb Lymphoedema Secondary to Breast Cancer: A Multicenter Controlled Clinical Trial. Journal of clinical medicine 11(8)	- Insufficient data to categorise intervention
Munoz-Alcaraz, Maria Nieves, Perula-de-Torres, Luis Angel, Serrano-Merino, Jesus et al. (2020) Efficacy and efficiency of a new therapeutic approach based on activity-oriented proprioceptive antiedema therapy (TAPA) for edema reduction and improved occupational performance in the rehabilitation of breast cancer-related arm lymphoedema in women: a controlled, randomized clinical trial. BMC cancer 20(1): 1074	- Study does not contain a relevant intervention
Ochalek, Katarzyna, Gradalski, Tomasz, Szygula, Zbigniew et al. (2018) Physical Activity With and Without Arm Sleeves: Compliance and Quality of Life After Breast Cancer Surgery-A Randomized Controlled Trial. Lymphatic research and biology 16(3): 294-299	- Does not contain a population of people with lymphoedema *Study aims to assess physical activity levels in patients after breast cancer surgery. Unclear if population has lymphoedema*
Osorio, F, Ferro, L, Garrido, L et al. (2017) Satisfaction with a therapeutic sleeve for arm lymphoedema secondary to breast cancer treatment: controlled crossover trial. Porto biomedical journal 2(1): 13-17	- Study does not contain a relevant intervention
Pajero Otero, Violeta, Garcia Delgado, Esther, Martin Cortijo, Concepcion et al. (2022) Intensive complex physical therapy combined with intermittent pneumatic compression versus Kinesio taping for treating breast cancer-related lymphoedema of the upper limb: A randomised cross-over clinical trial. European journal of cancer care 31(5): e13625	- Data not reported in an extractable format

Study	Reason for exclusion
Pajero Otero, Violeta, Garcia Delgado, Esther, Martin Cortijo, Concepcion et al. (2019) Kinesio taping versus compression garments for treating breast cancer-related lymphoedema : a randomized, cross-over, controlled trial. Clinical rehabilitation 33(12): 1887-1897	- Data not reported in an extractable format
Pekyavas, Nihan Ozunlu, Tunay, Volga Bayrakci, Akbayrak, Turkan et al. (2014) Complex decongestive therapy and taping for patients with postmastectomy lymphoedema : a randomized controlled study. European journal of oncology nursing : the official journal of European Oncology Nursing Society 18(6): 585-90	- Study used as primary study in included systematic review *Used in Kasawara 2018*
Pereira de Godoy, Jose Maria, Pereira de Godoy, Livia Maria, Pereira de Godoy, Henrique Jose et al. (2022) Reduction of Arm Lymphoedema Using Manual Lymphatic Therapy (Godoy Method). Cureus 14(8): e28374	- Data not reported in an extractable format
Petkov, A., Kashilska, Y., Uchikov, A. et al. (2016) Improving the quality of life through effects of treatment with low intensity extremely low-frequency electrostatic field with deep oscillation in patients with breast cancer with secondary lymphoedema to patients treated with standard lymph equipment. Journal of IMAB - Annual Proceeding (Scientific Papers) 22(3): 1248-1252	- Data not reported in an extractable format *Small participant numbers, limited raw event data reported*
Phatak, S and Kadam, N (2022) Efficacy of Complete Decongestive Therapy Versus Pneumatic Compression Against Faradism Underpressure in Patients with Lymphoedema Secondary to Breast Cancer. Indian journal of physiotherapy & occupational therapy 16(3): 86-91	- Insufficient information in the methods and results
Ridner, Sheila H, Shih, Ya-Chen Tina, Doersam, Jennifer K et al. (2014) A pilot randomized trial evaluating lymphoedema self-measurement with bioelectrical impedance, self-care adherence, and health outcomes. Lymphatic research and biology 12(4): 258-66	- Not a relevant study design *Feasibility/validation study with non-extractable data format*

Study	Reason for exclusion
Rockson, Stanley G and Skoracki, Roman (2023) Effectiveness of a Nonpneumatic Active Compression Device in Older Adults with Breast Cancer-Related Lymphoedema: A Subanalysis of a Randomized Crossover Trial. Lymphatic research and biology 21(6): 581-584	- Post-hoc analysis of included study
Sapula, R, Braniewska, J, Weremczuk, R et al. (2017) The evaluation of selected physiotherapeutic methods in the treatment of post-mastectomy lymphoedema. Advances in Rehabilitation 31(2): 5-15	- Not a relevant study design *Non-randomised trial*
Singh, B, Newton, R U, Cormie, P et al. (2015) EFFECTS OF COMPRESSION ON LYMPHOEDEMA DURING RESISTANCE EXERCISE IN WOMEN WITH BREAST CANCER-RELATED LYMPHOEDEMA: A RANDOMIZED, CROSS-OVER TRIAL. Lymphology 48(2): 80-92	- Data not reported in an extractable format
Smith, Caroline A; Pirotta, Marie; Kilbreath, Sharon (2014) A feasibility study to examine the role of acupuncture to reduce symptoms of lymphoedema after breast cancer: a randomised controlled trial. Acupuncture in medicine : journal of the British Medical Acupuncture Society 32(5): 387-93	- Study used as primary study in included systematic review *Used in Gao 2021*
Smykla, A, Walewicz, K, Trybulski, R et al. (2013) Effect of Kinesiology Taping on breast cancer-related lymphoedema : a randomized single-blind controlled pilot study. BioMed research international 2013: 767106	- Study used as primary study in included systematic review *Used in Kasawara 2018*
Sohl, Stephanie J, Dietrich, Mary S, Wallston, Kenneth A et al. (2017) A randomized controlled trial of expressive writing in breast cancer survivors with lymphoedema . Psychology & health 32(7): 826-842	- Study does not contain a relevant intervention
Tambour, Mette, Holt, Marianne, Speyer, Anette et al. (2018) Manual lymphatic drainage adds no further volume reduction to Complete Decongestive Therapy on breast cancer-related lymphoedema: a multicentre, randomised, single-blind trial. British journal of cancer 119(10): 1215-1222	- Study used as primary study in included systematic review *Used in Rangon 2022*

Study	Reason for exclusion
Taradaj, J, Halski, T, Rosinczuk, J et al. (2016) The influence of Kinesiology Taping on the volume of lymphoedema and manual dexterity of the upper limb in women after breast cancer treatment. European journal of cancer care 25(4): 647-60	- Study used as primary study in included systematic review *Used in Kasawara 2018*
Tastaban, Engin, Soyder, Aykut, Aydin, Elif et al. (2020) Role of intermittent pneumatic compression in the treatment of breast cancer-related lymphoedema: a randomized controlled trial. Clinical rehabilitation 34(2): 220-228	- Study used as primary study in included systematic review *Used in Rangon 2022*
Tsai HJ, Hung HC, Yang JL et al. (2009) Could Kinesio tape replace the bandage in decongestive lymphatic therapy for breast-cancer-related lymphoedema ? A pilot study. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 17(11): 1353-1360	- Study used as primary study in included systematic review *Used in Kasawara 2018*
Uzkeser, Hulya, Karatay, Saliha, Erdemci, Burak et al. (2015) Efficacy of manual lymphatic drainage and intermittent pneumatic compression pump use in the treatment of lymphoedema after mastectomy: a randomized controlled trial. Breast cancer (Tokyo, Japan) 22(3): 300-7	- Study used as primary study in included systematic review *Used in Rangon 2022*
van Mulken, Tom J M, Schols, Rutger M, Scharmga, Andrea M J et al. (2020) First-in-human robotic supermicrosurgery using a dedicated microsurgical robot for treating breast cancer-related lymphoedema : a randomized pilot trial. Nature communications 11(1): 757	- Study does not contain a relevant intervention *Technique of surgery, not different type of surgery*
Wang, Chunhui, Liu, Heng, Shen, Jing et al. (2023) Effects of Tuina Combined With Moxibustion on Breast Cancer-Related Lymphoedema: A Randomized Cross-Over Controlled Trial. Integrative cancer therapies 22: 15347354231172735	- Study does not contain a relevant intervention
Wang, Chunhui, Yang, Ming, Fan, Yingyi et al. (2019) Moxibustion as a Therapy for Breast Cancer-Related Lymphoedema in Female Adults: A Preliminary Randomized Controlled Trial. Integrative cancer therapies 18: 1534735419866919	- Study used as primary study in included systematic review *Used in Gao 2021*

Study	Reason for exclusion
Whatley, Judith, Street, Rachael, Kay, Sally et al. (2016) Use of reflexology in managing secondary lymphoedema for patients affected by treatments for breast cancer: A feasibility study. Complementary therapies in clinical practice 23: 1-8	- Not a relevant study design
Winkels, Renate M, Sturgeon, Kathleen M, Kallan, Michael J et al. (2017) The women in steady exercise research (WISER) survivor trial: The innovative transdisciplinary design of a randomized controlled trial of exercise and weight-loss interventions among breast cancer survivors with lymphoedema . Contemporary clinical trials 61: 63-72	- Not a relevant study design *Animal model*
Winters-Stone, Kerri M, Laudermilk, Monica, Woo, Kaitlin et al. (2014) Influence of weight training on skeletal health of breast cancer survivors with or at risk for breast cancer-related lymphoedema . Journal of cancer survivorship : research and practice 8(2): 260-8	- Data not reported in an extractable format *No extractable outcomes that match review protocol*
Wolfs, AGN (2021) Does lymphovenous anastomosis improve quality of life of patients with lymphoedema after breast cancer?: the LYMPH trial. Nederlands tijdschrift voor geneeskunde 165(5)	- Study not reported in English
Xiang-li, H. and Fang, C. (2021) Efficacy and effect on serum VEGF-C of mild moxibustion plus functional exercise for upper-limb lymphoedema after breast cancer surgery. Journal of Acupuncture and Tuina Science	- Does not meet PICO criteria *Uses Chinese medicine of lymphoedema VEGF-C Serum moxibustion which is a different intervention to moxibustion included in the review protocol.* .
XIONG, Z.-F., WANG, T., WANG, H.-L. et al. (2019) Sliding-cupping along meridian for lymphoedema after breast cancer surgery: A randomized controlled trial. World Journal of Acupuncture - Moxibustion 29(3): 179-185	- Study does not contain a relevant intervention
Yaman, Aysegul, Borman, Pinar, Inanli, Adeviye et al. (2021) The efficacy of different bandaging methods in patients with breast cancer-related lymphoedema : A prospective, randomized study. Turkish journal of physical medicine and rehabilitation 67(2): 155-166	- Study does not contain a relevant intervention

Study	Reason for exclusion
Yao, C, Xu, Y, Chen, L et al. (2016) Effects of warm acupuncture on breast cancer-related chronic lymphoedema : a randomized controlled trial. Current oncology (Toronto, Ont.) 23(1): e27-34	- Study used as primary study in included systematic review *Used in Gao 2021*
Zhao, W, Zhang, HR, Lu, P et al. (2023) Lidong needling therapy combined with functional exercise in treatment of upper limb lymphoedema after breast cancer surgery: a randomized controlled trial. Zhongguo zhen jiu [Chinese acupuncture & moxibustion] 43(10): 1123-1127	- Study not reported in English

Systematic reviews

Study	Reason for exclusion
(2022) Advanced lymphoedema: Can non-drug interventions alleviate symptoms? IQWiG Reports – Commission No. HT19-01. Institute for Quality and Efficiency in Health Care: Extracts	- SR does not contain quantitative analysis
Abouelazayem, Mohamed; Elkorety, Mohamed; Monib, Sherif (2021) Breast Lymphoedema After Conservative Breast Surgery: An Up-to-date Systematic Review. Clinical breast cancer 21(3): 156-161	- SR does not contain quantitative analysis
Al-Sakkaf, Ali M, Masia, Jaume, Auladell-Rispau, Ariadna et al. (2022) Evidence Mapping of the Treatments for Breast Cancer-related Lymphoedema. Plastic and reconstructive surgery. Global open 10(1): e4045	- SR is of non-randomised trials
Azuar, A.-S., Uzan, C., Mathelin, C. et al. (2024) Update of indications and techniques for the management of lymphoedema after breast cancer surgery. Gynecologie Obstetrique Fertilite et Senologie	- Data not reported in an extractable format
Baumann, F T, Reike, A, Reimer, V et al. (2018) Effects of physical exercise on breast cancer-related secondary lymphoedema : a systematic review. Breast cancer research and treatment 170(1): 1-13	- SR does not contain quantitative analysis

Study	Reason for exclusion
Blanco, E.G. and Gonzalez, M.S. (2020) Efficacy of kinesio taping in the treatment of lymphoedema after breast cancer: A systematic review. Journal of Lymphoedema 15(1): 71-76	- SR does not contain quantitative analysis
Blei, F. (2023) Biomaterials in the clinical treatment of lymphoedema - a systematic review. Lymphatic Research and Biology 21(5): 504-533	- Study does not contain a relevant intervention
Cendron, SW, Paiva, LL, Darski, C et al. (2015) Complex Decongestive Physiotherapy Associated Compression Therapy in the Treatment of Secondary Lymphoedema in Breast Cancer: a Systematic Review. Rev. bras. cancerol 61(1): 49-58	- PDF not available in english
Chien, Tsai-Ju; Liu, Chia-Yu; Fang, Ching-Ju (2019) The Effect of Acupuncture in Breast Cancer-Related Lymphoedema (BCRL): A Systematic Review and Meta-Analysis. Integrative cancer therapies 18: 1534735419866910	- More recent SR that contains all included studies found
Chocron, Yehuda, Azzi, Alain J, Bouhadana, Gabriel et al. (2022) Axilla versus Wrist as the Recipient Site in Vascularized Lymph Node Transfer for Breast Cancer-Related Lymphoedema: A Systematic Review and Meta-Analysis. Journal of reconstructive microsurgery 38(7): 539-548	- Comparator in study does not match that specified in protocol *Single arm studies. No direct comparisons between axilla and wrist*
Chun, Magnus J, Saeg, Fouad, Miller, Derek et al. (2022) Surgical Lymphoedema Treatment: A Meta-Analysis and Recommendations. Eplasty 22: e51	- SR is of non-randomised trials *Includes 14/15 cohort studies with RCT included in Winters 2021*
De Groef, A, Van Kampen, M, Dieltjens, E et al. (2015) Effectiveness of Postoperative Physical Therapy for Upper Limb Impairments Following Breast Cancer Treatment: A Systematic Review. Archives of physical medicine and rehabilitation 96:1140-1153	- Duplicate reference
De Groef, An, Van Kampen, Marijke, Dieltjens, Evi et al. (2015) Effectiveness of postoperative physical therapy for upper-limb impairments after breast cancer treatment: a systematic review. Archives of physical medicine and rehabilitation 96(6): 1140-53	- SR does not contain quantitative analysis

Study	Reason for exclusion
Demiri, Efterpi, Dionyssiou, Dimitrios, Tsimponis, Antonios et al. (2018) Donor-Site Lymphoedema Following Lymph Node Transfer for Breast Cancer-Related Lymphoedema: A Systematic Review of the Literature. Lymphatic research and biology 16(1): 2-8	- Study does not contain a relevant intervention
Domingues, Aline Cristina, Alves, Bárbara Cristina Alves, Miranda, Vania Cristina dos Reis et al. (2021) Descongestive complex therapy in the treatment of lymphoedema after mastectomy. Fisioter. Bras 22(2): 272-289	- SR does not contain quantitative analysis
Doubblestein, David, Campione, Elizabeth, Hunley, Julie et al. (2023) Pre- and Post-Microsurgical Rehabilitation Interventions and Outcomes on Breast Cancer-Related Lymphoedema: a Systematic Review. Current oncology reports 25(9): 1031-1046	- SR is of non-randomised trials
Ezzo, Jeanette, Manheimer, Eric, McNeely, Margaret L et al. (2015) Manual lymphatic drainage for lymphoedema following breast cancer treatment. The Cochrane database of systematic reviews: cd003475	- More recent SR that contains all included studies found
Fish, Morgan L; Grover, Ritwik; Schwarz, Graham S (2020) Quality-of-Life Outcomes in Surgical vs Nonsurgical Treatment of Breast Cancer-Related Lymphoedema: A Systematic Review. JAMA surgery 155(6): 513-519	- SR does not contain quantitative analysis
Forte, Antonio J, Cinotto, Gabriela, Boczar, Daniel et al. (2019) Omental Lymph Node Transfer for Lymphoedema Patients: A Systematic Review. Cureus 11(11): e6227	- SR does not contain quantitative analysis
Forte, Antonio J, Huayllani, Maria T, Boczar, Daniel et al. (2019) Lipoaspiration and Lymph Node Transfer for Treatment of Breast Cancer-related Lymphoedema: A Systematic Review. Cureus 11(11): e6096	- More recent SR that contains all included studies found
Gasteratos, Konstantinos, Morsi-Yeroyannis, Antonios, Vlachopoulos, Nikolaos Ch et al. (2021) Microsurgical techniques in the treatment of breast cancer-related lymphoedema : a systematic review of efficacy and patient	- More recent SR that contains all included studies found

Study	Reason for exclusion
outcomes. Breast cancer (Tokyo, Japan) 28(5): 1002-1015	
Gatt, M; Willis, S; Leuschner, S (2017) A meta-analysis of the effectiveness and safety of kinesiology taping in the management of cancer-related lymphoedema. European journal of cancer care 26(5)	- More recent SR that contains all included studies found
Haque, Mohammad Anamul (2018) Effects of physiotherapy on breast cancer related secondary lymphoedema : a systematic review. International Journal of Medical Science and Diagnosis Research (IJMSDR)	- SR does not contain quantitative analysis
Hasenoehrl, Timothy, Keilani, Mohammad, Palma, Stefano et al. (2020) Resistance exercise and breast cancer related lymphoedema - a systematic review update. Disability and rehabilitation 42(1): 26-35	- SR does not contain quantitative analysis *Reported outcomes are not listed in our protocol*
Hasenoehrl, Timothy, Palma, Stefano, Ramazanova, Dariga et al. (2020) Resistance exercise and breast cancer-related lymphoedema -a systematic review update and meta-analysis. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 28(8): 3593-3603	- Duplicate reference
Hayes, S., Singh, B., Bloomquist, K. et al. (2020) Do Women with Breast Cancer-related Lymphoedema Need to Wear Compression While Exercising?: Results from a Systematic Review and Meta-analysis. Current Breast Cancer Reports 12(3): 193-201	- More recent SR that contains all included studies found
Hormann, Julie, Vach, Werner, Jakob, Marcel et al. (2020) Kinesiotaping for postoperative oedema - what is the evidence? A systematic review. BMC sports science, medicine & rehabilitation 12: 14	- More recent SR that contains all included studies found - SR is of non-randomised trials
Hou, Wenzhen, Pei, Lixia, Song, Yafang et al. (2019) Acupuncture therapy for breast cancer-related lymphoedema : A systematic review and meta-analysis. The journal of obstetrics and gynaecology research 45(12): 2307-2317	- More recent SR that contains all included studies found *Gao et al. 2021*
Huang TW, Tseng SH, Lin CC, Bai CH, Chen CS, Hung CS, Wu CH, Tam KW (2013) Effects of manual lymphatic drainage on breast cancer-	- More recent SR that contains all included studies found

Study	Reason for exclusion
related lymphoedema : a systematic review and meta-analysis of randomized controlled trials. World Journal of Surgical Oncology 11: 15	
Inbal, A.; Teven, C.M.; Chang, D.W. (2017) Latissimus dorsi flap with vascularized lymph node transfer for lymphoedema treatment: Technique, outcomes, indications and review of literature. Journal of Surgical Oncology 115(1): 72-77	- SR does not contain quantitative analysis
Jang, Soobin, Ko, Youme, Sasaki, Yui et al. (2020) Acupuncture as an adjuvant therapy for management of treatment-related symptoms in breast cancer patients: Systematic review and meta-analysis (PRISMA-compliant). Medicine 99(50): e21820	- Does not contain a population of people with Lymphoedema *Only contains 2 studies with people who have lymphoedema.*
Jarvis, Nicholas R, Torres, Ricardo A, Avila, Francisco R et al. (2021) Vascularized omental lymphatic transplant for upper extremity lymphoedema : A systematic review. Cancer reports (Hoboken, N.J.) 4(4): e1370	- SR does not contain quantitative analysis
Jin, Huimin, Xiang, Yuying, Feng, Yuqian et al. (2020) Effectiveness and Safety of Acupuncture Moxibustion Therapy Used in Breast Cancer-Related Lymphoedema: A Systematic Review and Meta-Analysis. Evidence-based complementary and alternative medicine : eCAM 2020: 3237451	- More recent SR that contains all included studies found
Keilani, M, Hasenoehrl, T, Neubauer, M et al. (2016) Resistance exercise and secondary lymphoedema in breast cancer survivors-a systematic review. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 24(4): 1907-16	- More recent SR available
Kim, J K, Loo, C, Kim, J S et al. (2023) Can Acupuncture be a Part of the Treatment for Breast Cancer-Related Lymphoedema? A Systematic Review of the Safety and Proposed Model for Care. Lymphology 56(1): 27-39	- SR is of non-randomised trials - SR does not contain quantitative analysis
Levenhagen, K., Davies, C., Perdomo, M. et al. (2023) Effect of Yoga among Women at Risk and with Breast Cancer-Related Lymphoedema: A	- SR does not contain quantitative analysis

Study	Reason for exclusion
Systematic Review. Rehabilitation Oncology 41(3): 129-138	
Li, Jia-Xin, Gao, Jie, Song, Jiang-Yan et al. (2022) Compression Therapy for the Patients With Breast Cancer: A Meta-analysis of Randomized Controlled Trials. Cancer nursing 45(4): e736-e745	- More recent SR that contains all included studies found *Papers included in Qiao 2023*
Li, Lun, Yuan, Liqin, Chen, Xianyu et al. (2016) Current Treatments for Breast Cancer-Related Lymphoedema: A Systematic Review. Asian Pacific journal of cancer prevention : APJCP 17(11): 4875-4883	- SR does not contain quantitative analysis
Liang, Mining, Chen, Qiongni, Peng, Kanglin et al. (2020) Manual lymphatic drainage for lymphoedema in patients after breast cancer surgery: A systematic review and meta-analysis of randomized controlled trials. Medicine 99(49): e23192	- More recent SR that contains all included studies found *Papers included in Qiao 2023*
Lin, Yan, Yang, Yan, Zhang, Xiaoyu et al. (2022) Manual Lymphatic Drainage for Breast Cancer-related Lymphoedema: A Systematic Review and Meta-analysis of Randomized Controlled Trials. Clinical breast cancer 22(5): e664-e673	- More recent SR that contains all included studies found *Papers included in Qiao 2023*
Lin, Yawei, Chen, Yi, Liu, Rongrong et al. (2023) Effect of exercise on rehabilitation of breast cancer surgery patients: A systematic review and meta-analysis of randomized controlled trials. Nursing open 10(4): 2030-2043	- Study does not contain a relevant intervention and population *Studies/interventions not specific to lymphoedema management*
Maccarone, Maria Chiara, Venturini, Erika, Menegatti, Erica et al. (2023) Water-based exercise for upper and lower limb lymphoedema treatment. Journal of vascular surgery. Venous and lymphatic disorders 11(1): 201-209	- SR does not contain quantitative analysis
Markkula, Silja P, Leung, Nelson, Allen, Victoria B et al. (2019) Surgical interventions for the prevention or treatment of lymphoedema after breast cancer treatment. The Cochrane database of systematic reviews 2: cd011433	- Does not contain a population of people with Lymphoedema *Includes 2/3 studies on the prevention of lymphoedema with surgery, 1/3 included in Winters 2021*
Marotta, Nicola, Lippi, Lorenzo, Ammendolia, Valerio et al. (2023) Efficacy of kinesio taping on upper limb volume reduction in patients with breast cancer-related lymphoedema : a	- SR does not contain quantitative analysis

Study	Reason for exclusion
systematic review of randomized controlled trials. European journal of physical and rehabilitation medicine 59(2): 237-247	
Muller, Martin, Klingberg, Karsten, Wertli, Maria M et al. (2018) Manual lymphatic drainage and quality of life in patients with lymphoedema and mixed oedema: a systematic review of randomised controlled trials. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation 27(6): 1403-1414	- SR does not contain quantitative analysis
Munoz-Alcaraz, Maria Nieves, Jimenez-Vilchez, Antonio Jose, Perula-de Torres, Luis Angel et al. (2023) Effect of Conservative Rehabilitation Interventions on Health-Related Quality of Life in Women with Upper Limb Lymphoedema Secondary to Breast Cancer: A Systematic Review. Healthcare (Basel, Switzerland) 11(18)	- SR does not contain quantitative analysis
Naghibi, S. and Varshoie Tabrizi, F. (2018) Exercise training and breast cancer-related lymphoedema : A systematic review. Razavi International Journal of Medicine 6(1): e11967	- SR does not contain quantitative analysis *Includes observational studies pre-dating 2016*
Nelson, Nicole L (2016) Breast Cancer-Related Lymphoedema and Resistance Exercise: A Systematic Review. Journal of strength and conditioning research 30(9): 2656-65	- SR does not contain quantitative analysis
Ozturk, Cemile Nurdan, Ozturk, Can, Glasgow, Mark et al. (2016) Free vascularized lymph node transfer for treatment of lymphoedema : A systematic evidence based review. Journal of plastic, reconstructive & aesthetic surgery : JPRAS 69(9): 1234-47	- SR does not contain quantitative analysis
Perdomo, Marisa, Davies, Claire, Levenhagen, Kimberly et al. (2023) Patient education for breast cancer-related lymphoedema : a systematic review. Journal of cancer survivorship : research and practice 17(2): 384-398	- SR does not contain quantitative analysis *Narrative description of RCTs. Used as a source of references*
Panchik, Daniel, Masco, Sarah, Zinnikas, Patrice et al. (2019) Effect of Exercise on Breast Cancer-Related Lymphoedema: What the Lymphatic Surgeon Needs to Know. Journal of reconstructive microsurgery 35(1): 37-45	- More recent SR that contains all included studies found

Study	Reason for exclusion
Pylkkanen, L., Uluturk, A., Parkinson, Z.S. et al. (2016) A systematic review on the effects of manual lymphatic drainage in operated breast cancer patients with lymphoedema. Annals of Oncology 27(supplement6): vi517	- Conference abstract
Rafn, Bolette Skjodt, Bodilsen, Anne, von Heymann, Annika et al. (2024) Examining the efficacy of treatments for arm lymphoedema in breast cancer survivors: an overview of systematic reviews with meta-analyses. EClinicalMedicine 67: 102397	- Study used for background information - Not a relevant study design *Systematic review of systematic reviews/meta-analyses.*
Reger, Maren, Kutschan, Sabine, Freuding, Maren et al. (2022) Water therapies (hydrotherapy, balneotherapy or aqua therapy) for patients with cancer: a systematic review. Journal of cancer research and clinical oncology 148(6): 1277-1297	- SR does not contain quantitative analysis
Ribeiro, Rafael Vilela Eiras; Dos Santos-Júnior, Lucio Henrique Romão; Barra, Irene Daher (2020) Lymph node transplantation in the management of post-mastectomy lymphoedema : a systematic review with meta-analysis. Rev. bras. cir. plást 35(3): 334-339	- SR does not contain quantitative analysis
Riobo Garcia, B. and Soto Gonzalez, M. (2018) Effects of resistance exercises in post-mastectomy lymphoedema, a systematic review. Fisioterapia 40(4): 199-207	- PDF not available in English
Rogan, Slavko, Taeymans, Jan, Luginbuehl, Helena et al. (2016) Therapy modalities to reduce lymphoedema in female breast cancer patients: a systematic review and meta-analysis. Breast cancer research and treatment 159(1): 1-14	- More recent SR that contains all included studies found
Romesberg, M., Rodzewich, A., Tucker, A. et al. (2017) Effects of Resistance Exercises on Secondary Lymphoedema Due to Treatment of Breast Cancer: A Systematic Review. Journal of Women's Health Physical Therapy 41(1): 55-56	- Conference abstract *Poster abstract for included SR*
Romesberg, M., Tucker, A., Kuzminski, K. et al. (2017) The Effects of Resistance Exercises on Secondary Lymphoedema Due to Treatment of Breast Cancer: A Review of Current Literature.	- SR does not contain quantitative analysis

Study	Reason for exclusion
Journal of Women's Health Physical Therapy 41(2): 91-99	
Saraswathi, Vasudevan, Latha, Satish, Niraimathi, K et al. (2021) Managing Lymphoedema, Increasing Range of Motion, and Quality of Life through Yoga Therapy among Breast Cancer Survivors: A Systematic Review. International journal of yoga 14(1): 3-17	- SR does not contain quantitative analysis
Shah, Chirag, Arthur, Douglas W, Wazer, David et al. (2016) The impact of early detection and intervention of breast cancer-related lymphoedema : a systematic review. Cancer medicine 5(6): 1154-62	- SR does not contain quantitative analysis
Shamoun, Shaimaa and Ahmad, Muayyad (2023) Complete Decongestive Therapy Effect on Breast Cancer Related to Lymphoedema: A Systemic Review and Meta-Analysis of Randomized Controlled Trials. Asian Pacific journal of cancer prevention : APJCP 24(7): 2225-2238	- More recent SR that contains all included studies found
Shao, Y and Zhong, D-S (2017) Manual lymphatic drainage for breast cancer-related lymphoedema. European journal of cancer care 26(5)	- More recent SR that contains all included studies found
Shao, Yi, Qi, Kang, Zhou, Qing-Hua et al. (2014) Intermittent pneumatic compression pump for breast cancer-related lymphoedema : a systematic review and meta-analysis of randomized controlled trials. Oncology research and treatment 37(4): 170-4	- Insufficient detail on methods and data reported *Unclear search and study selection criteria. Only one outcome on lymphoedema meta-analysed. All 6RCTs were reviewed independently by NICE*
Sousa, Marisa Augusta Gomes, Cecatto, Rebeca Boltes, Rosa, Chennyfer Dobbins Paes et al. (2014) Ultrasound therapy and transcutaneous electrical neuromuscular stimulation for management ofpost-mastectomy upper limb lymphoedema . Acta fisiátrica 21(4)	- Study does not contain a relevant intervention
Thompson, Belinda, Gaitatzis, Katrina, Janse de Jonge, Xanne et al. (2021) Manual lymphatic drainage treatment for lymphoedema : a systematic review of the literature. Journal of cancer survivorship : research and practice 15(2): 244-258	- SR does not contain quantitative analysis

Study	Reason for exclusion
Tremback-Ball, A., Harding, R., Heffner, K. et al. (2018) The Efficacy of Kinesiology Taping in the Treatment of Women with Post-Mastectomy Lymphoedema: A Systematic Review. Journal of Women's Health Physical Therapy 42(2): 94-103	- SR does not contain quantitative analysis
Tsai, Chi-Lin, Chih-Yang, Hsu, Chang, Wei-Wen et al. (2020) Effects of weight reduction on the breast cancer-related lymphoedema : A systematic review and meta-analysis. Breast (Edinburgh, Scotland) 52: 116-121	- Study does not contain a relevant intervention *3 studies are weight loss interventions, only one study is exercise but included in another systematic review.*
Tsai, Yu Lin, I, Ting Jie, Chuang, Ya Chi et al. (2021) Extracorporeal Shock Wave Therapy Combined with Complex Decongestive Therapy in Patients with Breast Cancer-Related Lymphoedema: A Systemic Review and Meta-Analysis. Journal of clinical medicine 10(24)	- Study does not contain a relevant intervention
Wanchai, A. and Armer, J.M. (2020) The effects of yoga on breast-cancer-related lymphoedema : a systematic review. Journal of Health Research 34(5): 409-418	- SR does not contain quantitative analysis
Wanchai, Ausanee and Armer, Jane M (2019) Effects of weight-lifting or resistance exercise on breast cancer-related lymphoedema : A systematic review. International journal of nursing sciences 6(1): 92-98	- SR does not contain quantitative analysis
Wanchai, Ausanee and Armer, Jane M (2021) Manual Lymphoedema Drainage for Reducing Risk for and Managing Breast Cancer-Related Lymphoedema After Breast Surgery: A Systematic Review. Nursing for women's health 25(5): 377-383	- SR does not contain quantitative analysis
Wang, H.-X., Li, H.-P., Yang, Y.-J. et al. (2017) Effect of intermittent pneumatic compression in the prevention and treatment of breast cancer-related lymphoedema :A Meta-analysis. Chinese Journal of Cancer Prevention and Treatment 24(11): 773-778	- PDF not available in english
Ward, Joseph, King, Ian, Monroy-Iglesias, Maria et al. (2021) A meta-analysis of the efficacy of vascularised lymph node transfer in reducing limb volume and cellulitis episodes in patients with cancer treatment-related lymphoedema.	- SR is of non-randomised trials *Only contains 1 RCT* - More recent SR that contains all included studies found

Study	Reason for exclusion
European journal of cancer (Oxford, England : 1990) 151: 233-244	*Papers included in Winters 2021*
Wei, Ching-Wen, Wu, Yi-Chen, Chen, Pei-Yi et al. (2019) Effectiveness of Yoga Interventions in Breast Cancer-Related lymphoedema : A systematic review. Complementary therapies in clinical practice 36: 49-55	- SR does not contain quantitative analysis
Whitworth, P, Vicini, F, Valente, S et al. (2023) Reducing Rates of Chronic Breast Cancer Related Lymphoedema with Screening & Early Intervention: an Update of Recent Data. Cancer research 83(5)	- Not a relevant study design *Abstract of poster session found only. Includes studies that are relevant to prevention of lymphoedema rather than management*
Xing, W., Duan, D., Ye, C. et al. (2023) Effectiveness of manual lymphatic drainage for breast cancer-related lymphoedema: an overview of systematic reviews and meta-analyses. European Journal of Gynaecological Oncology 44(1): 1-16	- Not a relevant study design *Systematic review of systematic reviews/meta-analyses.* - Study used for background information
Yu, Shibo, Zhu, Lizhe, Xie, Peiling et al. (2020) Effects of acupuncture on breast cancer-related lymphoedema: A systematic review and meta-analysis. Explore (New York, N.Y.) 16(2): 97-102	- More recent SR that contains all included studies found *Papers included in Gao 2021*
Zhang, Xinliang, Beeraka, Narasimha M, Sinelnikov, Mikhail Y et al. (2023) Breast Cancer-related Lymphoedema: Recent Updates on Clinical Efficacy of Therapies and Bioengineering Approaches for a Personalized Therapy. Current pharmaceutical design	- Study does not contain a relevant intervention
Zhang, Xinyan, Wang, Xiuli, Zhang, Bingyan et al. (2019) Effects of acupuncture on breast cancer-related lymphoedema: a systematic review and meta-analysis of randomised controlled trials. Acupuncture in medicine : journal of the British Medical Acupuncture Society 37(1): 16-24	- More recent SR that contains all included studies found *Papers included in Gao 2021*

Economic study

Study	Reason for exclusion
Dionyssiou, Demiri, Tsimponis et al. (2016) A randomized control study of treating secondary	The study was assessed as not applicable due to the fact that no

Study	Reason for exclusion
stage II breast cancer-related lymphoedema with free lymph node transfer. Breast cancer research and treatment; 2016; vol. 156 (no. 1); 73-9	discount rate was applied to a lifetime cost estimation. Moreover, the study was found to have very serious limitations as the assumption that surgery's benefits are always permanent is not confirmed by clinical evidence

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Appendix K– Research recommendations – full details

K1.1 Research recommendation

What are the most reliable, valid and clinically relevant outcomes and measures for assessing the severity and treatment effectiveness of lymphoedema, and what is the acceptability of the intervention for different groups, such as:

- women, men, trans people and non-binary people
- people from ethnic minority backgrounds
- people with disabilities.

K1.1.1 Why this is important

Identifying the most reliable, valid, and clinically relevant outcome measures for assessing lymphoedema severity and treatment will help with creating standardised outcome sets and measures. Standardising outcome measures will facilitate the comparison of results across studies, enable the further development of evidence-based guidelines, and guide clinical decision-making. Moreover, focusing on clinically relevant outcome measures will ensure that treatment goals align with patients' needs and preferences. Addressing the heterogeneity in lymphoedema measurements will ultimately lead to a stronger evidence base for lymphoedema management, helping healthcare professionals provide the most effective care for their patients.

K1.1.2 Rationale for research recommendation

Table: Rationale for research recommendation

Importance to ‘patients’ or the population	Identifying reliable, valid, and clinically relevant outcome measures for lymphoedema will ensure that treatment goals align with patients' needs and preferences, promoting patient-centred care and ultimately improving patients' quality of life and functional abilities.
Relevance to NICE guidance	Different interventions for managing BCRL were evaluated in this guideline, however due to the high heterogeneity in the outcomes and outcome measures reported in the studies it was not possible to determine the most effective treatments. As such, it is important create a core outcome set.

Relevance to the NHS	Identifying a core outcome set will enable the NHS to improve patient outcomes, better resource allocation and increase cost-savings as it will help with standardising which treatment approaches are the most effective.
National priorities	Low
Current evidence base	Minimal long-term data
Equality considerations	None known

K1.1.3 Modified PICO table

Table: Modified PICO for research recommendation

Population	All adults (aged 18 or over) who have, or have had, breast cancer and have lymphoedema of the upper limb (including axilla, hands and fingers), chest wall or breast.
Intervention	Any non-pharmacological interventions/strategies, as well as surgical interventions for managing BCRL
Comparator	Usual care
Outcome	• Incidence and severity of lymphoedema • Adverse events • Quality of life outcomes • Patient reported outcomes (including cosmetic impact) • Changes in tissues and skin condition
Study design	Phase 1: Systematic search to identify existing or ongoing studies on developing a core outcome set using the COMET online database and studies reporting on Patient Reported outcome measures (PROMS) Phase 2: Systematic review to evaluate current outcome measures used in trials, identifying the frequency of use of each outcome and validation data. In line with the four-step process for developing core outcome sets outlined in the COMET handbook, this is to initially identify and agree on potential outcomes, to define and determine how they will be measured. These should include family reported outcome measures as well as patient reported outcome measures. Phase 3: To reach consensus on which outcomes should be included in the core outcome set, their definition and measurement, a Delphi consensus technique of multiple rounds, involving specialists, research experts

	and people with lived experience of BCRL in the UK will be used.
Timeframe	Long term
Additional information	None

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K1.2 Research recommendation

What is the effectiveness and cost-effectiveness of lymphaticovenous anastomosis (LVA) and vasularised lymph node transfer (VLNT) in the management of breast cancer-related lymphoedema , and what is the acceptability of the intervention for different groups, such as:

- women, men, trans people and non-binary people
- people from ethnic minority backgrounds
- people with disabilities.

K1.1.1 Why this is important

Determining the effectiveness and cost-effectiveness of lymphaticovenous anastomosis (LVA) and vascularised lymph node transfer (VLNT) in the management of breast cancer-related lymphoedema is crucial. Lymphoedema is a significant condition that impacts patients' quality of life, long-term health outcomes and incurring additional costs for both patients and the healthcare system. Evaluating these surgical interventions will provide valuable evidence to guide clinical decision-making and resource allocation, with the potential of early intervention for the management of lymphoedema, thereby improving outcomes for patients while reducing long-term costs for the healthcare system. This research will strengthen the evidence base for lymphoedema management, enabling healthcare professionals to offer the most appropriate and effective treatments to their patients at varying stages of the condition to ensure optimal outcomes

.K1.1.2 Rationale for research recommendation

Table: Rationale for research recommendation

Importance to 'patients' or the population	Understanding the effectiveness of LVA and VLNT is of utmost importance to patients with breast cancer-related lymphoedema. These surgical interventions have the potential to significantly improve lymphatic function, reduce swelling, and alleviate associated symptoms. Effective management of lymphoedema can enhance patients' physical comfort, functional capacity, and overall quality of life. Moreover, knowing the efficacy of these procedures can help patients make informed decisions about their treatment options, potentially reducing the long-term physical and psychological burden of lymphoedema.
Relevance to NICE guidance	This research is highly relevant to NICE guidance as it will inform recommendations for the surgical management of breast cancer-

	related lymphoedema. Evaluating the effectiveness and cost-effectiveness of LVA and VLNT will help standardise best practices across the healthcare system. It may lead to updates in existing guidelines on lymphoedema management, ensuring that guidance reflects the most current evidence on surgical interventions. Additionally, this research addresses specific techniques that may not be fully covered in current guidance, thus filling an important gap in treatment recommendations for lymphoedema.
Relevance to the NHS	This research holds significant relevance to the NHS as it can optimise resource allocation for lymphoedema management. By determining the effectiveness and cost-effectiveness of LVA and VLNT, the NHS can ensure that it is providing the most efficient and beneficial treatments to patients. This could potentially reduce the long-term costs associated with ongoing lymphoedema management and improve overall patient outcomes. Furthermore, offering effective surgical interventions may decrease the need for lifelong conservative treatments, leading to more sustainable care practices and improved patient satisfaction with NHS services.
National priorities	Medium
Current evidence base	Minimal randomised trial data, limited long-term data.
Equality considerations	None known

K1.1.3 Modified PICO table

Table: Modified PICO for research recommendation

Population	All adults (aged 18 or over) who have, or have had, breast cancer and have lymphoedema of the upper limb (including axilla, hands and fingers), chest wall or breast.
Intervention	Lymphaticovenous anastomosis (LVA Vascularised lymph node transfer
Comparator	Usual care
Outcome	• Severity of lymphoedema • Adverse events • Quality of life outcomes • Patient reported outcomes (including cosmetic impact) • Changes in tissues and skin condition

Study design	• Systematic review of RCTs • RCTs
Timeframe	Long term
Additional information	None

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K1.3 Research recommendation

What are the most effective interventions for the management of breast oedema in people who have or have had breast cancer , and what is the acceptability of the intervention for different groups, such as:

- women, men, trans people and non-binary people
- people from ethnic minority backgrounds
- people with disabilities.

K1.1.1 Why this is important

Identifying the most effective interventions for the management of breast oedema in people who have or have had breast cancer is crucial. Breast oedema is a common complication that significantly impacts patients' quality of life. Determining evidence-based interventions will guide clinical practice, ensuring healthcare professionals can provide optimal care. This research will strengthen the evidence base for breast oedema management, ultimately improving patient outcomes and well-being.

K1.1.2 Rationale for research recommendation

Table: Rationale for research recommendation

Importance to ‘patients’ or the population	Understanding the most effective interventions for breast oedema is of paramount importance to patients. Breast oedema can cause considerable discomfort and functional impairment, affecting daily activities and long-term quality of life. Improved management techniques will enhance recovery and help patients regain a sense of normalcy. Moreover, effective interventions may alleviate the psychological impact of breast oedema, addressing issues related to body image and self-esteem that many patients experience.
Relevance to NICE guidance	This research is highly relevant to NICE guidance as it will inform future recommendations for breast cancer care and survivorship. Identifying effective interventions will help standardise best practices for managing breast oedema across the healthcare system. It may lead to necessary updates in existing guidelines on breast cancer treatment and follow-up care, ensuring that guidance reflects the most current and effective approaches.

	Additionally, this research addresses a specific complication that may not be fully covered in current guidance, thus filling an important gap in patient care recommendations.
Relevance to the NHS	This research holds significant relevance to the NHS as it can optimise resource allocation for breast cancer care. By identifying the most effective interventions, the NHS can ensure the provision of efficient and beneficial treatments, potentially reducing the need for repeated interventions or consultations. Effective management of breast oedema could also reduce long-term complications and associated healthcare costs, leading to more sustainable care practices. Furthermore, improved patient outcomes resulting from better oedema management may increase patient satisfaction with NHS services, contributing to overall positive perceptions of the healthcare system.
National priorities	Medium
Current evidence base	Minimal long-term data
Equality considerations	None known

K1.1.3 Modified PICO table

Table: Modified PICO for research recommendation

Population	All adults (aged 18 or over) who have, or have had, breast cancer and have breast oedema
Intervention	Any non-pharmacological interventions/strategies, as well as surgical interventions for managing breast oedema
Comparator	Usual care
Outcome	• Severity of lymphoedema • Adverse events • Quality of life outcomes • Patient reported outcomes (including cosmetic impact) • Changes in tissues and skin condition
Study design	• Systematic review of RCTs • RCTs
Timeframe	Long term
Additional information	None