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Review Article

Conservative management of lymphoedema in children: A systematic review

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Abstract.
PURPOSE: A systematic literature review was conducted to determine best practice conservative management of pediatric lymphoedema.
METHOD: The PRISMA protocol was followed; a search of Ovid Medline, Cinahl and Scopus was conducted using the search terms children OR pediatric OR adolescent AND lymphoedema OR lymphedema. Studies about management or treatment of lymphoedema in children were included while studies about filariasis, imaging, pathology, secondary lymphoedema, surgical techniques, central lymphoedema and those with participants with a median age greater than 18 years were excluded.
RESULTS: Of 738 possible studies identified, eight studies were eligible for inclusion in the review: four case reports, two retrospective service reviews and two prospective studies investigating different interventions. All studies were rated using the NHMRC hierarchy of evidence and appraised by both authors using the McMaster University Critical Review Form. Studies were of low quality with poor descriptions of management, small sample size, unclear and inconsistent methodology and irreproducible outcome measures.
CONCLUSION: This review identified low level evidence to support the use of pneumatic compression in the management of pediatric lymphoedema. Further research is required to identify optimal parameters for application of pneumatic compression and to investigate the use of other interventions for conservative management of pediatric lymphoedema.

Keywords: Lymphoedema, pediatric, therapeutics, management: self-management, disease-management

1. Introduction

Primary lymphoedema occurs due to a developmental lymphatic abnormality, which may appear at birth, during childhood, adolescence, or even much later in life. In contrast, secondary lymphoedema occurs as a result of damage to the lymphatic system most frequently due to cancer and its treatment, or filariasis, a parasitic infection, which occurs in many tropical countries. Primary lymphoedema has been estimated to occur in approximately 1 in 6000 children; this figure is based on the report of a London clinic, nearly 30 years ago [1] and no more recent report of prevalence has been published. Paediatric lymphoedema differs from adult lymphoedema in several ways: it is commonly of primary origin [2], depending on the malformation may involve more than one limb or body area and pitting oedema is not always present [3].

Although children with lymphoedema are estimated to be few in number, the impact on their lives and that of their families is large as parents struggle to manage the psychological and financial impact of lymphoedema and worry about the long term implications for their child [4,5]. Diagnosis of lymphoedema is of-

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ten delayed: a review of services for people of any age having lymphoedema in Victoria, Australia found that it took an average of 9.4 years for those with primary lymphoedema to be diagnosed, in contrast to an average of 1.5 years for those with secondary lymphoedema [6]. The National Lymphoedema Practitioners Register, established by the Australasian Lymphology Association (ALA) in 2010, provides a list of lymphoedema practitioners who fulfil ALA accreditation criteria. Out of a total of 168 lymphoedema therapists in rural and metropolitan, private and public services, only 27 (16%) are listed as treating children [7].

Historic literature describing management of pediatric lymphoedema indicates that treatment has long been based on the principles of adult management and applied using a recipe approach [3,8,9] because it was not considered that diagnostic measures would alter treatment [9]. Compression, diuretics, surgery and no treatment were all adult treatment options described for children in the 1980s [9].

In the 21st century, management strategies for adult lymphoedema evolved and have been applied to pediatric management; these currently include skin care, exercise, manual lymphatic drainage (MLD), use of medication to control infections and compression therapy [2,10,11]. Genetic phenotyping for diagnosis, management and follow-up has been recommended for children with no systemic involvement and for those with systemic involvement a multidisciplinary management approach, which includes both geneticists and pediatricians, has been recommended [2]. While a commentary paper by Schook et al. [11] provides a flow chart for management of pediatric lymphoedema it was based on research completed with adults who had secondary lymphoedema. It has also been suggested that pediatric specific management strategies including teaching parents to participate in management, encouraging normal physical activity and the importance of psychological support and self-management are required for optimal outcomes [2].

Compression therapy has been consistently described to manage pediatric lymphoedema with reports from small populations indicating that its use may have increased from 46% in 1985 [9] to 75.4% in 2011 [11]. The type of compression described has altered from compression garments and bandaging – either alone or in combination with diuretics – in 1985 [9] to pneumatic compression, and "controlled compression therapy: custom-fitted layered stockings that are progressively tightened" in 2011 [11].

Manual lymphatic drainage has long been recommended for treatment of adult lymphoedema [12,13] but was not described for pediatric lymphoedema management until more recently with the acknowledgement there was a lack of evidence for its use in children [2].

While there seems to be variation in management of pediatric lymphoedema according to the therapist and their country, guidelines for pediatric lymphoedema management are non-existent. An international consensus document on 'Best practice for the management of lymphoedema' has no mention of children [14] and a pediatric Lymphoedema Framework document developed in 2010 provides advice regarding access, diagnosis and service provision but does not provide any guidelines for physical treatment [15].

This systematic review was undertaken to identify and assess the evidence regarding conservative physical management of pediatric lymphoedema.

2. Methods

In undertaking this literature review, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol was followed [16], which may be accessed at www.prisma-statement.org. The review has PROSPERO registration, number CRD 42012003260.

2.1. Search strategy

A search of Medline, Scopus and Cinahl was undertaken on 14th February 2014 using the search terms and limits in Fig. 1. Reference lists of key articles and literature reviews were hand searched for further eligible articles and citations of these articles were then searched for other appropriate articles. A search of the indices of the Journal of Lymphoedema, established in 2006, was undertaken as this journal is an important journal in the field and does not appear in the databases searched.

2.2. Inclusion criteria and study characteristics

Children were defined by an upper age limit of 18 years. Studies were selected on the basis of conservative or physical therapy for lymphoedema where the study population was children or included children and the results for children were reported separately and management or therapy or treatment appeared in the title or abstract, or a physical treatment method was specified. Case studies were also included unless it was clear from the abstract that no management was investigated or they were exclusively diagnostic.

1. Lymphedema* OR "milroy disease" OR "nonne-milroy-meige disease" OR "nonne-milroy lymphedema" OR "nonne milroy" OR "milroy's disease" OR "milroys disease" OR lymphoedema* OR elephantias* OR "verrucosis lymphostatic" OR "mossy foot" OR "microcrystal diseases" OR "lymphostatic verrucoses" OR "microcrystal disease" OR "diseases microcrystal" OR "lymphostatic verrucosis" OR "bigfoot disease" OR "bigfoot diseases" OR "verrucoses lymphostatic" OR "mossy foots" OR "Lymphatic System Abnormalities" OR "Lymph System Abnormalities"
2. Treatment* OR therap* OR manage*
3. Child* OR youth* OR adolesce* OR infant* OR toddler* OR teen*
4. 1 AND 2 AND 3.
5. Limit 4 to English and Human
6. 5 not filaria*.mp

Fig. 1. Search terms 14th February 2014 (Ovid Medline, Cinahl and Scopus).

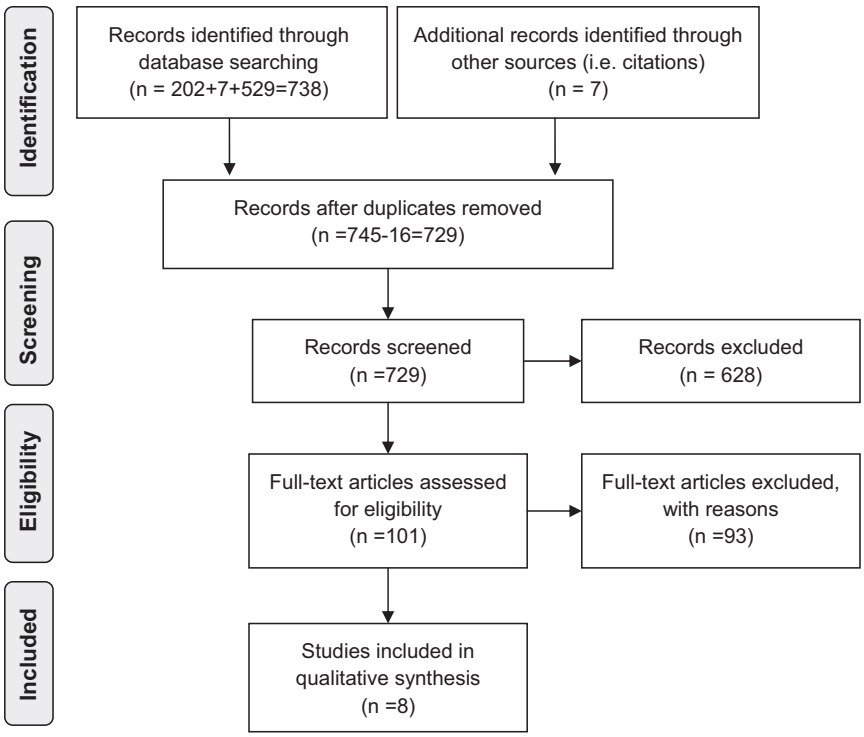

Fig. 2. Prisma flow diagram of literature search[16].

2.3. Exclusion criteria

Studies were excluded if they were about secondary or genital lymphoedema, or surgical management. Letters and editorials were also excluded. A flow chart depicting the process for inclusion and exclusion is provided in Fig. 2.

Included studies were ranked using the National Health and Medical Research Council (NHMRC) hierarchy of evidence (Level I systematic review of level II studies, Level II a randomized controlled trial, Level III-1 a pseudo-randomized controlled trial, Level III-2 a comparative study with concurrent controls, Level III-3 a comparative study without concurrent controls and Level IV case series) and appraised using the McMaster University Critical Review Form [17].

3. Results

The searches returned a total of 738 studies for possible inclusion. A search of the indices of the Journal of Lymphoedema identified a further two papers and examination of reference lists of the most relevant, a further seven papers. Sixteen duplicates were removed; screening of the remaining studies via title and abstract

Table 1
Study comparison table

Author, study type, setting	Participants	Management/ Intervention	Outcome measures	Statistical analysis	Results	Limitations
Alexander et al. [21] Case report DT Watson Rehabilitation Hospital for Children Pennsylvania USA	9 yr old female Park-Weber Syndrome RUL+RLL	8 hours use of Linear Pump overnight + use of CG during the day for 4/12	12 CM: 4 foot/4 knee/ 4 knee to upper thigh. Diagram provided. Change in CM = pre CM less post CM/(pre CM less CM of normal leg)	Descriptive results	Reduction of 53% mid-thigh, 70% mid-calf and 27% foot arch at 4/12	Comparator not described, no blinding of assessors. Coincidental use of CG
Avery et al. [22] Case report Montgomery Hospital, Pennsylvania USA	5/12 old male Congenital RLL LO Onset 4/12 old	Use of pneumatic compression for 2/12	CM at foot arch, ankle, mid-calf and inferior knee at baseline, 12, 28, 40 and 63 days	Descriptive results	At 2/12 Reduction CM 3 cm at ankle and 1 cm mid-calf Increase CM 1.5 cm at foot and 3.5 cm below knee	No clinically relevant change defined. No long term follow-up. Use of unaffected limb as comparator
Akbayrak et al. [24] Case report Hacettepe University School of Physical Therapy and Rehabilitation, Ankara, Turkey	6.5/12 female Congenital, Bi LL Onset 2/12 old	Physiotherapist applied MLD, multi-layered compression bandaging. 5 days/wk for 2.5/12 Home program remedial exercises and skin care by mother during 2.5/12 and after.	CM at 2 cm intervals ankle to 10 cm above the knee Water displacement – no description. Measurement pre-, 2.5/12 (end of intervention) + 6/12 post intervention	Descriptive results	CM and volumetric measures "reflected reduction in swelling" after 2.5/12 TT and at 6/12 post TT	No description of "exercise or home program" for a 6/12 baby. Limited description of intervention and control measures. No consideration of a clinically relevant change
Mahram et al. [23] Case report Qazvin, Iran.	15 year old female LO praecox RLL	Use of 4 LLLT probes (wavelength 630 or 890 nm) Probes and positions described. TT cycle of 12 TT sessions (on alternate days, over 1/12) with 1/12 rest then a second cycle of 1/12	CM just below the knee, 15 cm below the knee and above the ankle	Descriptive results	Decrease of 2 cm below the knee, 2 cm at the ankle and 4 cm at 15 cm below the knee after the 2nd intervention cycle. No side effect noted during TT. No significant increase in CM three months after intervention ceased	No information regarding blinding of assessors or protocol of assessment. No data provided at 3 months after intervention (discussed in report)

Table 1, continued

Author, study type, setting	Participants	Management/ Intervention	Outcome measures	Statistical analysis	Results	Limitations
De Godoy et al. [19] Prospective Case Report 2004–2009 Godoy Clinic, Sao Jose do Rio Preto, Brazil	Inclusion criteria: clinical diagnosis LL LO by CM at 2 points on the feet 9 males, 5 females (N = 14) Age range: 2/12 to 8.5 yrs Group 1 (N = 10) Group 2 (N = 4) participants had fibrosis, LO > 3 yrs	Group 1cervical stimulation Group 2 cervical stimulation + CGs Mothers trained in manual cervical stimulation technique applied: 15–20 mins/day 20–30 stimuli/minute. Intervention period 2 years	2004–2009 Followed for 2 years CM: feet at 3 cm and 6 cm superior to the base of the big toe.	2-tailed t-test and Wilcoxon's matched pair test Alpha error of 5% ($P < 0.05$) acceptable	Group 1 Pre between feet $p < 0.0001$ Post between feet $p < 0.02$ Pre to post same foot $p = 0.0001$ Group 2 Pre between feet $p < 0.0002$ Post between feet $p < 0.08$ Pre to post same foot $p < 0.002$ No between group analysis	Confounding of results by indiscriminate selective addition of other forms of TT including manual and mechanical lymph drainage during the trial.
Hassall et al. [25] Retrospective review records from 1987–1997 The Hospital for Sick Children, Toronto Canada	7 male, 9 female Age range At diagnosis 0.1–14 yrs Start 0.8–16 yrs End 6–26 yrs Primary or secondary LO UL 3 Ui LL 7 Ui LL 6 Bi Exclusion: vascular involvement	Pneumatic compression pump, wearing CGs and advice on exercise and skin hygiene. Pump pressure TT phase 50–140 mmHg Mean 84.29 ± 24.72 mmHg. Maintenance phase 35–100 mmHg Mean 58.57 ± 19.05 mmHg	CM 7 points LL: groin, thigh, calf, 3 cm above and at the ankle, midfoot and toes 8 points UL: axillary fold, mid and lower upper arm, elbow crease, mid and lower forearm, wrist crease and hand. Water displacement to the groin; >10% difference significant	Paired t-tests $p < 0.05$ significant; CI based on expert opinion Ui LO CM >5% change CI <5% change M >−5% change D Ui LO Volume >10% change CI <10% change M > −10% change D Bi LO Thigh to foot ratio change > 2 = CI	20% limbs CI, 73% M, 7 % D Increased pump pressure, initial vs end $p = 0.0036$ Volume, CM and ratio pre and post TT – no statistical difference No complications in 88%, 2 (12%) complications: 1 cellulitis/ 1 pressure sore on heel in a patient with cerebral palsy	Use of unaffected limb as comparator. Variation in TT duration from 19–96/12 M TT varied from 2–8 times per week; hours of TT varied from 1–8 hours per day

Table 1, continued

Author, study type, setting	Participants	Management/ Intervention	Outcome measures	Statistical analysis	Results	Limitations
Hutzschenreuter and Herpertz [26] Retrospective review dates unspecified 1983–1992 likely University of Ulm, Germany	N = 50, 43 primary & 7 secondaryLO Age range: 3/12–16 years 12 primary hereditary: LL 7 Bi/UL 3 Bi/ 4 limbs/Half body1 31 primary sporadic: LL 16 Bi LL11Ui UL 2 Ui UL + face1 UL + Bi LL1	Inpatient 4/52 < 2 yrs old: MLD twice/day > 2 yrs old: MLD twice/day plus compression bandaging. MTM CG at end of TT. Short "stress" bandages used for compression bandaging.	Measures taken pre + 4/52 (post) Volumes calculated using Kuhnke method: the volume of a 4 cm segment of a limb is $V = \frac{c^2}{4\pi}$ and the volume of a whole limb is $= \frac{\Sigma c^2}{\pi}$.	Leg volume change pre and post Wilcoxon matched pairs test Primary arm and secondary (due variable sites) volume change descriptive results due to small numbers Description by limb dominance	Primary Bi LO reduction (R leg dominant) ($p < 0.025$); R Ui LO unaffected L leg reduction in volume $p < 0.05$ Arm or leg volume decrease N = 47 (94%) No effect in 3 UL with lymphangioma cysticus.	Difficult to interpret graphs provided. No table of results No description of method No conclusions provided that are pertinent to the results
McLeod et al. [20] Prospective study The Hospital for Sick Children, Toronto Canada	7 girls 2 boys 8 congenital LO; 1 secondary to Hodgkins lymphoma and XRT; 6 RLL 3 LLL Mean age of onset: 2.6 yrs (range 0–14); Mean age at start of study: 13 yrs (range 5.5–17)	Comparison 3 Pneumatic Compression devices Wright Linear Pump: MPs 85/65/45 distal to proximal over the length of the pneumatic sleeve; Lympha-Press: MP1 22.5 mmHg Hemaflo 2: MP:43 mmHg TT: 2/7 bed rest, elevation, pump on 2/24, off 0.5/24 Night: 6/24 pump. Home program overnight pump + daily 5 minutes step up exercises + CG	CM 2/3 distance medial malleolus to base of patella per Swedborg[38]. Volumetric measures – base of the patella (with leg extended) % increase in volume or CM compared to normal limb Measured pre-TT; on release from hospital; at 1, 2, 3, 4, 12, 18 and 24 months	Descriptive statistics	Volumetric reduction in all ($N = 9$); Greater decreases in volume and CM noted with Lympha-Press ($N = 3$) Acknowledgement of effect of bed rest and limitations of using indirect method of measurement – using girth CM to calculate LL volume	Hemaflo 2units broke after 4/12; 3 subjects transferred to Lympha-Press No description of randomisation Limited information co-interventions (exercise, CGs) Results incomplete; no explanation of patient loss provided. Use of unaffected limb as control.

Legend: LO = lymphoedema; UL = Upper limb; LL = Lower limb. CI = clinical improvement, M = maintenance, D = deterioration, CM = Circumferential measure, Bi = Bilateral, Ui = Unilateral, TT = treatment, CG = compression garment, MP = Mean pressure.

Table 2
Evaluation questions – quantitative studies critical appraisal tool (McMaster)

1. Was the study purpose stated clearly?
2. Was relevant background literature reviewed?
3. Was the design appropriate for the study question?
4. Was the sample described in detail?
5. Was the sample size justified?
6. Were the outcome measures valid?
7. Were the outcome measures reliable? (Threats to internal validity controlled?)
8. Was the intervention described in detail?
9. Was contamination avoided?
10. Was co-intervention avoided?
11. Were the results reported in terms of statistical significance?
12. Was the analysis method appropriate?
13. Were the conclusions appropriate given study methods and results?
14. Were the main limitations and biases discussed?

excluded 628 studies; these consisted of those on filariasis, genetics, case studies (descriptive or diagnostic), imaging, pathology (including physiology and anatomical descriptions), surgery (as a treatment for lymphoedema), cancer and surgery (as a cause of lymphoedema). The full-text of 101 papers were screened (JJP) to assess for eligibility and any uncertainty regarding inclusion was discussed between the authors.

Articles excluded from this review included recent research about management of pediatric lymphoedema, which has concentrated on the development of an appropriate response to children within an adult service [18], and the psychosocial support needed by the families of children with lymphoedema [4,5].

Eight studies were appropriate to include in the review. Two were prospective clinical reports: one investigated a new manual massage technique [19] while the other compared three different pneumatic compression machines [20]. Four case studies were included with two reporting the outcomes of pneumatic compression [21,22], one low level laser therapy [23] and another bandaging of an infant's legs [24]. The remaining studies retrospectively evaluated the use of pneumatic compression [25] and manual lymphatic drainage and compression bandaging [26]. (See Table 1)

All studies were level III-3 or IV based on the NHMRC hierarchy of evidence. Papers were assessed by both authors for quality using the McMaster critical appraisal tool [17] (see Table 2). Where ratings differed between authors discussion occurred to arrive at consensus. A score of one was allocated where the response to the question was yes, a zero was allocated where the answer was no or insufficient detail was provided. Where the question was not applicable to the study type, the total score was reduced by one, and the scores have therefore been presented as percentages to enable comparison (see Table 3). The highest score for a study was 67% [25] and the lowest was 14% [26].

4. Study description: Prospective studies

4.1. Intervention

Two different interventions for lower limb lymphoedema were investigated: manual cervical stimulation [19] and comparison of three different pneumatic compression devices [20]. The method and length of intervention was not comprehensively described in either study and were therefore not reproducible. Neither study provided standardized intervention for each participant. During the compression study one machine malfunctioned and that study group was allocated to a different machine during the trial [20] while De Godoy et al [19] inconsistently added other interventions to the manual cervical stimulation during the trial. Therefore any treatment outcomes reported by these studies cannot be attributed to any specific intervention.

4.2. Sample characteristics

The sample sizes of the studies were small and no sample size calculation or post-hoc power calculations were provided. De Godoy et al. [19] provided limited description of participants, and while treating the whole lower limb only feet measurements were reported. Although, McLeod et al. [20] stated that the mean age of onset and the mean age at commencement of the study were similar across groups, on examination of the raw data there was a large variation [20].

4.3. Outcome measures

Random assignment to pneumatic compression intervention groups was not described. Both studies used the unaffected limb for comparison. Outcome measures used to assess lower limb lymphoedema varied in type and measurement protocol between studies. De Godoy et al. [19] arbitrarily considered a two-centimeter reduction in foot circumference as a significant change while the results presented by McLeod et al. [20] are difficult to interpret due to poor description of data management and results.

4.4. Findings

McLeod et al. [20] reported lower volumetric measures after 18 to 24 months of treatment no mat-

Table 3
NHMRC ratings and McMaster critical appraisal ratings

First author	L	1	2	3	4	5	6	7	8	9	10	11	12	13	14	TS	%
Akbayrak	<IV	N	N	Y	Y	A	Y	Y	N	Y	N	A	Y	Y	N	7/12	58
Alexander	<IV	Y	Y	Y	Y	D	Y	D	Y	N	N	N	Y	N	N	7/14	50
Avery	<IV	N	Y	Y	Y	D	Y	D	N	D	D	N	Y	N	N	5/14	36
De Godoy	IV	N	N	Y	N	N	D	D	N	N	N	Y	Y	N	N	3/14	21
Hassall	III-3	Y	Y	Y	Y	N	Y	N	N	A	A	Y	Y	Y	N	8/12	67
Mahram	<IV	Y	Y	Y	Y	D	Y	D	N	D	D	N	N	Y	N	6/14	43
McLeod	III-3	Y	Y	Y	N	N	Y	N	Y	A	D	N	N	N	N	5/13	38
Hutzschen-reuter	III-3	Y	N	Y	N	N	D	D	N	D	D	Y	N	N	N	2/14	14
TS		5	5	8	5	0	6	1	2	1	0	3	5	3	0		

Legend: L = level of NHMRC evidence, Y = yes, N = no, D = not described, A = not applicable, TS = total score.

ter which pneumatic compression device was used. However no attempt was made to relate the amount of change in volumetric measure to a clinically relevant change. The research primarily assessed the relative merits of each pneumatic machine and reported that all were safe and easy to use. The authors also concluded that pneumatic compression could alleviate skin changes and improve quality of life; however they did not include outcome measures that assessed either skin change or quality of life.

The use of manual cervical stimulation was reported to significantly reduce foot volume; however there was considerable difference in treatment between individuals and non-random allocation to groups, which undermined conclusions about the efficacy of the intervention [19].

5. Study description: Retrospective studies

5.1. Intervention

A case note audit was undertaken to assess the use of pneumatic compression in pediatric lymphoedema management [25] at the same hospital where the prospective comparison of three pneumatic compression machines was conducted [20]. There were large differences in the treatment duration (months), the number of sessions per week during the maintenance phase and the number of hours per day the compression was applied. Ten years of patient care were reviewed to assess the outcome of four weeks of inpatient MLD and compression bandaging [26]. Children two years and older were treated with MLD twice a day and compression bandaging, while those under two years only had MLD twice a day. No further description of the intervention was given.

5.2. Sample characteristics

Sixteen children of both genders were included in the study on pneumatic compression and were subgrouped into unilateral upper limb, unilateral lower limb or bilateral lower limb lymphoedema, resulting in sample sizes of three to seven in each group. Mean age at diagnosis and commencement of treatment were provided and by the end of the study the age range extended over 18 years [25]. Fifty children (43 primary and 7 secondary) were included for analysis of MLD and compression therapy [26], with an age range of three months to 16 years. The majority of children studied had one or both legs involved (37).

5.3. Outcome measures

Hassall et al. [25] provided details of initial pressure setting, pressure reduction, treatment duration, frequency per week of treatment or maintenance, and hours per day of treatment. Circumferential measures at seven points on the lower limb and eight points on the upper limb as well as water displacement volume to the groin or axilla were measured. Water displacement measures were presented as a percentage change in volume using the unaffected limb as the comparator. A difference in volumetric percentage of greater than 10% or less than minus 10% were considered to be a clinically significant improvement or deterioration. Percentage change, which fell between 10% and minus 10%, indicated maintenance of limb size. Circumferential measures at each point were summed and the mean value used to calculate a percentage difference in limb circumference, using the unaffected limb as the comparator. For those children with bilateral lymphoedema the authors devised and applied a thigh to foot ratio to calculate change in the absence of an unaffected "control" limb. An increase in the ratio of greater than two units was interpreted as a decrease

in lymphoedema while a decrease of greater than two units indicated an increase in lymphoedema. The authors state that the level of clinical significance for all measures in this study was set at an arbitrary point deemed significant by an expert physical therapist and physician in the absence of guidelines.

In contrast, no detail of outcome measure was given by Hutzschenreuter and Herpertz [26], advising that the measures were taken and calculated according to the method devised by Kuhnke [27] and reported in German in 1979 (in [26,28]) and that the measures were taken at the pre- and post-treatment point as well as the end of each week of the four weeks of treatment.

5.4. Findings

Although, Hassall et al. [25] found a trend towards clinical improvement in limb size and volume with pneumatic compression the statistical analysis was not significant. However a statistically significant reduction in pump pressure between the initial and maintenance periods of the study was reported; this indicated less pressure was required over time to maintain limb size but there is no definition, measure or parameter provided to describe the transition to maintenance care. The authors acknowledged the limitations of the study, including the small sample size, and lack of reliability and validity studies of outcome measures. Hutzschenreuter and Herpertz [26] found reductions in both lymphoedema and "healthy" leg volumes. While statistical analysis was not provided, participants with secondary lymphoedema were reported to have a larger reduction in limb size than those with primary lymphoedema. The results were not discussed; instead the authors postulated about the mode of fluid movement with manual lymphatic drainage.

6. Study description: Case reports

1) A comprehensive physiotherapy program that included MLD, remedial exercises, bandaging (by both therapist and mother during treatment phase and mother during follow-up) and skin care information for a six month old female with bilateral lower limb lymphoedema was reported by Akbayrak et al. [24]. Volumetric and circumferential measures were reported pre- and post-intervention, and at six month follow-up. A reduction in swelling was reported in circumferential measures post-intervention and volumetric changes at six months follow-up, with measures given for right and left limb. Control measures for the right and left lower limb were included in the results table, but it was unclear if these were the pre-intervention measures. No specific information was provided regarding the intervention, or the method of volume calculation, rendering the study not reproducible. The effect of growth was not discussed, although six centimeters increase in height was reported. A reduction in leg lymphoedema may be observed in some children undergoing a growth spurt, where limb length has increased over a short period (author's observation).
2) Alexander et al. [21] reported that the use of a linear pneumatic compression pump overnight for four months resulted in reductions in mid-thigh, mid-calf and foot arch circumferential measures in a nine-year-old female with Park-Weber syndrome. However there was no blinding of assessors or long term follow-up, and coincidental use of compression garments indicate caution in attributing this outcome solely to pneumatic compression.
3) Five treatments of sequential pneumatic compression were used by Avery et al. [22] over two months, at intervals varying from 12 to 23 days to treat a five month old male with congenital lower limb lymphoedema. Results included decreased ankle and mid-calf but increased foot and below knee circumferential measures. No detail was provided regarding the method or timing of application and hence this study is not reproducible.
4) Low level laser therapy (LLLT) applied on alternate days for 12 sessions to a 15-year-old female resulted in decreased limb circumference, which was maintained three months after cessation of treatment [23]. No side effects from the use of LLLT were reported [23]; limitations of this study include a variation in the dosage reported, lack of information regarding prior or concurrent management strategies and the lack of long term follow-up.

7. Discussion

The eight studies that met the criteria for this review provide poor quality, low level evidence (level III-3 & IV) to guide the management of pediatric lym-

phoedema. Small sample sizes and variability in participant demography limited the power and decreased the generalizability of the research findings.

Management of pediatric lymphoedema provides different challenges due to the implications of normal growth, and childhood understanding and therefore cooperation with management practices. The clinical presentation of primary lymphoedema may affect many body parts depending on the malformation within the lymphatic system. Properties of the tissues differ with pediatric lymphoedema being described as non-pitting [3]. Developmental changes require monitoring in both psychological and physical domains for children [2].

Researchers have variously suggested that fungal infections and cellulitis are less common in children than adults [2,29]; or very common in children [19]. While skin care to prevent infection has been a longstanding, universally accepted management practice for secondary, adult lymphoedema, given the various opinions regarding childhood susceptibility, it is not surprising that only one recent study in this review included preventative skin care measures [19]. However avoidance of infections continues to be recommended for pediatric lymphoedema management [2].

Due to the shorter duration of pediatric lymphoedema, children have been reported to have less functional impairment and malignant degeneration [11] than the adult lymphoedema population. However this is a broad generalization as pediatric lymphoedema can be extremely debilitating. Exercise is important to maintain function and in children, it can be challenging to prescribe or manage the amount of exercise, particularly in preschool years. While the description of differences in pediatric presentation is widespread there is limited information about the underlying physiological and tissue factors which contribute to these differences. Without this knowledge the management approach is likely to be sub-optimal and will continue to default to adoption of adult management regimes.

The outcome measures used in the studies in this review reflected the lack of international agreement regarding a standardized measurement protocol to monitor limb size and volume. Due to the effect of normal growth a different approach to monitoring pediatric lymphoedema is required [2,5]. In an adult, monitoring of body weight and limb circumferential measures will identify if a limb is increasing in size, potentially indicating worsening lymphoedema; whereas in children there will be a natural increase in size due to limb growth. The use of an unaffected limb as a control to compare to the affected limb is common practice both in research and clinically. Most studies have compared the affected with an unaffected limb to evaluate management interventions. This assumes that if girth difference is stable, the unaffected limb can be used as a control for comparison during normal growth. However often in pediatric lymphoedema both lower limbs are affected and post-cancer adult arm lymphoedema studies have reported that when lymphoedema is present in the limb of the operated side, subclinical changes occur in the limb of the unoperated side [12, p. 283][30]. Although this may only apply to the post-operative state, the validity of using measures of the unaffected limb as a control is contestable. Moreover comparisons over time in pediatric lymphoedema are not useful due to the natural changes in length and circumference, rendering volumetry measures not appropriate [2].

Due to the challenges posed by growth, Hassall et al. [25] proposed a ratio of foot to thigh volume to assess change in limb volume in children with bilateral lymphoedema. Unfortunately the calculation was not provided in the publication and there is no way to assess the validity of the calculation used or reproduce the method. The authors were unable to find any further reference to this method in later pediatric literature. The use of a ratio warrants further investigation, as it is a plausible method to monitor change within a limb in a growing child or where bilateral lymphoedema is present.

Despite the suggested differences in pediatric lymphoedema presentation the research about pediatric lymphoedema management has mostly assessed the outcomes of adult management practices based on the outcomes of secondary lymphoedema research [2,31, 32]. Historic literature recommends the use of compression using garments or bandaging [3,8,9]; although the style and options for application of compression have changed over time, its use has been consistent in the management of lymphoedema. Single use cohesive bandages changed only two or three times per week, and padded systems that may be re-used are now available for use clinically compared with traditional short-stretch elastic bandages changed daily. Pneumatic compression has evolved from being non-segmented and beginning distally [9,21] to a segmented, sequential application [22,25]. The use of pneumatic compression devices varies considerably globally: in some countries it is used as standard treatment in home programs; in other countries it is a novel treatment modality or compression whether pneumatic or not, is un-

available due to factors of cost and availability. Five studies in this review (retrospective, prospective and case study) assessed pneumatic compression and all reported favorable outcomes without adverse effects in the management of pediatric lymphoedema. While larger, more robust research, which defines optimal application parameters is required, it appears that pneumatic compression is useful in the management of pediatric lymphoedema.

A novel approach using cervical stimulation for the management of pediatric lymphoedema has been investigated [19]. Although positive outcomes were reported, some participants were concurrently prescribed compression garments to manage fibrosis noted in the limb [19] and the outcomes of treatment may not be a direct result of the stimulation.

The first trials of low level laser therapy (LLLT) for lymphoedema management were published in 1998 [33]. Since then there have been favorable reports regarding its use in the management of breast cancer related lymphoedema (BCRL) [34–36]. Only one case study (N = 1) has investigated the use of LLLT for primary, pediatric lymphoedema [23]. While the outcome was positive and there were no adverse effects, further research is required.

While it is reassuring that no adverse effects from adult management strategies were reported, the literature did not provide evidence that current, adult based management interventions are providing optimal outcomes for children. Further research is needed to determine if the different precipitator of lymphoedema in different age groups (congenital versus trauma) requires a different treatment approach. No studies were identified that compared adult and pediatric outcomes using the same management.

Seven studies in this review cited the prevalence of primary lymphoedema from Smeltzer et al. [9] who calculated an incidence rate of 1.15/100,000 population less than age 20 years. This rate was based on one town that over the study period (1955–1974) had an average population of 17,800 people. Four diagnoses of primary lymphoedema were made during the twenty years of this study and from this, an incidence rate was calculated. The external validity of extrapolating these figures as the prevalence worldwide and over time is questionable.

Many interventions described in this review required substantial and ongoing parental time and significant costs were likely to have been incurred where therapist intervention was provided on a daily basis [19, 20,24,25]. As the number of working mothers has increased the impost of attending treatment, and its impact on employment as well as the ongoing time commitment to supervise and deliver home therapy may contribute to increased family distress. The psychological impact of pediatric lymphoedema on families has been reported [4,5] and the financial and time costs of treatment which contribute to this impact, has been noted in pediatric chronic illness [37]. Further, access to pediatric services in Australia is limited to a few specialist centers and small numbers of therapists. Poor access to treatment and limited services underpin the need for efficient evidence based practice in order to minimize the burden of treatment on families and optimize self-management.

8. Limitations of this systematic review

This review did not include languages other than English; however the use of broad search terms, examination of study reference lists and unrestricted dates provides confidence in the rigor of this English language review.

9. Conclusion

Limited, poor quality evidence is available to guide management of pediatric lymphoedema. This review has found limited evidence to support the use of compression therapy, including the use of pneumatic compression, in pediatric lymphoedema; however specific parameters for application of compression are unable to be provided. While descriptive studies report differences in pediatric and adult lymphoedema presentation, there is no research that has investigated the response of different age groups within the lymphoedema community to the same intervention and no large scale, high quality studies to evaluate interventions commonly used in the management of pediatric lymphoedema. This research is vital to ensure treatment resources are efficiently allocated and provide optimal outcomes for children with lymphoedema.

Conflict of interest

The authors have no conflict of interest to declare.

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