

# Prevalence and incidence of cancer related lymphedema in low and middle-income countries: A systematic review and meta-analysis.

Eric Torgbenu (✉ [ERIC.L.TORGBENU@student.uts.edu.au](mailto:ERIC.L.TORGBENU@student.uts.edu.au))

University of Technology Sydney

Tim Lockett

University of Technology Sydney

Mark A. Buhagiar

University of Technology Sydney

Sungwon Chang

University of Technology Sydney

Jane L. Phillips

University of Technology Sydney

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## Research article

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# Abstract

**Background** Little is known about the prevalence and incidence in low and middle-income countries (LMICs) of secondary lymphedema due to cancer. This study aims to estimate the prevalence and incidence in LMICs of secondary lymphedema related to cancer and/or its treatment(s) and identify risk factors.

**Method** A systematic review and meta-analysis was conducted. Medline, EMBASE and CINAHL were searched in June 2019 for peer-reviewed articles that assessed prevalence and/or incidence of cancer-related lymphedema in LMICs. Risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies. Estimates of pooled prevalence and incidence estimates were calculated with 95% confidence intervals (CI), with sub-group analyses grouping studies according to: country of origin, study design, risk of bias, setting, treatment, and lymphedema site and measurement. Heterogeneity was measured using  $X^2$  and  $I^2$ , with interpretation guided by the Cochrane Handbook for Systematic Reviews.

**Results** Of 8766 articles, 36 were included. Most reported on arm lymphedema secondary to breast cancer treatment (n=31), with the remainder reporting on leg lymphedema following gynecological cancer treatment (n=5). Arm lymphedema was mostly measured by arm circumference (n=16/31 studies), and leg lymphedema through self-report (n=3/5 studies). Eight studies used more than one lymphedema measurement. Only two studies that measured prevalence of leg lymphedema could be included in a meta-analysis (pooled prevalence =10.0%, 95%CI 7.0 – 13.0,  $I^2$  =0%). The pooled prevalence of arm lymphedema was 27%, with considerable heterogeneity (95%CI 20.0 – 34.0,  $I^2$  =94.69%, n =13 studies). The pooled incidence for arm lymphedema was 21%, also with considerable heterogeneity (95%CI 15.0 – 26.0,  $I^2$  =95.29%, n =11 studies). There was evidence that higher BMI (>25) was associated with increased risk of arm lymphedema (OR: 1.98, 95%CI 1.45 – 2.70,  $I^2$  =84.0%,  $P$ < 0.0001, n =4 studies).

**Conclusion** Better understanding the factors that contribute to variability in cancer-related arm lymphedema in LMICs is an important first step to developing targeted interventions to improve quality of life. Standardising measurement of lymphedema globally and better reporting would enable comparison within the context of information about cancer treatments and lymphedema care.

## Background

Lymphedema is a distressing and often persistent condition that occurs when fluid accumulates in the extracellular tissue spaces causing swelling, predominately in the extremities (1). Lymphedema is classified as congenital, primary or secondary. Secondary lymphedema occurs as a sequelae to another condition, such as the surgical and/or radiation treatments of cancer (2, 3).

Lymphedema is characterised by heaviness and discomfort, decreased range of motion, recurrent skin infections, elephantiasis verruca nostra, recurrent skin ulcers, cutaneous angiosarcoma, as well as

psychological effects including depression, anxiety, and negative body image (4). These effects impact adversely on quality of life (5).

Systematic reviews of the estimates incidence and prevalence of cancer-related lymphedema have focused almost exclusively on high-income countries (HICs). A 2013 systematic review and meta-analysis found the incidence of unilateral arm lymphedema post breast cancer treatment ranged from 8.4% to 21.4% (6). Another systematic review estimated the prevalence of secondary lymphedema due to non-specific cancer in United Kingdom (UK) lymphedema specialist clinics (n=11,555) to be 2.05–3.99:1000 (7). Risk factors for lymphedema identified in the literature have included obesity at the time of a cancer diagnosis, receipt of chemotherapy, adjuvant radiation therapy, type of surgery, physiotherapeutic modalities, and number of lymph nodes removed (6, 8).

No review to date has reported on the pooled prevalence or incidence of lymphedema in LMICs and associated risk factors, making it difficult to advocate for and plan appropriate services to manage this condition.

### **Aim:**

To estimate the prevalence and incidence in LMICs of secondary lymphedema related to cancer and/or its treatment(s) and identify risk factors.

## **Methods**

A systematic review and meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO) [CRD42019137641] (9). This review is reported in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (10). This paper reports on the cancer-related lymphedema component of a larger review across lymphedema from all causes.

### **Eligibility Criteria**

Primary studies in peer-reviewed journals of any design that estimated prevalence or incidence of secondary lymphedema in a sample from a LMIC, as defined by The World Bank Group (11) criteria. Where studies evaluated an intervention, only the baseline data were included. Studies using various measures of secondary lymphedema, including self-report and objective measures were included. Where studies were published in languages other than English, native language speakers were contacted to do the extraction according to the predefined criteria. Editorials, comment papers, review papers, case reports, and case series were excluded.

### **Information Sources:**

Database searches were conducted of Medline, Excerpta medica database (EMBASE) and Cumulative Index of Nursing and Allied Health Literature (CINAHL). A hand search of the reference lists of included

studies was also performed.

## **Search Strategy**

Databases were searched on seventh of June 2019 without any limit on date or language. Subject headings and keywords related to lymphedema and LMICs. The initial search strategy was developed in Medline and adapted for other bibliographic databases (refer to Table 1).

[Insert Table 1]

## **Study Selection**

The first author (E.T.) assessed titles and abstracts of all citations retrieved by the search for relevance against the inclusion criteria, obtaining full texts as required to make a decision. 10% of articles were independently screened by a second author (T.L., M.B. or J.P.), with screening continued by E.T. alone after finding 100% agreement.

## **Data extraction**

Data were extracted by the first author (E.T.), with random checks performed by a second (T.L.). Data items extracted included: year and country, setting, aims, study design, sample size, sampling method, lymphedema site, stage, severity and duration, the type of management reported, and estimates of lymphedema prevalence or incidence.

## **Risk of bias (quality) assessment**

The first author (E.T.) independently assessed risk of bias for each study using the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies (12). 20% of articles were independently assessed by the second author (T.L.), with the remaining risk of bias assessment continued by E.T. alone after a 100% agreement. Disagreements were resolved by discussion or, and when necessary, a third person arbitrating. The tool consists of 9 items which assess the internal and external validity of studies included in the quantitative analysis (12). Studies were classified into low or high risk of bias using a cut-off of 70%.

## **Statistical Analysis**

Meta-analyses of incidence and prevalence data were undertaken separately in accordance with the Cochrane Handbook for Systematic Reviews, using a random effects models (13). The summary measure was the prevalent or incident percentage of people with lymphedema, with 95% confidence intervals. Following Ressing et al Heterogeneity between estimates was measured using  $\chi^2$  and  $I^2$  statistics, using recommended thresholds (15). For studies that used multiple lymphedema measurements, we prioritized the following measures based on level of objectivity (16, 17): 1) circumferential measurement (18); 2) perimetry (assessing difference in limb sizes, similar to the

circumferential measurement) (6); 3) limb volume measurement; 4) bioimpedance spectroscopy; or 5) self-report.

### **Analysis of subgroups or subsets**

Subgroup analyses were conducted on an a priori basis for studies classified according to whether or not estimation of prevalence/incidence was a stated aim of the study, and low risk of bias. Further subgroup analyses were conducted post hoc to explore any significant heterogeneity based on study characteristics such as country, setting, sample size, site and measurement of lymphedema and study design. Where studies were not considered sufficiently similar to be included in a meta-analysis, synthesis used a narrative approach based on the methods published by the Lancaster University, UK (19).

## **Results**

Of the 8766 articles that were retrieved, 1,231 articles were excluded due to duplication. The remaining 7,535 articles were evaluated, and 7,109 were excluded based on their title and abstract. Next, 426 full-text articles were assessed and 389 were excluded, leaving 36 articles for inclusion reporting 36 studies (Refer to Figure 1).

[Insert Figure 1]

### **Characteristics of included studies**

The majority of studies (n=34) focused on women (n=12145), while two studies (20, 21) involved both men and women. All studies were conducted between 2001 and 2019 and three studies (22-24) were reported in non-English language publications (Refer to table 2).

While the majority of studies were conducted in Brazil (n=12) and Turkey (n=9), most other regions with LMIC were represented, including: South America (n=12) (5, 20, 24-33), Europe (n=11) (21, 23, 34-42), Southern Asia (n=6) (43-48), West Africa (n=3) (22, 49, 50), Middle East (n=3) (51-53) and East Asia and Pacific (n=1) (54).

[Insert Table 2]

Most studies were cross-sectional (n=21), with a smaller number of prospective cohort (n=8), retrospective cohort (n=3) and case-control studies (n=4). The majority of studies (n=34) reported exclusively on either arm (n=30) or leg (n=4) lymphedema, while two (20, 50) reported on both. One study reported on lymphedema of the chest and arm secondary to breast cancer treatment (28). This study was the only study to use bioelectric impedance to diagnose lymphedema (28). Other methods used for measuring and defining lymphedema included: tape measurement (n=16) (21, 25, 32-34, 38, 39, 41-45, 48, 51-53); patient self-report (n= 8) (22, 26, 30, 40, 46, 47, 49, 54); water volumeter (n=2) (27, 35); palpation and clinical diagnosis (n=2) (29, 50); and perometer (n=1) (31).

Twenty-five studies reported lymphedema prevalence and 11 studies reported incidence.

Of the three studies that explored the risk of developing lymphedema associated with cancer staging both in the leg and arm, two involved women with breast cancer (41, 45) and the other, women with vulvar cancer (29). Four studies reported on the risk of developing arm lymphedema associated with breast cancer treatment among women who had sentinel lymph node biopsy (5, 21, 32, 42). Variations in the timing or the onset of cancer related lymphedema ranged from three months to over five years post diagnosis and treatment. The type of management received by women with cancer related lymphedema included: lymphatic drainage (42), physiotherapeutic modalities such as care for the affected limb, home exercises and self-lymphatic drainage (24, 26, 34), hormonal therapy (51) and neo-adjuvant therapy including radiotherapy and chemotherapy (25, 31).

## Synthesis

### Arm Lymphedema Following Breast Cancer Treatment

The majority of studies (n=31) reported arm lymphedema secondary to breast cancer treatment. However, lymphedema was defined differently based on the method of measurement used. Half of these studies (n=16) used circumferential measurements (21, 25, 32-34, 38, 39, 41-45, 48, 51-53). The remainder either used self-reports of swelling in the arms (n=5) (26, 30, 46, 47, 54), volumetric measurement (n=2) (27, 35), perimetry (n=1) (31) and/or bioimpedance spectrometry (n=1) (37). Six studies used more than one method of arm lymphedema diagnosis (5, 20, 23, 24, 27, 36).

Eleven studies (n=11) compared circumferential measurement in bilateral limbs using a range difference of  $\geq 2$  cm as indicative of lymphedema. One study from Brazil only used a difference of  $\geq 1$  cm circumferential measurement in the presence of any other two lymphedema symptoms of heaviness, swelling, tightness or firmness in the affected limb (5). Another study (23) which examined the upper extremity disorders among breast cancer women undergoing surgery measured lymphedema as circumferential measurement difference  $\geq 1.5$  cm in the affected limb. There was only one large population study involving Turkish women with breast cancer (n=5064), which used a cut-off difference of  $\geq 5$  cm in the affected limb as a diagnosis for lymphedema (34). All Turkish studies (n=7) measured arm lymphedema by the circumferential method, while the Brazilian (n=3) (24, 26, 30) and Indian (n=2) (46, 47) studies used patients' self-reports.

Studies which used the volumetric measurement defined lymphedema to be a cut-off difference in volume based on circumferential measurements of both limbs  $> 10\%$  percent (27, 35). Lymphedema was diagnosed as an impedance ratio of greater than 10 in the affected limb using the bioimpedance spectrometer (37).

### Prevalence of arm lymphedema following breast cancer treatment

The most common method of arm lymphedema measurement was arm circumference (n=16), while several studies (n=9) also used more than just one lymphedema measurement. One study used

lymphoscintigraphy as a technique in the measurement of lymphedema among Brazilian post-breast cancer women (32). All studies included in this review reported prevalence of arm lymphedema secondary to breast cancer treatment. Twenty-five studies reported prevalence estimates (5, 22, 23, 25-33, 35, 36, 38-40, 43, 44, 49-54). The prevalence estimate among post breast cancer treated women varied from 0.4% in Papua New Guinea (54) to 92.5% reported by a Brazilian study (35). The lowest estimate of 0.4% was reported by self-report of lymphedema(54). Of the two studies that reported on sentinel lymph node biopsy, the prevalence estimates were relatively low compared with other studies; 4.4% (95% CI 1.0 – 15.0) (32) and 17.0% (95% CI 11.0 – 27.0) (5).

Using data abstracted from 13 studies the pooled estimate for prevalence of breast cancer related lymphedema was 30 % (95% CI 24 – 37). There was considerable heterogeneity among studies ( $I^2=91.66\%$ ,  $p=0.001$ ) (refer to Figure 2). Heterogeneity was not reduced in a subgroup analysis of studies grouped by a single country, Brazil (pooled prevalence = 31%, 95% CI 19.0 – 43.0,  $I^2 = 87.21\%$ ,  $n = 5$  studies). Studies from the Middle East (i.e. Iran (51), Jordan (53) and Turkey (23)) demonstrated considerable heterogeneity ( $I^2= 94.69\%$ ,  $p=0.001$ ), which increased to considerable heterogeneity when a second Turkish study (39) was included ( $I^2= 99.67\%$ ,  $p=0.001$ ). The pooled prevalence recorded by the two Turkish studies was 37% (95% CI 32 – 42) among breast cancer women receiving treatment in cancer units (refer to Figure 3).

[Insert Figures 2 and 3]

#### Incidence of arm lymphedema following breast cancer treatment

Eleven (11) studies reported incidence of unilateral arm lymphedema (20, 21, 24, 34, 37, 41, 42, 45-48), while one study reported lymphedema of both arm and leg (20). The follow up periods varied among studies from 6 months to over 5 years post- cancer treatment.

The lowest incidence was 5.9% after breast cancer treatment in Romania (21) with a mean follow up period of 24 months, who received sentinel lymph node biopsy. The highest incidence was 56.7% recorded in an Indian study with 6-month follow up after modified radical mastectomy treatment for breast cancer patients (47). Breast cancer related lymphedema incidence in Turkey ranged from 7.2% recorded within a population sample with a median follow up of 64 months with a median follow up of 30 months after breast cancer treatment (41). The incidence of arm lymphedema reported by the Brazilian studies ranged from 17.5% to 23.2% (20, 24). The pooled incidence was 21% (95% CI 15.0 – 26.0,  $I^2 = 95.29\%$ ,  $n=11$  studies) with considerable heterogeneity, while that reported by circumferential measurement was 16% (95% CI 9.0 – 23.0,  $I^2=96.54\%$ ,  $n=6$  studies) (refer to Figure 4). The estimated pooled incidence by all other methods of assessment was between 16.0% (circumferential measurement) and 26.0% (self-report).

[Insert Figure 4]

#### Risk factors of lymphedema following breast cancer treatment

Ten of the 11 studies reporting on lymphedema risk factors, focused on the risk of developing arm lymphedema following breast cancer treatment (21, 31, 34, 38, 41-43, 45, 48, 52). One study (34) reported that individuals with body mass index (BMI) of  $\geq 30$  were 6.64 times more likely to develop arm lymphedema than those with BMI  $\leq 17.9$ . The risk of developing arm lymphedema among breast cancer women with BMI  $\geq 25$  ranges from the odds ratio (OR) of 1.5 to 5.9 compared to participants with BMI  $< 25$  (34, 38, 41, 48, 52). We obtained a pooled effect estimate OR of 1.98, 95% confidence interval (CI): 1.45 to 2.70 ( $P < 0.0001$ ;  $I^2 = 84.0\%$ ) in a random effect meta-analysis (refer to figure 5).

[Insert Figure 5]

Axillary radiotherapy treatment is a significant risk with an OR ranging from 2.7 to 4.4 (21, 38, 42). Four studies examined the risk of developing arm lymphedema associated with higher number of lymph node removal among breast cancer survivors (21, 38, 48, 52). The removal of lymph nodes of  $>25$  during mastectomy was associated with a risk of developing arm lymphedema [4.88 (OR 2.25–10.58)] among breast cancer woman compared with when less number of lymph nodes were removed (21). Higher nodal ratio [1.135 (Hazard ratio (HR) 1.037-1.243)] was also found to be associated with higher risk of arm lymphedema (48). Lumpectomy was not a significant risk factor for arm lymphedema (38).

Modified radical mastectomy was associated with an OR of 4.3 (95% CIs: 2.3 – 7.9) risk than those who did not and participants who received radiotherapy had an OR of 3.9 (95% CIs: 1.8 – 8.2) risk of developing arm lymphedema compared with those who did not (52). The length of time after surgery for breast cancer was also reported to be 9.7 times higher among breast cancer women who had surgery more than 5 years as compared to those with less years (31).

Other risk factors identified to significantly affect lymphedema among breast cancer survivors include: past history of limb damage had an OR of 1.7 (95% CIs: 0.9 – 3.1) (52), presence of a co-morbid condition with a HR of 0.1593 (95% CIs: 1.1441 – 2.9369) (43), post radiotherapy moist desquamation had an OR of 4.34 (95% CIs: 1.07–17.65) (45), and presence of seroma after breast cancer surgery (31). Women with breast cancer tumour invasion were 13.7 times at risk of developing arm lymphedema compared to those women who did not receive tumour invasion (52). Cancer stage was not significant in arm lymphedema following breast cancer treatment (31, 45) (refer to Table 3).

[Insert Table 3]

### **Leg lymphedema following gynecological cancer treatment**

All five studies that reported leg lymphedema used either patient self-report ( $n=3$ ) or palpation or clinical diagnosis ( $n=2$ ). Studies which used the self-report method of lymphedema diagnosis only used either palpation or observation methods of identifying lymphedema in the affected limbs of the patients (22, 40, 49). These were based on patients' reports of swelling in the legs alone. In the case of the clinical diagnosis, lymphedema was identified as present when a positive Stemmer's sign was recorded (50).

## Prevalence of leg lymphedema following gynecological cancer treatment

Of the five studies reporting on leg lymphedema, three focused on the prevalence of leg lymphedema secondary to cervical cancer treatment; two West African and one Romanian (22, 40, 50). The prevalence estimates were similar; 7.0% (95% CI 3 – 15) (22), 11.0% (95% CI 8 – 15) (40) and 13% (95% CI 7 – 23) (50). The three studies (22, 40, 50) that reported on leg lymphedema following cervical cancer reported a pooled prevalence of 10% (95% CI 7 – 13) with considerable heterogeneity. The method of measurement of lymphedema was self-report and none of these studies explored leg lymphedema risk factors.

Two studies reported leg lymphedema prevalence based on clinical diagnosis among women who received vulvectomy (29, 49). The prevalence varied widely from 60.1% in the Brazilian study to 9.1% in the Nigerian study (49).

The incidence of leg lymphedema was reported in only one study, which focused on patients following inguinal and ilioinguinal lymphadenectomies in Brazil and identified an incidence of 59.1% (20).

## Risk factors of lymphedema following vulvar cancer treatment

One study reported the risk of developing leg lymphedema following vulvar cancer treatment (29). The risk of leg lymphedema following vulvar cancer included age associated with an OR of 1.09 (95% CIs: 1.00 – 1.18) and a BMI with an OR of 1.34 (1.01 -1.77) (29) (refer to Table 3).

## Sub-group analyses

Planned sub-group analyses failed to significantly reduce heterogeneity. Heterogeneity based on: country of study publication and the type of cancer was 95.29%; study region was 93.85%; sample size, the type of measurement of lymphedema, and the design of the study were 94.69%. The level of heterogeneity was 97.2% ( $n=5$  studies) for incidence and 94.89% ( $n=6$  studies) for prevalence when focusing on low risk of bias studies (refer to table 4).

[Insert Table 4]

A post-hoc subgroup analysis was also conducted in which we removed from the meta-analyses all studies that had less than 24 months follow up ( $n = 5$ ). This too resulted in minimal improvement in heterogeneity.

## **Discussion**

This systematic review and meta-analysis is the first to attempt to estimate prevalence and incidence of lymphedema in LMICs. Arm lymphedema results were too heterogeneous to reliably estimate prevalence or incidence. Two studies suggest that the prevalence of leg lymphedema may be between 7% and 13% (22, 40), while only one study estimated incidence of leg lymphedema, estimating it to be 59.1%, focusing specifically on Brazilian patients following ilioinguinal lymphadenectomy (20).

Differences in study quality, sample size estimations, technique of sampling and study methodology typically form the bases for heterogeneity in meta-analysis of prevalence or incidence data, and this review is likely to be no exception. Lymphedema following cancer treatment might be influenced by lymphatic drainage, adjuvant radiation therapy, hormonal therapy, skin care, physiotherapeutic modalities such as simple home exercises, and self-lymphatic drainage techniques (55) and trastuzumab therapy and taxane-based chemotherapy but none of these variables were reliably reported. Risk factors for arm lymphedema following breast cancer treatment identified by this review did not differ from those identified by studies in HICs (6, 57, 58). BMI  $\geq 25$ , age above 60 years, having axillary radiotherapy treatment with axillary lymph node dissection,  $\geq 16$  lymph nodes removed, higher lymph node ratio, and increased engagement in moderate to severe physical activity were identified as the most significant risk factors of arm lymphedema. The number of lymph nodes typically removed in LMICs may be more compared to HICs because of later detection of cancer and differences in the type of treatment provided as standard. Such differences in treatments and health management practices in LMICs are likely to have accounted for at least some of the variation found between the current review and that conducted in HICs

While several different methods are available for measuring lymphedema, the majority of studies included in this review used the circumferential measurements and patients' self-reports. Circumferential measurement is a non-invasive, inexpensive and practical method of lymphedema measurement in the clinical setting (6, 60) with established reliability (61). Self-report, on the other hand, is open to subjective variability between patients and is typically used in the clinic to assess the patient's view of improvement (6, 60) and likely to report higher rates compared with the more objective lymphedema measurement methods like circumferential measurements (62). One study (37) reported on the use of bioimpedance spectroscopy in diagnosing lymphedema. Although this method has demonstrated high sensitivity and specificity, the equipment is expensive and few health facilities even in HICs are able to afford it (63), prohibiting its use in LMICs.

## **Limitations**

The limitations of this study arise from the limited number of available studies and incomplete reporting, especially with regard to disease stage and treatment. Studies were limited to a small range of countries in certain geographical regions. None of the studies controlled for premorbid lymphedema.

## **Implications for Future Research**

Notable gaps that should be filled by future research include studies of the prevalence of lymphedema in certain geographical regions, such as Africa. Because affected people may sometimes resort to traditional and other alternative treatment rather than hospitals in the first instance (64), community-based research may be necessary. In the absence of a gold standard lymphoedema measurement, reaching global consensus on the most reliable and feasible method of identifying lymphedema in LMICs would do much to enable comparability between studies, and to assess the impact of any treatments. Understanding the impact the role of social-determinates of health and culture have on lymphedema prevalence and incidence rates in LMICs are important areas for future research.

Lymph node sparing is considered an invaluable surgical method for lymphedema prevention (65). However, due to the quality of reporting we were unable to examine its impact on lymphedema prevalence or incidence in LMICs.

## Conclusion

This systematic review and meta-analysis was unable to reliably estimate the prevalence or incidence of lymphedema in LMICs due to heterogeneity (arm lymphedema) and small numbers of studies (leg lymphedema). Heterogeneity among estimates is likely due to differences in measurement methods, as well as variability in stage of cancer, treatments and other variables not reliably reported. Rates were higher according to self-report or compared with more objective measures, such as the clinical diagnosis or the circumferential measurements. Gaining consensus on how best to measure lymphedema in LMICs would enable comparability between studies and more reliable estimates. Better understanding the factors contributing to the wide variability in arm lymphedema is an important first step to developing targeted interventions to improve the quality of life of people living with cancer related lymphedema in LMICs.

## Abbreviations

LMIC: Low and middle-income countries

EMBASE: Excerpta medica database

CINAHL: Cumulative Index of Nursing and Allied Health Literature

CI: Confidence interval

PROSPERO: Prospective Register of Systematic Reviews

PRISMA: Preferred reporting items for systematic reviews and meta-analyses

BMI: Body mass index

HIC: High-income countries

UK: United Kingdom

OR: Odds ratio

HR: Hazard ratio

## Declarations

**Ethics approval and consent to participate**

This article is based on a secondary analysis of the existing literature and does not contain any studies with human participants or animals performed by any of the authors. The PRISMA guideline for conducting systematic and meta-analysis was followed.

### **Consent for publication**

Not applicable

### **Availability of data and material**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interests**

The authors declare that they have no competing interest.

### **Funding**

None

### **Authors' contributions**

All authors developed the protocol, and contributed to the study design, manuscript development, editing, and completion of the manuscript. The article search and management were performed by EL. Article screening was completed by EL, and TL, MAB, and JLP independently screened 10% of the articles. Quality assessment and study description were performed by EL and TL. The data analysis was done by SC and consensus discussions and finalising with EL, JP, TL, and MAB. Table design was completed by EL, JP, MAB, SC and TL.

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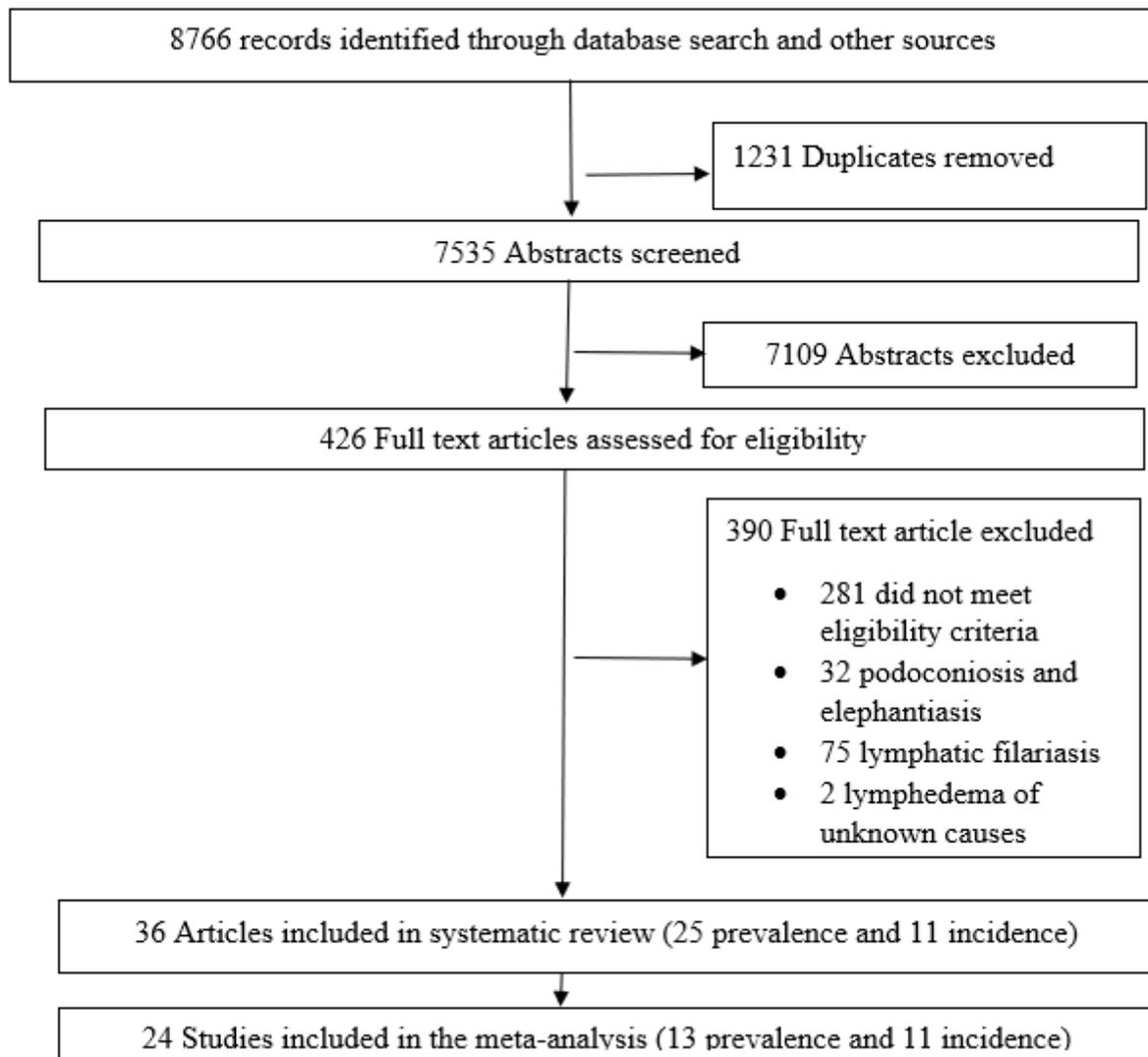
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## Tables

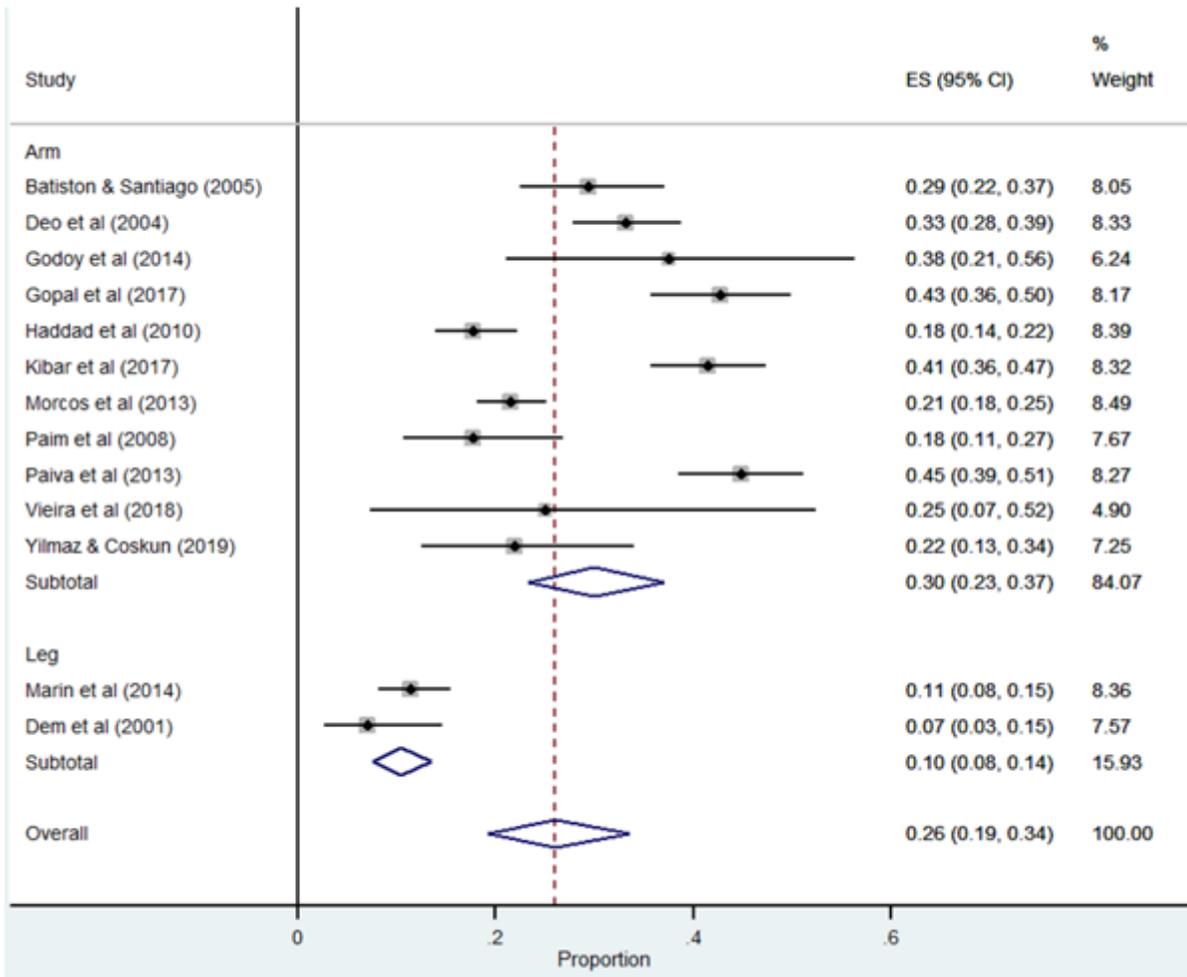
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## Figures



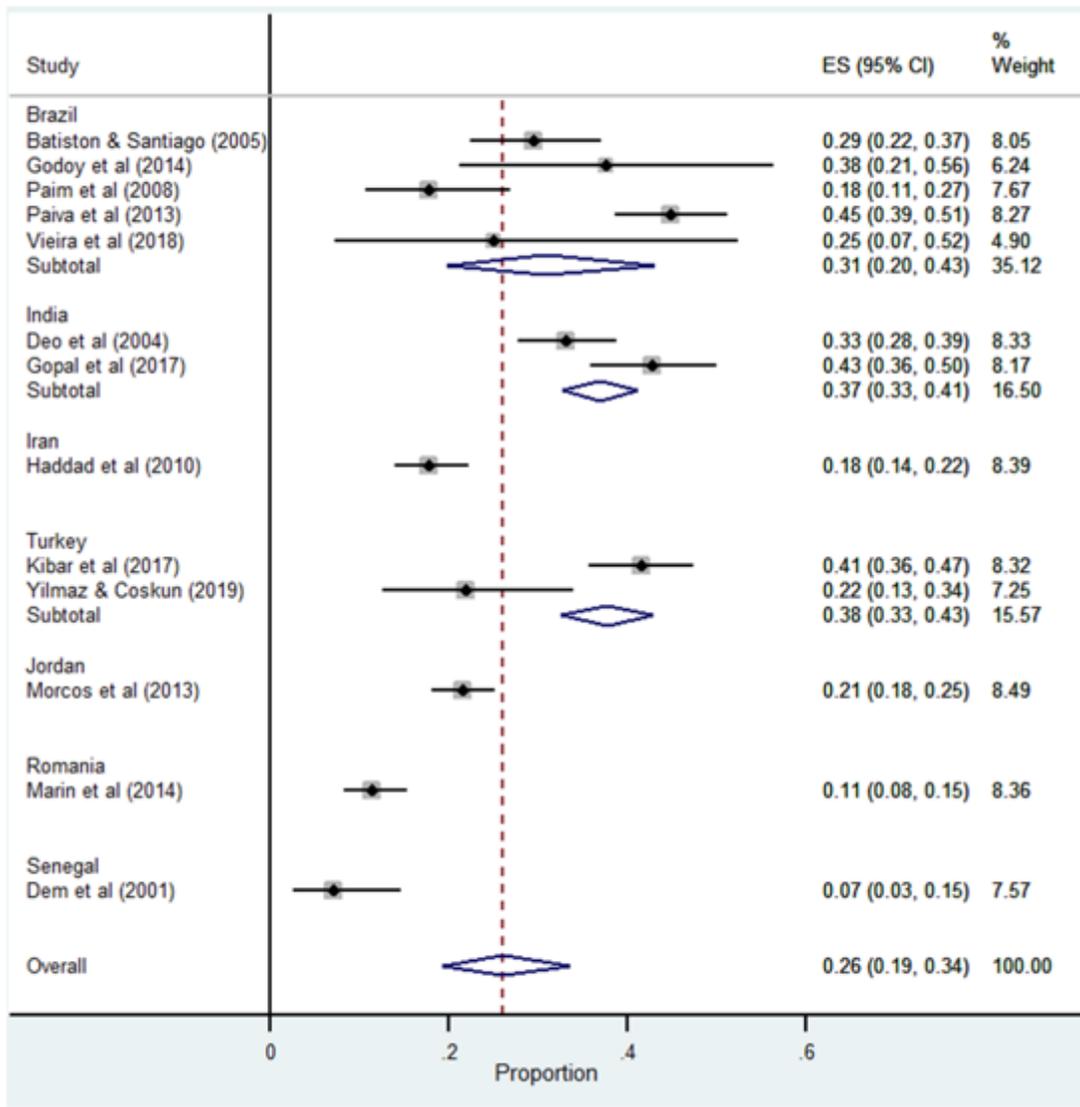
**Figure 1**

Flow diagram of study selection for inclusion in this review and meta-analysis



**Figure 2**

Forest plot of pooled prevalence of arm and leg lymphedema



**Figure 3**

Forest plot of pooled prevalence of cancer related lymphedema based on country of study publication

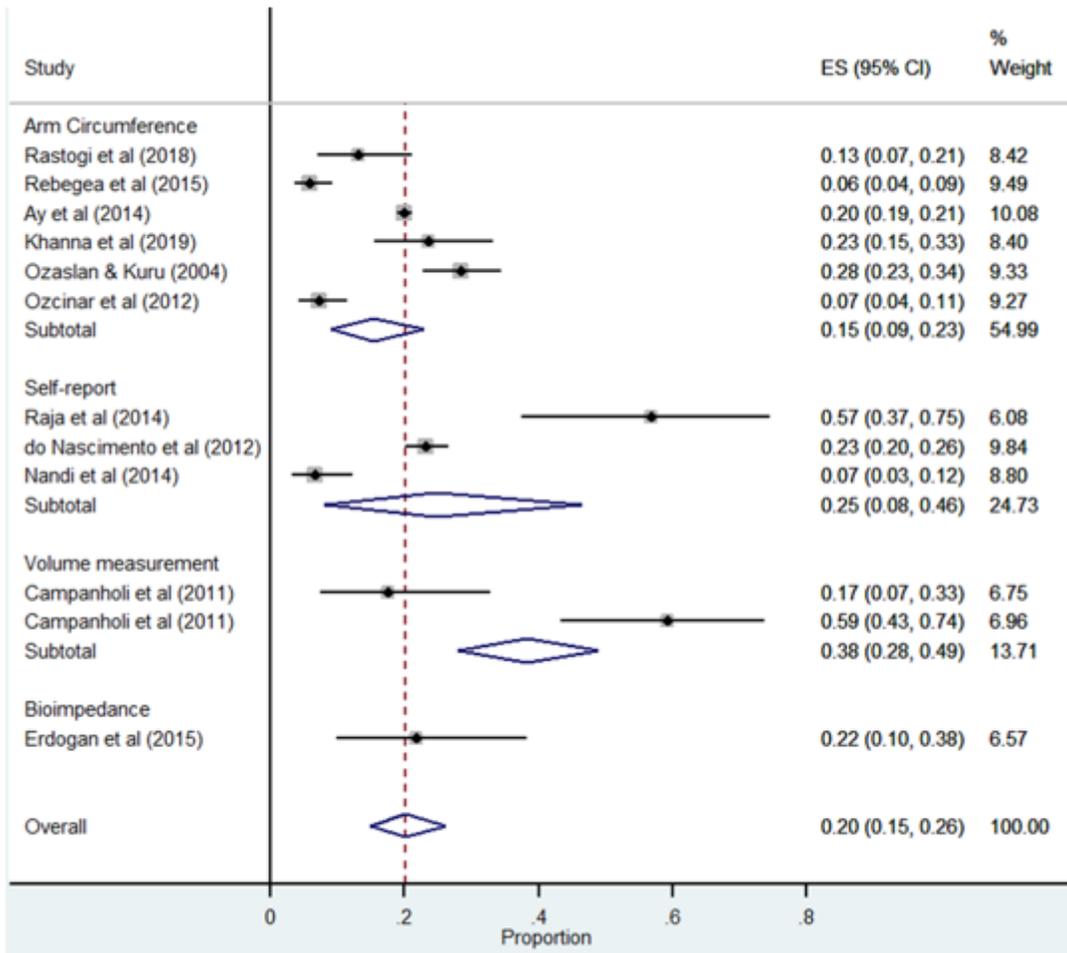
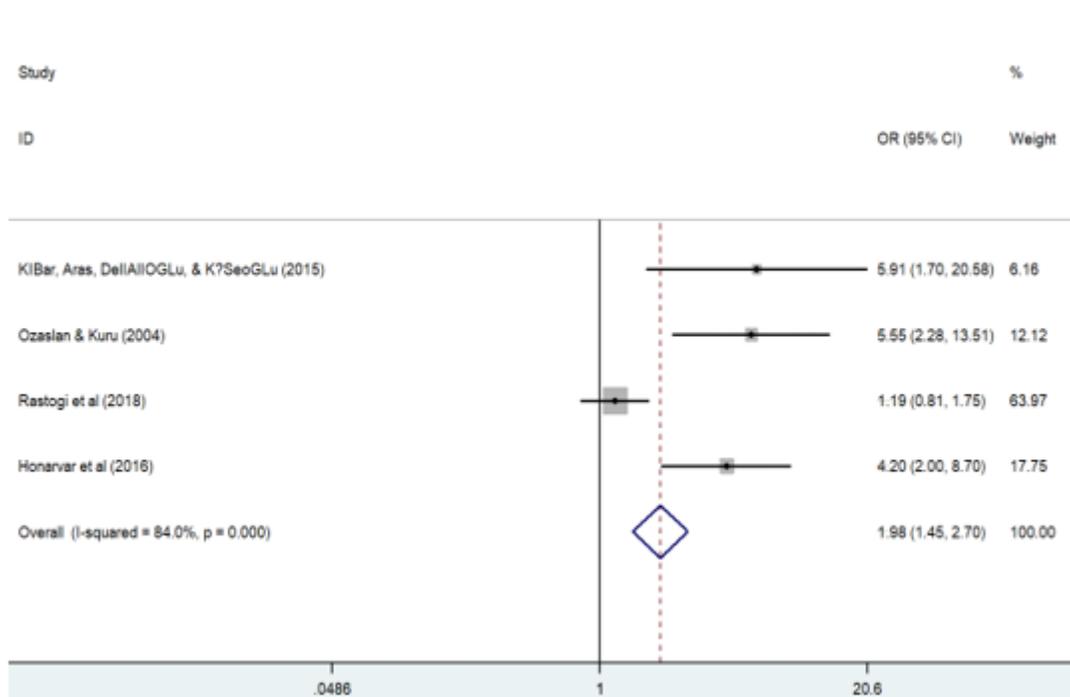


Figure 4

Forest plot of pooled lymphedema incidence according to arm lymphedema measurement methods



## Figure 5

Effect of BMI on risk of arm lymphedema: adjusted effect measure and 95% confidence interval (CI) by study

## Supplementary Files

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