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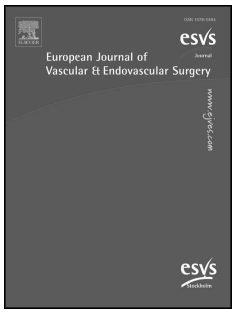

Prevalence and Clinical Characteristics of Chronic Venous Insufficiency among Individuals with Lower Extremity Lymphoedema: A Systematic Review and Meta-analysis

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<RRH>Venous Insufficiency in Lower Extremity Lymphoedema: Systematic Review

<LRH>Daniel Önefäldt *et al.*

<DOC>SYSTEMATIC REVIEW

<AT>Prevalence and Clinical Characteristics of Chronic Venous Insufficiency among Individuals with Lower Extremity Lymphoedema: A Systematic Review and Meta-analysis

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<TXBX>WHAT THIS PAPER ADDS

Chronic venous insufficiency (CVI) is increasingly recognised as a contributor to lower extremity lymphoedema, but its prevalence in patients suffering from lymphoedema remains inconsistently reported. This systematic review and meta-analysis provides pooled prevalence estimates showing that approximately half of individuals with lower extremity lymphoedema have coexisting CVI, with similar findings in sensitivity analyses restricted to studies with clearer diagnostic definitions. The review also highlights substantial heterogeneity and inconsistent reporting of diagnostic criteria and clinical characteristics, underscoring the need for standardised venous and lymphatic assessment and reporting frameworks in clinical practice and future research.

<BEGIN ABSTRACT>

Objective: Lower extremity lymphoedema is increasingly recognised as a multifactorial condition in which chronic venous insufficiency (CVI) may play an important role. This study aimed to estimate the pooled prevalence of CVI among individuals with lower extremity lymphoedema and to summarise clinical characteristics of patients with combined disease.

Data Sources: PubMed, Web of Science, and the Cochrane Library were searched from database inception through 13 November 2025.

Review Methods: Observational studies reporting CVI among individuals with lower extremity lymphoedema were included. Study selection, data extraction, and risk of bias assessments were performed independently by two reviewers. Pooled prevalence was estimated using a random effects generalised linear mixed model.

Results: Eighteen studies were included; 12 contributed to the prevalence meta-analysis, comprising 1 563 individuals with lower extremity lymphoedema, of whom 570 had coexisting CVI. The pooled prevalence was 45.7% (95% confidence interval [CI] 31.0 – 61.2%; GRADE, very low certainty evidence), with substantial heterogeneity (I^2 = 95.6%). In a restricted analysis limited to five studies with clearer case definitions, systematic venous assessment, and well defined denominators, pooled prevalence was 48.8% (95% CI 23.1 – 75.1%; very low certainty evidence), with persistent heterogeneity (I^2 = 92.2%). Ten studies reported descriptive data, including 1 111 individuals with combined disease. The pooled female proportion was 66.3%. Age and body mass index varied widely. Diagnostic criteria and clinical characteristics were inconsistently

reported. Quality of life outcomes were assessed infrequently and inconsistently. Most studies demonstrated moderate to high risk of bias.

Conclusion: CVI was present in approximately half of patients with lower extremity lymphoedema across diverse clinical settings. Marked heterogeneity reflects differences in diagnostic criteria, study populations, and reporting practices. Routine evaluation of venous disease in patients with lower extremity lymphoedema should be considered. Standardised diagnostic and reporting frameworks are needed in future research.

<END ABSTRACT>

<KW>**Keywords:** Lower extremity, Lymphoedema, Meta-analysis, Prevalence, Systematic review, Venous insufficiency

<H1>INTRODUCTION

<p>Lymphoedema is a chronic, progressive disorder of interstitial fluid homeostasis that produces profound functional impairment, recurrent infection, and reduced quality of life (QoL). Lower extremity lymphoedema is increasingly recognised as a multifactorial disorder in which venous pathology may play an important role. Several studies have shown that chronic venous insufficiency (CVI) or “phlebolymphoedema” contributes to lower extremity lymphoedema in real world vascular practice.[1–5]

<p>Anatomic and physiological coupling of the venous and lymphatic systems may explain this clinical overlap. Venous hypertension increases capillary filtration and interstitial protein load and, over time, produces dermal fibrosis and lymphatic overload; conversely, lymphatic failure alters interstitial compliance and calf pump dynamics, promoting venous stasis and valvular incompetence.[6–9] These bidirectional mechanisms produce a continuum of disease, from primarily venous oedema with secondary lymphatic impairment to primary lymphatic failure complicated by venous incompetence, which has been termed phlebolymphoedema.[10–12]

<p>The clinical implications of concomitant CVI and lower extremity lymphoedema are significant. Patients with combined disease demonstrate greater limb volumes, more severe skin trophic change, higher cellulitis rates, and poor responses to conventional decongestive therapies than patients with isolated lymphoedema.[2,13,14] Equivalently, patients with combined venous and lymphatic pathology are more likely to present with higher clinical class in the Clinical–Etiological–Anatomical–Pathophysiological (CEAP)

scoring of CVI, as lymphoedema related swelling and skin changes overlap with features defining C3 and C4 disease and may inflate clinical severity scores independent of venous disease.[7,15] In patients referred for evaluation of lower extremity lymphoedema or chronic swelling, duplex ultrasonography and magnetic resonance venography can reveal concomitant venous reflux or obstruction not suspected on clinical assessment alone, indicating potential under recognition of venous contributors in routine diagnostic pathways.[4,16,17] Lymphoscintigraphy remains the reference technique for assessing lymphatic dysfunction but cannot adequately assess concurrent venous pathology.

<p>There is limited knowledge on the prevalence of CVI in patients with lower extremity lymphoedema across heterogenous populations and diagnostic methods.[6,18,19] Although the CEAP classification offers a standardised approach to grading chronic venous disease, it does not account for lymphatic dysfunction and may have limited discriminatory value in patients with combined CVI and lower extremity lymphoedema, where oedema, skin changes, and tissue fibrosis may arise from overlapping mechanisms.[15,17] If venous disease is a common and underappreciated finding in patients with lower extremity lymphoedema, then screening algorithms (duplex imaging), compression strategies, and indications for venous intervention should be explicitly integrated into lymphoedema care pathways. Currently, there are no established guidelines or recommendations on when and how concomitant evaluation of venous and lymphatic dysfunction should be performed in patients with lower extremity lymphoedema. The European Society for Vascular Surgery (ESVS) guidelines on the

management of chronic venous disease of the lower limbs do not propose evaluation of the lymphatic system in any of their recommendations.[20] Equivalently, there is no established consensus on whether evaluation of the venous system should be an integrated part of clinical assessment of patients presenting to lymphoedema clinics with lower extremity lymphoedema.[21,22]

<p>This systematic review and meta-analysis was designed to determine the pooled prevalence of CVI among individuals with lower extremity lymphoedema and to compare the clinical characteristics of patients with combined CVI and lower extremity lymphoedema to those with lower extremity lymphoedema alone.

<p>The specific aims were as follows. The primary aim was to estimate the pooled prevalence of CVI among individuals with lower extremity lymphoedema. Secondary aims were to assess venous disease features (CEAP class, reflux segments) in patients with combined lower extremity lymphoedema and CVI and to compare demographic and clinical characteristics (e.g., age, sex, body mass index [BMI], comorbidities), limb burden (volume, bioimpedance), and QoL between combined lower extremity lymphoedema and CVI and lower extremity lymphoedema only.

<H1>METHODS

<p>This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.[23] The study protocol was prospectively registered and is available in the

International Prospective Register of Systematic Reviews (PROSPERO; registration no. CRD420251170287).

<p>Studies were eligible if they included individuals with lower extremity lymphoedema, regardless of aetiology, clinical setting, or geographic location. Eligible study designs included cohort studies, analytical cross sectional studies, registry or administrative database analyses, and case series with at least ten participants. Eligibility was restricted to full text articles published in English from 1990 onward.

<p>For the primary outcome, studies were required to report sufficient data to calculate the prevalence of CVI among individuals with lower extremity lymphoedema, defined as the number of participants with CVI and lower extremity lymphoedema divided by the total number of participants with lower extremity lymphoedema. Studies in which these groups could not be reliably determined were not eligible for the prevalence meta-analysis.

<p>For secondary outcomes, studies were eligible if they reported descriptive clinical characteristics of a clearly defined CVI and lower extremity lymphoedema subgroup, even if prevalence data were not available or could not be validly calculated.

<p>Studies were excluded if they: (1) included only upper extremity lymphoedema; (2) reported mixed limb populations without separable lower extremity data; (3) examined oedema not attributed to lymphatic dysfunction unless lower extremity lymphoedema

was explicitly diagnosed by the study authors, regardless of whether the diagnostic method was fully specified; (4) were interventional studies without baseline data; or (5) were case reports or case series with fewer than ten participants. Reviews, editorials, and conference abstracts without full data were excluded.

<p>A systematic literature search was conducted across PubMed, Web of Science, and the Cochrane Library from database inception through 13 November 2025. Eligibility criteria were applied during the screening process. Full search strategies and documentation are provided in Supplementary Table S1.

<p>Following deduplication, titles and abstracts were screened independently by two reviewers (D.Ö. and S.H.A.) using a blinded process. After completion of blinded screening, disagreements were resolved by consensus, and records meeting inclusion criteria by consensus proceeded to full text review.

<p>Full text articles were assessed independently by two reviewers (D.Ö. and S.H.A.), with discrepancies resolved through discussion or adjudication by a third reviewer (M.M.). Reasons for exclusion at the full text stage were documented and are reported in the PRISMA flow diagram (Fig. 1).

<p>Data extraction was performed using a standardised data collection form with pre-specified variables that was iteratively refined during extraction. Two reviewers extracted study characteristics, diagnostic criteria for lower extremity lymphoedema and

CVI, and outcome data relevant to the primary and secondary objectives. Data extraction was completed by both reviewers, with discrepancies resolved by discussion.

<p>For the primary outcome, data extracted included the total number of participants with lower extremity lymphoedema and the number of participants with combined CVI and lower extremity lymphoedema, allowing calculation of study level prevalence estimates where reported.

<p>Secondary data were extracted descriptively for participants with combined CVI and lower extremity lymphoedema and included demographic characteristics (age, sex), anthropometric measures (BMI), venous disease features (e.g., CEAP class), and QoL instruments used. Comorbidities, limb volume, and bioimpedance measures were largely missing and were not synthesised. Secondary outcomes were summarised descriptively only.

<p>Outcomes reported using different summary measures were recorded as reported.

<p>Risk of bias was assessed using the Joanna Briggs Institute (JBI) critical appraisal tools appropriate to each study design (cohort, analytical cross sectional, or case series).[24,25] Because prevalence of CVI was a secondary finding in most included studies, an additional prevalence specific risk of bias assessment was conducted using a three item domain evaluating: (1) clarity of case definitions for CVI and lower extremity lymphoedema; (2) completeness and consistency of CVI assessment across

participants; and (3) clarity of the denominator used for prevalence estimation, i.e., the total lower extremity lymphoedema group. Each item was judged as low, high, or unclear risk of bias.

<p>The prevalence specific domain did not replace the design specific JBI appraisal but supplemented it for the purpose of the prevalence meta-analysis. Sensitivity analyses were performed excluding studies at high risk of prevalence extraction bias and, in addition, excluding studies with exclusively primary lymphoedema patients.

<p>Certainty of evidence for the primary outcome was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework adapted for prognostic and risk estimates in observational studies, in which evidence from observational studies start at high certainty and may be downgraded based on methodological limitations.[26,27]

<H2>Statistical analysis

<p>Pooled prevalence estimates were calculated using a random effects generalised linear mixed model with a logit link function, implemented using the *metaprop()* function in R. Between study variance (τ^2) was estimated using maximum likelihood, and random effects confidence intervals (CIs) were calculated using the Hartung–Knapp method.

<p>Statistical heterogeneity was assessed using Cochran's *Q* statistic, the I^2 statistic, and τ^2. Prediction intervals were calculated to reflect between study variability.

Individual study confidence intervals were calculated using the Clopper–Pearson method.

<p>A pre-specified sensitivity analysis restricted the meta-analysis to studies meeting all three prevalence specific methodological criteria (clear case definitions, complete CVI assessment, and a clearly defined denominator for the lower extremity lymphoedema group).

<p>Secondary outcomes describing clinical characteristics of participants with combined CVI and lower extremity lymphoedema were summarised descriptively. The proportion of females was pooled using the method described above; otherwise meta-analysis or meta-regression of secondary outcomes was not performed because of sparse and heterogeneous reporting.

<p>All analyses were performed using R version 4.5.2 (R Foundation for Statistical Computing, Vienna, Austria). Data are available from the corresponding author upon reasonable request.

<H1>RESULTS

<H2>Study selection

<p>The database search identified 1 749 records. After removal of duplicates, 835 unique records were screened at the title and abstract level, of which 779 were

excluded. Eighteen studies met the inclusion criteria and were included in the systematic review and meta-analysis.[2,4,6,8,9,11–13,17,28–36] One study was excluded during the review process due to absent outcomes.[37] The study selection process is summarised in the PRISMA flow diagram (Fig. 1).

<H2>Study characteristics

<p>The characteristics of the 18 included studies are summarised in Table 1. Studies were published between 2000 and 2025 and were conducted across multiple geographic regions, including North America, Europe, Africa, and Asia.

<p>Included studies comprised cohort studies, analytical cross sectional studies, and case series. Twelve studies reported data suitable for inclusion in the primary prevalence meta-analysis.[2,4,6,8,9,11,28,32–36] Of these, four studies also reported descriptive clinical characteristics of participants with combined CVI and lower extremity lymphoedema,[6,8,32,33] while six additional studies contributed secondary descriptive data only.[12,13,17,29–31]

<p>Diagnostic criteria for CVI and lower extremity lymphoedema varied substantially across studies (Supplementary Table S2), as did the scope and completeness of outcome reporting.

<H2>Risk of bias

<p>Risk of bias assessments for the included studies are summarised in Supplementary Figure S1. Overall, most studies demonstrated moderate to high risk of bias, reflecting limitations in study design, outcome assessment, and reporting.

<p>In addition, a prevalence specific methodological assessment evaluated three criteria relevant to prevalence estimation: (1) clarity of case definitions; (2) whether CVI was assessed in all lower extremity lymphoedema participants included in the study sample; and (3) whether the total number of participants with lower extremity lymphoedema used to calculate prevalence was clearly defined. These factors informed the restricted sensitivity analysis of prevalence estimates.

<p>Regarding publication bias, visual inspection of the funnel plot for the primary prevalence meta-analysis did not demonstrate pronounced asymmetry (Fig. 2). Interpretation is limited by the small number of included studies and substantial between study heterogeneity; therefore, formal statistical tests for funnel plot asymmetry were not performed.

<H2>Prevalence of chronic venous insufficiency in lower extremity lymphoedema

<p>The 12 studies reporting data on the prevalence of CVI among individuals with lower extremity lymphoedema included a total of 1 563 participants with lower extremity lymphoedema, of whom 570 had coexisting CVI.[2,4,6,8,9,11,28,32–36] These 1 563 patients were identified from a combined study population consisting of 2 437 patients, which in

several studies also included participants without lower extremity lymphoedema. In accordance with the study objective, prevalence calculations were restricted to participants with lower extremity lymphoedema. Demographic data were inconsistently reported for the extracted CVI and lower extremity lymphoedema subgroup; therefore, demographics are summarised at the total study population level ($n = 2\,437$). Across 12 studies reporting sex distribution, the pooled proportion of female participants was 46.0% (95% CI 26.9 – 66.4%), with substantial between study heterogeneity ($I^2 = 97.1\%$; $\tau^2 = 1.67$).[2,4,6,8,9,11,28,32–36]

<p>Age was reported as a mean in nine studies (range 54.0 – 69.9 years) and as a median in two studies (range 58.0 – 68.4 years), although these two studies also reported mean age. Three studies did not report age at the study level. Study level demographics and clinical characteristics are summarised in Supplementary Table S3.

<p>The pooled prevalence of CVI among individuals with lower extremity lymphoedema was 45.7% (95% CI 31.0 – 61.2%) (Fig. 3). Substantial between study heterogeneity was observed ($I^2 = 95.6\%$; $\tau^2 = 0.84$), and the Q test for heterogeneity was statistically significant ($p < .001$). The certainty of evidence for this estimate was rated as very low according to GRADE (Supplementary Table S4), reflecting serious limitations across multiple domains.

<p>The prediction interval for the pooled prevalence estimate ranged from 9.2% to 87.5%, indicating considerable between study variability. The numeric table including meta-analysis weights is available in Supplementary Table S5.

<H2>Sensitivity analysis

<p>In the restricted sensitivity analysis including only studies meeting all three prevalence specific methodological criteria (five studies), the pooled prevalence of CVI among individuals with lower extremity lymphoedema was 48.8% (95% CI 23.1 – 75.1%; very low certainty evidence) (Fig. 4).[4,6,33,34,36] The numeric table including meta-analysis weights is available in Supplementary Table S6. Duplex ultrasonography was used to assess CVI in all participants in three of the five studies. All studies included populations with secondary or mixed lymphoedema aetiology. Four studies were cohort studies and one was a case series.

<p>Between study heterogeneity remained substantial but was reduced compared with the primary analysis ($I^2 = 92.2\%$; $\tau^2 = 0.76$). The prediction interval in the restricted analysis ranged from 6.1% to 93.3%.

<p>Exclusion of studies with exclusively primary lymphoedema patients (one study[11]) from the primary analysis resulted in a pooled prevalence of CVI among individuals with lower extremity lymphoedema of 43.5% (95% CI 28.9 – 59.3%; very low certainty evidence) with persistent heterogeneity ($I^2 = 95.9\%$; $\tau^2 = 0.80$) in the 11 included studies.[2,4,6,8,9,28,32–36]

<H2>Secondary outcomes

<p>Ten studies contributed secondary descriptive data, including a total of 1 111 participants with combined CVI and lower extremity lymphoedema.[6,8,12,13,17,29–33] Demographic characteristics are summarised in Supplementary Table S7, while categorical clinical variables related to lymphoedema aetiology, laterality, diagnostic criteria, and venous disease classification are presented in Supplementary Table S8. Secondary outcome data were heterogeneous and incompletely reported.

<p>Across nine studies reporting sex distribution for the combined CVI and lower extremity lymphoedema subgroup, the pooled proportion of female participants was 66.3% (95% CI 50.1 – 79.4%), with substantial between study heterogeneity (I^2 = 90.9%; τ^2 = 0.66). Female proportions ranged from 31.3% to 88.9%.[6,8,12,13,17,29–32] Reported age and BMI varied widely. Mean age ranged from 40.2 to 71.7 years and median age from 48 to 63 years. BMI was generally in the obese range, with the mean BMI ranging from 25.0 to 45.6 kg/m^2 and the median BMI from 33.0 to 42.8 kg/m^2 where reported, although BMI data were missing in five of the ten studies contributing demographic information.

<p>Lymphoedema aetiology was most commonly reported as secondary (four studies), while three additional studies included mixed aetiologies. Bilateral (one study) or mixed unilateral and bilateral presentation (four studies) predominated, although laterality was unclear in five studies. Diagnostic methods were unclear in three studies for lower

extremity lymphoedema and three studies for CVI. Formal venous disease classification using CEAP was reported in six studies.[6,17,29–32] One study included exclusively C6 patients,[31] one included only C3 patients,[17] and one reported proportions across CEAP classes C3–C6.[29] In the remaining studies, CEAP classes were mixed or insufficiently reported to allow reliable extraction (Supplementary Table S8).

<p>QoL outcomes were reported infrequently and assessed using multiple instruments. Instruments used included the SF-36 (three studies[2,33,35]), CIVIQ-20 (two studies[17,30]), CIVIQ-2 (one study[34]), LYMQOL (one study[33]), and Wound-QoL-17 (one study[28]). No single QoL instrument was used consistently across studies, precluding quantitative synthesis. In addition, no study reported QoL outcomes stratified by venous status, precluding comparison between individuals with lower extremity lymphoedema and those with combined CVI and lower extremity lymphoedema.

<p>Limb volume measurements, bioimpedance data, and comorbidity information were sparsely reported and therefore not synthesised.

<H1>DISCUSSION

<p>In this systematic review and meta-analysis, CVI was identified in nearly half of individuals diagnosed with lower extremity lymphoedema, with a pooled prevalence of 45.7% (very low certainty evidence). This estimate remained stable (48.8%; very low certainty evidence) in a restricted analysis limited to studies with clearer case definitions, systematic venous assessment, and well defined denominators, suggesting

that CVI is commonly observed in adult lower extremity lymphoedema populations rather than an incidental finding. Despite the high pooled prevalence, only a limited number of studies reported both prevalence data and detailed clinical characteristics of the combined CVI and lower extremity lymphoedema population. Secondary outcomes were inconsistently reported, highlighting important gaps in the existing literature. Despite the very low certainty of evidence, the consistency of findings across sensitivity analyses and the biological plausibility of venous–lymphatic interaction supports the clinical relevance of these observations. Importantly, this review was designed to estimate the prevalence of CVI among individuals with lower extremity lymphoedema and does not permit inference regarding the directionality or causality of this association. The included studies were not designed to evaluate whether CVI leads to lower extremity lymphoedema, or *vice versa*, and the findings should therefore be interpreted strictly within this descriptive framework.

<p>These results challenge the traditional conceptual separation between venous oedema and lymphoedema that continues to shape diagnostic algorithms and referral pathways. Instead, they support the growing recognition of phlebolymphoedema as a frequent and clinically important phenotype in adult patients presenting with chronic lower extremity swelling, particularly in vascular and wound care settings.[18,38]

<p>Prevalence estimates of CVI among individuals with lower extremity lymphoedema varied substantially across included studies, ranging from 12.5% to 77.8%. Heterogeneity was substantial in both the primary and restricted analyses ($I^2 > 90\%$).

This degree of heterogeneity is expected in prevalence syntheses spanning diverse aetiologies, clinical settings, and diagnostic approaches. Such heterogeneity indicates that most of the observed variability in prevalence estimates reflects real differences between studies rather than random sampling error. Lower extremity lymphoedema constitutes a heterogeneous clinical syndrome resulting from multiple primary and secondary pathophysiological mechanisms.[18,19,22] Differences in case definitions and ascertainment methods likely contributed materially: CVI was variably defined using clinical criteria with or without CEAP classification, duplex ultrasonography, or venography, while lower extremity lymphoedema diagnosis ranged from clinical assessment to lymphoscintigraphy. In addition, reliance on clinical criteria alone may introduce misclassification, as features such as oedema and stasis related skin changes can occur in obesity and lymphoedema in the absence of demonstrable venous reflux, potentially leading to overestimation of CVI prevalence in studies without systematic duplex or imaging confirmation. Variation in lymphoedema aetiology, including primary or genetically defined disease, may also have contributed to heterogeneity through differences in underlying pathophysiology. Referral and spectrum bias may further contribute to this variability, as studies derived from venous or wound care settings may apply different diagnostic thresholds and include patients with different underlying disease distributions than cohorts recruited from lymphoedema or reconstructive surgery services. These methodological differences directly affect case diagnosis and are known to yield substantially different prevalence estimates.[4,9] Accordingly, the pooled estimate should not be interpreted as a true population level prevalence but rather as an average across heterogeneous contexts, and the wide prediction intervals

observed in both analyses emphasise that prevalence is likely to differ substantially across specific clinical populations.

<p>The frequent coexistence of CVI and lower extremity lymphoedema observed in this review is consistent with established concepts of venous–lymphatic interdependence; however, the present findings do not allow conclusions regarding causal or bidirectional relationships between these conditions. Obesity is likely to contribute to this overlap, as higher BMI is associated with both lymphatic dysfunction and more severe chronic venous disease. Increased adiposity may increase venous hypertension and tissue fluid burden while also impairing lymphatic transport capacity, potentially inflating the observed prevalence of combined CVI and lower extremity lymphoedema in cohorts with high mean BMI.[39,40] Chronic venous hypertension can increase capillary filtration and interstitial protein load, which may progressively overwhelm lymphatic transport capacity and lead to lymphatic dilation, valvular incompetence, inflammation, and fibrosis.[18,20] Over time, this process results in structural lymphatic failure rather than purely functional overload. Conversely, primary or secondary lymphatic dysfunction alters interstitial compliance, increases tissue pressure, and impairs calf muscle pump efficiency, thereby promoting venous stasis and reflux.[21] These mechanisms provide a biologically plausible framework that may explain the observed coexistence of CVI and lower extremity lymphoedema, consistent with the concept of phlebolymphoedema.[18,38]

<p>While imaging based studies have reported venous reflux or obstruction in patients referred for presumed primary lymphoedema, the findings of this review do not establish

causality or directionality; rather, they support routine consideration of both venous and lymphatic contributors when evaluating chronic lower extremity swelling.[4,41]

<p>The findings of this review have practical clinical implications. Underdiagnosis of CVI may partially explain suboptimal responses to conservative decongestive therapies, as persistent venous hypertension continues to drive interstitial fluid accumulation despite appropriately targeted lymphatic interventions. Components of complex decongestive therapy, particularly manual lymphatic drainage, can reduce venous reflux indices, oedema, clinical severity, and symptoms in CVI, and can increase venous flow velocity on duplex assessment, indicating that lymphatic focused techniques may positively influence venous haemodynamics when venous dysfunction is concurrently recognised and addressed.[42] Misclassification of underlying venous disease risks delaying appropriate intervention in patients with treatable reflux or obstruction, potentially allowing progression to more advanced combined venous–lymphatic dysfunction. These considerations support routine venous assessment, most commonly with duplex ultrasonography, as part of the diagnostic workup for adults presenting with lower extremity lymphoedema.

<p>Beyond individual clinical decision making, these findings also have implications at the guideline level, as current venous and lymphoedema management frameworks largely address these conditions separately, despite their frequent coexistence in clinical practice. These findings primarily support improved diagnostic standardisation and more systematic assessment of venous disease within future guideline frameworks.

From a health system perspective, recognition of combined venous–lymphatic disease is also relevant, as phlebolymphoedema has been associated with higher infection rates, increased symptom burden, impaired QoL, and greater healthcare utilisation.[18,43]

<p>This study has several limitations, including the very high between study heterogeneity, limiting the generalisability of a single pooled prevalence estimate. In particular, the included studies were not designed to evaluate causal relationships between CVI and lower extremity lymphoedema. Diagnostic criteria for both CVI and lower extremity lymphoedema varied substantially across studies, and many studies provided limited methodological detail. Reporting of secondary outcomes was sparse and inconsistent, precluding quantitative synthesis of clinical characteristics such as limb volume, bioimpedance, comorbidities, and QoL outcomes. QoL outcomes were additionally difficult to interpret because instruments were heterogeneous and not consistently aligned with the combined CVI and lower extremity lymphoedema phenotype. The SF-36 is a generic health status measure and may lack sensitivity to detect disease specific change in chronic limb swelling.[44] CIVIQ-20 and CIVIQ-2 were developed for chronic venous disease and therefore may not capture key lymphoedema specific domains such as infection related morbidity and functional limitations driven by lymphatic failure.[45] Conversely, Wound-QoL is designed for chronic wound populations and may be poorly applicable to participants without active ulceration.[46] This variability, together with sparse reporting, limited comparability across studies and reinforces the need for future prospective cohorts to use both general and disease specific validated instruments selected to reflect venous, lymphatic, and (when relevant) wound related

burden. Finally, most included studies were observational and assessed as having moderate to high risk of bias, particularly case series.

<p>Clinically, the findings underscore the need to routinely consider both venous and lymphatic contributors when evaluating adults with lower extremity lymphoedema, rather than approaching these conditions as distinct entities. From a research perspective, the existing literature is limited by inconsistent diagnostic definitions and reporting practices for both CVI and lower extremity lymphoedema. Future studies should prioritise standardised diagnostic criteria and consistent assessment protocols, ideally within prospective cohorts that systematically report patient centred outcomes with both general and disease specific validated questionnaires. Addressing these gaps will be essential to improve comparability across studies and to better characterise populations with combined venous and lymphatic dysfunction.

<p>These findings generate the hypothesis that recognising and treating coexisting venous pathology may improve responses to conservative therapies, optimise outcomes of lymphatic surgical interventions, prevent disease progression, and reduce patient morbidity and healthcare burden. These hypotheses should be explored in prospective studies.

<H2>Conclusions

<p>CVI appears to be common among individuals with lower extremity lymphoedema; however, the certainty of evidence is very low and substantial heterogeneity limits the

generalisability of this estimate. Clinically, these findings underscore the importance of standardised integrated assessment and management strategies that address both venous and lymphatic components and prospective studies to better define the clinical relevance of concomitant disease.

<H1>CONFLICTS OF INTEREST

The authors declare that they have no financial or personal relationships that could have inappropriately influenced this work. No organisation or sponsor had any role in the study design; collection, analysis, or interpretation of data; writing of the report; or the decision to submit the article for publication.

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<H1>USE OF GENERATIVE AI TOOLS

During the preparation of this work the authors used ChatGPT 5.2 in order to support language editing, clarity, and organisation of the manuscript during drafting and

revision. All study design decisions, data extraction, analysis, interpretation of results, and final manuscript content were performed and verified by the authors. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Figure 1. PRISMA flow diagram illustrating identification, screening, eligibility assessment, and inclusion of the 18 studies included in the systematic review and meta-analysis of chronic venous insufficiency among individuals with lower extremity lymphoedema. Records were identified through a structured search across online databases. After removal of duplicates, records were screened at the title and abstract level, followed by full text assessment for eligibility. Reasons for exclusion at the full text stage are shown.

Figure 2. Funnel plot of prevalence estimates of chronic venous insufficiency among 1 563 individuals with lower extremity lymphoedema from 12 studies included in the primary meta-analysis. Funnel plot showing logit transformed prevalence estimates plotted against standard error. Each circle represents one study. The vertical dashed line indicates the pooled estimate and the diagonal dashed lines represent pseudo 95% confidence limits.

Figure 3. Forest plot showing study level prevalence estimates of chronic venous insufficiency (CVI) among 1 563 individuals with lower extremity lymphoedema (LEL) from 12 studies included in the primary meta-analysis. Squares represent study specific prevalence estimates and horizontal lines indicate 95% confidence intervals (CIs). The diamond represents the pooled random effects estimate, and the red line represents the prediction interval. Weights are approximate calculations presented for descriptive purposes only and not directly reported by the generalised linear mixed model.

Figure 4. Forest plot showing prevalence estimates of chronic venous insufficiency (CVI) among 660 individuals with lower extremity lymphoedema (LEL) from five studies included in the restricted sensitivity analysis. Squares represent study specific prevalence estimates and horizontal lines indicate 95% confidence intervals (CIs). The diamond represents the pooled random effects estimate, and the red line represents the prediction interval. Weights are approximate calculations presented for descriptive purposes only and are not directly estimated by the generalised linear mixed model.

Table 1. Characteristics of the 18 studies included in the systematic review of chronic venous insufficiency among individuals with lower extremity lymphoedema.

Author	Country/region	Design	Outcomes reported	Total study population	Total LEL	Total CVI	Diagnostic method for LEL	Diagnostic method for CVI
de Carvalho, 2020[32]	Brazil	Cross sectional	Both	64	34	9	Combined	Combined
Maldonado, 2021[33]	USA	Cohort	Both	178	74	53	Clinical	Imaging
Dean, 2020[6]	USA	Cohort	Both	440	440	184	Combined	Combined
Padovese, 2016[8]	Ethiopia	Case series	Both	511	511	64	Clinical	Clinical
Dissemond, 2025[28]	Germany	Cohort	Primary	343	118	73	Unclear	Clinical
Padberg, 2024[2]	USA	Cohort	Primary	179	179	112	Clinical	Unclear
Finkelstein, 2023[4]	USA	Cohort	Primary	121	25	12	Imaging	Imaging
Blumberg, 2016[34]	USA	Cohort	Primary	100	100	18	Clinical	Imaging
Baulieu, 2013[9]	Europe	Case series	Primary	41	41	19	Imaging	Clinical
Gethin, 2012[35]	Ireland	Cross sectional	Primary	418	11	4	Clinical	Clinical
Dean, 2011[36]	USA	Case series	Primary	21	21	15	Clinical	Combined
Mellor, 2010[11]	UK	Cross sectional	Primary	21	9	7	Clinical	Imaging

Murray-Ramcharan 2024[29]	USA	Cohort	Secondary	52	52	52	Unclear	Unclear
Jayaraj, 2024[30]	USA	Cohort	Secondary	192	192	192	Imaging	Imaging
Moon, 2023[31]	USA	Cohort	Secondary	5 466	299	5 466	Unclear	Clinical
Raju, 2012[17]	USA	Cohort	Secondary	443	72	443	Imaging	Combined
Mellor, 2007[12]	UK	Cross sectional	Secondary	30	15	NA	Clinical	Imaging
Földi, 2000[13]	Germany	Case series	Secondary	261	171	171	Clinical	Clinical

LEL = lower extremity lymphoedema; CVI = chronic venous insufficiency; NA = ??.

Studies are summarised according to geographic region, study design, outcomes reported, population size, and diagnostic methods used for LEL and CVI.

Diagnostic methods for LEL and CVI were categorised as clinical, imaging, combined (use of both clinical and imaging based assessments), or unclear if insufficient detail was available. Diagnostic approaches and reporting completeness varied substantially across studies.