

The BiomolBiomed publishes an “Advanced Online” manuscript format as a free service to authors in order to expedite the dissemination of scientific findings to the research community as soon as possible after acceptance following peer review and corresponding modification (where appropriate). An “Advanced Online” manuscript is published online prior to copyediting, formatting for publication and author proofreading, but is nonetheless fully citable through its Digital Object Identifier (doi®). Nevertheless, this “Advanced Online” version is NOT the final version of the manuscript. When the final version of this paper is published within a definitive issue of the journal with copyediting, full pagination, etc., the new final version will be accessible through the same doi and this “Advanced Online” version of the paper will disappear.

## META-ANALYSIS

**Chen et al: PRE for BCRL prevention**

# **Progressive resistance exercise for preventing breast cancer-related lymphedema after breast cancer surgery: A systematic review and meta-analysis**

**Shufang Chen\*, Sijing Wu, Yanzhi Chen, Wenting Tan**

Department of General Surgery, Guangzhou Panyu District Maternal and Child Health Hospital (Affiliated Hospital Group of Guangdong Medical University Panyu HeXian Memorial Hospital), Guangzhou, Guangdong, China

\*Correspondence to **Shufang Chen**: [shufangchen\\_2025@hotmail.com](mailto:shufangchen_2025@hotmail.com)

DOI: <https://doi.org/10.17305/bb.2026.14006>

---

## ABSTRACT

Breast cancer-related lymphedema (BCRL) is a prevalent and debilitating complication following breast cancer surgery. Progressive resistance exercise (PRE) has been proposed as a preventive strategy, yet evidence from randomized controlled trials (RCTs) remains inconclusive. This meta-analysis aimed to evaluate the impact of PRE on the incidence of postoperative BCRL. We conducted a comprehensive search of PubMed, Cochrane Library, Embase, and Web of Science for RCTs comparing PRE with non-PRE interventions in adults undergoing breast cancer surgery without baseline lymphedema. Risk ratios (RRs) with 95% confidence intervals (CIs) were aggregated using a random-effects model to address potential heterogeneity. A total of eleven RCTs involving 1,450 women were included in the analysis. The findings indicated that PRE significantly reduced the risk of BCRL compared to control groups (RR = 0.68, 95% CI: 0.53–0.88;  $p = 0.003$ ), with no significant heterogeneity observed ( $I^2 = 0\%$ ). The results were consistent in leave-one-out sensitivity analyses and remained robust after excluding two high-risk studies (RR = 0.65, 95% CI: 0.49–0.85). Furthermore, subgroup analyses revealed no significant modifications in results based on age, baseline body mass index, axillary lymph node dissection status, timing of PRE initiation, intervention duration, follow-up length, or diagnostic criteria (all  $p$  for subgroup difference  $> 0.05$ ). Egger's test showed no significant risk of publication bias ( $p = 0.68$ ). The certainty of evidence was rated as moderate, primarily downgraded due to the risk of bias associated with the open-label design of the included RCTs. In conclusion, PRE may be linked to a reduced incidence of BCRL following breast cancer surgery, supported by moderate-certainty evidence. Therefore, PRE should be considered as a component of postoperative rehabilitation and a potential strategy for lymphedema prevention, although further high-quality studies are necessary to validate these findings.

**Keywords:** Breast cancer-related lymphedema, progressive resistance exercise, incidence, randomized controlled trials, meta-analysis.

---

## INTRODUCTION

Breast cancer–related lymphedema (BCRL) has become one of the most common and disabling long-term complications after breast cancer surgery (1, 2). Clinically, BCRL is characterized by chronic swelling of the affected upper limb resulting from impaired lymphatic drainage following axillary surgery and adjuvant treatments (3). The incidence of BCRL varies widely according to previous reports, which ranges from approximately 4% to over 30%, depending on diagnostic criteria, follow-up duration, and treatment modalities (4). The established risk factors for BCRL include axillary lymph node dissection (ALND), radiotherapy, higher body mass index, postoperative infection, and reduced shoulder mobility (3, 4). Clinically, BCRL has been associated with pain, heaviness, restricted range of motion, functional impairment, recurrent cellulitis, and substantial reductions in quality of life (5). Therefore, prevention of BCRL has become a major priority in survivorship care for patients with breast cancer.

In recent years, exercise-based rehabilitation has emerged as an important preventive and therapeutic strategy for BCLR (6). Progressive resistance exercise (PRE), defined as structured strength training with gradually increasing external load over time, has gained particular attention. PRE may improve lymphatic transport through enhanced skeletal muscle pumping, promote collateral lymphatic drainage, reduce inflammation and tissue fibrosis, and improve body composition and functional recovery (7-9). Historically, resistance training was discouraged in breast cancer survivors due to concerns that vigorous upper-limb loading could exacerbate or trigger lymphedema (10). However, accumulating evidence from clinical trials has challenged this paradigm (10). A 2014 meta-analysis reported that PRE may reduce the risk or the exacerbation of BCRL (11). However, only five studies were available and both patients with and without confirmed diagnosis of BCRL were included (11), which may confound the results. More recent meta-analyses have further suggested that resistance exercise does not negatively affect lymphedema in patients with confirmed diagnosis of BCRL and may even improve objective measures such as bioimpedance spectroscopy (12, 13). Nevertheless, prior meta-analyses were limited by heterogeneous study designs, mixed exercise modalities, inclusion of non-randomized trials, inconsistent outcome definitions, and a lack of updated evidence incorporating newer randomized controlled trials (RCTs) and standardized preventive endpoints

---

(11-13). Therefore, an updated and focused synthesis of randomized evidence is needed. The present meta-analysis aimed to evaluate whether PRE initiated after breast cancer surgery reduces the incidence of postoperative BCRL, and to explore whether its preventive effects vary according to patient characteristics, intervention timing, duration, follow-up length, and diagnostic criteria.

## **MATERIAL AND METHODS**

This systematic review and meta-analysis followed established methodological guidance from the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) reporting framework (14) and the Cochrane Handbook for Systematic Reviews of Interventions (15). The review protocol was registered prospectively with the PROSPERO international prospective register of systematic reviews (CRD420261303945).

### **Study inclusion and exclusion criteria**

Study screening was conducted independently by two reviewers based on titles/abstracts and full texts. Discrepancies were resolved through discussion with a third author. Eligible studies were selected based on predefined criteria structured according to the PICOS framework.

Population (P): Adults ( $\geq 18$  years) undergoing breast cancer surgery (with or without sentinel lymph node biopsy or ALND), free of lymphedema at baseline, regardless of adjuvant therapy status, or time since surgery at enrollment. For trials enrolling mixed populations, data were included only when outcomes for participants without baseline BCRL could be extracted separately; otherwise, the study was excluded to ensure that all analyzed events represented incident (new-onset) BCRL.

Intervention (I): PRE initiated after breast cancer surgery, defined as a structured resistance/strength-training program involving upper-limb and/or whole-body exercises performed against external load (e.g., free weights, machines, resistance bands, or body weight with quantifiable progression), in which training workload is progressively increased over time (e.g., increased load, resistance level, repetitions, sets, or advancement in exercise difficulty) according to a prespecified protocol or individual progression rule; delivered in supervised, partially supervised, or home-based formats.

---

Comparator (C): Any non-PRE control condition, including (1) usual care/standard postoperative rehabilitation without progressive resistance training; (2) no structured exercise or wait-list; (3) education-only/self-management advice; or (4) an alternative exercise program without progressive resistance overload (e.g., stretching/range-of-motion, physiotherapy focused on mobility, aerobic-only exercise), provided it does not include structured progressive resistance training.

Outcomes (O): incidence of postoperative breast cancer–related lymphedema (new-onset BCRL) diagnosed clinically or by objective criteria. For studies reporting outcomes at multiple timepoints, data from the longest available follow-up were extracted to reflect cumulative incidence. All included trials enrolled participants free of lymphedema at baseline, ensuring that all analyzed events represented incident BCRL.

Study design (S): RCTs with parallel group.

Studies were excluded if they were non-randomized or quasi-experimental studies, observational designs, case series/case reports, or trials enrolling participants with established lymphedema at baseline or lymphedema not attributable to breast cancer treatment. Studies were also excluded if the intervention was not PRE as defined above (e.g., aerobic-only, stretching/yoga, range-of-motion only, education-only, or resistance training with no progression described) or if the comparator included a structured progressive resistance program. Reviews, editorials, conference abstracts, protocols, or reports without sufficient quantitative data to estimate effect sizes for eligible outcomes were also excluded. When multiple reports from the same trial were identified, overlap was determined based on trial name/acronym, study design, recruitment period, sample size, study setting, and author group. For overlapping publications, only one report was included, preferentially selecting the study that provided the most complete data on incident BCRL at the longest available follow-up, while secondary or ancillary analyses from the same cohort were excluded to avoid double-counting.

### **Database search**

PubMed, Cochrane Library, Embase, and Web of Science were systematically searched using the combined terms including: (1) "breast cancer" OR "breast tumor" OR "breast tumour" OR "breast neoplasm\*" OR "breast carcinoma"; (2) "lymphedema" OR "lymphoedema" OR "secondary lymphedema" OR "arm

---

lymphedema" OR "arm swelling" OR "upper extremity edema"; (3) "resistance exercise" OR "progressive resistance exercise" OR "progressive resistance training" OR "strength exercise" OR "strength training" OR "weight lifting" OR "weight training"; and (4) "random" OR "randomly" OR "randomized" OR "control" OR "allocated" OR "placebo" OR "randomised". We considered only peer-reviewed, English-language full-text studies conducted in human participants. In addition, the bibliographies of relevant reviews and eligible articles were manually screened to identify any additional records. The final search update was performed on December 22, 2025. The detailed search strategies for all databases were provided in the **Supplemental File 1** and were carefully reviewed and corrected to ensure accurate Boolean syntax.

### **Study quality evaluation**

Risk-of-bias assessment was conducted at the study level. The quality of the included RCTs was assessed using the Cochrane Risk of Bias tool (RoB 2), which evaluates potential bias across five key domains: the randomization procedure, deviations from intended interventions, completeness of outcome data, outcome measurement, and selective reporting of results (15). Each domain was judged as presenting low risk, some concerns, or high risk of bias, and these assessments were combined to determine an overall risk-of-bias rating for each study.

### **Data extraction**

Data extraction was performed independently by two reviewers using a standardized form, and any disagreements were resolved through discussion with a third author. Extracted data included general study information (first author, publication year, and country), study design (double-blind, single-blind, or open-label), patient characteristics (sample size, mean age, baseline mean body mass index [BMI], cancer stage, and proportions of patients who received ALND), details of the intervention (timing, protocol, and treatment duration of PRE), comparator (non-PRE control), follow-up durations, and diagnostic criteria for BCRL of each study.

### **Statistical analysis**

The association between progressive resistance exercise and the risk of developing BCRL was summarized using risk ratios (RRs) with 95% confidence intervals (CIs) (15). In trials with multiple eligible intervention arms, each comparison was included

---

separately. When a shared control group was used, its sample size was proportionally divided to avoid double-counting, in accordance with Cochrane Handbook recommendations (15). Statistical heterogeneity across studies was examined using Cochran's Q test and further quantified with the  $I^2$  statistic, with values below 25%, between 25% and 75%, and above 75% reflecting low, moderate, and substantial heterogeneity, respectively (16). Pooled estimates were generated using a random-effects model to account for anticipated clinical and methodological diversity among trials (15). The stability of the findings was evaluated through leave-one-out analyses, and additional sensitivity analyses were conducted after excluding studies judged to be at high risk of bias (15). Prespecified subgroup analyses were performed based on participant and trial characteristics, including mean age, baseline BMI, the proportion of patients undergoing ALND, timing of intervention initiation, intervention duration, length of follow-up, and BCRL diagnostic approach (arm volume-based versus circumference-based criteria). Subgroup analyses according to intervention timing were defined based on the initiation of PRE relative to surgery (e.g., preoperative vs. postoperative), regardless of chemotherapy timing. For continuous moderators, median values were applied as cut points to achieve balanced subgroup distributions. Potential publication bias was explored using funnel plot inspection and Egger's regression test (17). Statistical significance was defined as a two-sided  $p$  value  $< 0.05$ . All analyses were carried out using RevMan (version 5.3, Cochrane Collaboration, Oxford, UK) and Stata (version 17.0, StataCorp, College Station, TX, USA) software.

### **Certainty of evidence**

The overall certainty of evidence was independently evaluated by two reviewers using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework, which rates confidence in the findings across domains including risk of bias, inconsistency, indirectness, imprecision, and potential publication bias (18). The certainty of evidence was categorized as high, moderate, low, or very low, and any differences in judgment were resolved through discussion and agreement.

---

## RESULTS

### Literature search

The study selection process is illustrated in **Figure 1**. A total of 300 records were initially identified from the database search, of which 82 duplicates were removed, leaving 218 unique articles. Following title and abstract screening, 191 records were excluded as they did not meet the eligibility criteria. The full texts of the remaining 27 articles were then reviewed in detail, and 16 were excluded for the reasons provided in **Figure 1**. In addition, three secondary publications (19-21) originating from the same randomized trial (22) were identified; to avoid duplication of participants, only the primary report was included. Ultimately, 11 randomized controlled trials (22-32) were included in the quantitative synthesis.

### Study characteristics

An overview of the included RCTs is presented in Table 1. This meta-analysis incorporated 11 RCTs (22-32) published between 2006 and 2026, conducted across North America (United States and Canada), Europe (Norway and Denmark), and Asia-Pacific (Australia, China, and South Korea). One trial (32) included two eligible PRE intervention arms (low- and high-intensity), which were analyzed as separate comparisons using a shared control group with appropriate adjustment, resulting in 12 independent datasets from 11 RCTs. Collectively, these studies enrolled 1,450 breast cancer survivors undergoing surgery for stage I–III disease, with sample sizes ranging from 45 to 213 participants. The mean age of participants varied from 48.3 to 71.9 years, and baseline mean BMI ranged from 23.4 to 30.1 kg/m<sup>2</sup>. Six trials included patients all receiving ALND (22-25, 27, 32). The timing of PRE initiation differed substantially, beginning as early as within 1 week postoperatively in four studies (25, 30-32), while others initiated resistance training within 1 to 9 weeks after surgery (24, 26-28) or even after 1 year postoperatively (22, 23, 29). Intervention protocols generally involved supervised or hybrid progressive resistance training performed two to three times per week (where reported), using free weights, machines, elastic bands, or home-based exercises with gradual load progression over time. Control groups typically received usual care without structured resistance training, activity restriction advice, or non-exercise supportive programs. The treatment durations of PRE varied from 1 to 12 months and the follow-up durations ranged from 4 to 24 months.

---

Diagnostic criteria for incident BCRL varied across trials, including arm circumference thresholds ( $\geq 2$  cm) (23, 32) and arm girth estimated volume increase ( $> 3\%$ ) (29), absolute volume increases ( $\geq 200$  mL) (24), relative interlimb volume differences ( $\geq 5$ – $10\%$ ) (22, 25–28, 30), or clinician-defined diagnoses (31), highlighting important methodological diversity in outcome ascertainment. All included studies explicitly recruited participants without lymphedema at baseline, confirming that the reported outcomes represent incident BCRL.

### **Study quality assessment**

As summarized in Table 2, the overall methodological quality of the included RCTs was generally acceptable, with nine trials (22–27, 29, 30, 32) judged as having “some concerns” of bias according to the Cochrane RoB 2 tool. Randomization procedures were consistently well described, and all studies were rated as low risk in the randomization domain, commonly using computer-generated or block randomization with appropriate allocation concealment. Given the nature of exercise interventions, blinding of participants and personnel was not feasible, leading several trials to be rated as having some concerns regarding deviations from intended interventions, particularly due to moderate adherence or potential contamination in control groups. Outcome data were largely complete across studies, with most trials assessed as low risk for missing outcome data; however, one study had notable attrition over longer follow-up, contributing to some concerns. Outcome measurement was generally robust because BCRL was primarily assessed using objective volumetric or circumference-based criteria, and several trials employed blinded assessors, resulting in low risk ratings in this domain. Nevertheless, two studies were judged as high risk overall, driven by substantial contamination or reduced contrast between intervention and control conditions (28), or insufficiently specified diagnostic procedures with unblinded outcome assessment (31). Selective reporting was largely unlikely, as most trials reported prespecified outcomes and several were prospectively registered, although uncertainty remained in one unregistered study. Overall, the evidence base comprises well-conducted exercise RCTs with objective outcome ascertainment and minimal attrition, while acknowledging unavoidable limitations related to open-label design and occasional contamination in control arms.

---

## Meta-analysis results

The total number of participants included in the meta-analysis ( $n = 1,450$ ) corresponds to the randomized populations summarized in **Table 1** and is consistent with the denominators presented in **Figure 2A**. For each study, event counts were extracted based on the number of participants analyzed at the selected endpoint (longest follow-up), and trials with multiple intervention arms were handled using shared control group adjustment in accordance with Cochrane recommendations. Overall, this meta-analysis included 12 comparisons from 11 RCTs (22-32) and involved 1,450 women with breast cancer after surgery (749 patients in the PRE group and 701 patients in the control group). Overall, 207 patients developed BCRL during follow-up. The pooled results with a random-effects model showed that PRE after breast surgery significantly reduced the risk of BCRL (RR: 0.68, 95% CI: 0.53 to 0.88,  $p = 0.003$ ; **Figure 2A**) without significant heterogeneity ( $p$  for Cochrane Q test = 0.84,  $I^2 = 0\%$ ). The sensitivity analysis by excluding one dataset at a time showed consistent results (RR: 0.64 to 0.71,  $p$  all < 0.05). In addition, further sensitivity analysis excluding the two studies with high risk of bias (28, 31) also showed similar results (RR: 0.65, 95% CI: 0.49 to 0.85,  $p = 0.003$ ;  $I^2 = 0\%$ ). Subsequent subgroup analysis showed similar results in studies with the mean ages of the patients < 52 years and  $\geq 52$  years (RR: 0.60 vs. 0.71,  $p$  for subgroup difference = 0.55; **Figure 2B**), between women with the mean BMI at baseline  $\leq$  or  $> 26.0$  kg/m<sup>2</sup> (RR: 0.52 vs. 0.75,  $p$  for subgroup difference = 0.22; **Figure 3A**), and between studies with patients who all or partially received ALND (RR: 0.69 vs. 0.63,  $p$  for subgroup difference = 0.81; **Figure 3B**). Furthermore, the preventive efficacy of PRE against BCRL did not differ significantly among patients who initiated PRE within 1 week after surgery, between 1 and 9 weeks, or more than 1 year postoperatively (RR: 0.52, 0.77, and 0.70,  $p$  for subgroup difference = 0.45; **Figure 4A**), and between studies with the intervention during < 6 months and  $\geq 6$  months (RR: 0.69 vs. 0.66,  $p$  for subgroup difference = 0.88; **Figure 4B**). Finally, consistent results were observed for studies with the follow-up durations < 12 months and  $\geq 12$  months (RR: 0.68 vs. 0.69,  $p$  for subgroup difference = 0.97; **Figure 5A**), and between studies with BCRL diagnosed with the objective arm volume-based and circumference-based criteria (RR: 0.69 vs. 0.60,  $p$  for subgroup difference = 0.73, **Figure 5B**).

---

### Publication bias

The funnel plots for the meta-analysis evaluating the effect of PRE on the risk of BCRL are shown in **Figure 6**. These plots are symmetrical on visual inspection, suggesting a low risk of publication bias. Egger's test detected no evidence of small-study effects ( $p = 0.68$ ).

### Certainty of evidence

A summary of the certainty of evidence evaluated using the GRADE approach is presented in **Table 3**. The certainty for the outcome of BCRL incidence was rated as moderate, downgraded by one level due to risk of bias. Although all included studies were RCTs and most applied objective lymphedema measurements, the exercise interventions were necessarily open-label, and two studies were judged at high overall risk of bias because of contamination or unclear outcome assessment (28, 31). No downgrading was applied for inconsistency, as effects were consistent across trials with negligible heterogeneity ( $I^2 = 0\%$ ). Similarly, the evidence was not downgraded for indirectness or imprecision, since the included populations, interventions, and outcomes directly addressed the review question and the pooled confidence interval excluded no effect with an adequate total sample size. Overall, PRE may reduce the risk of developing BCRL after breast cancer surgery with moderate certainty.

## DISCUSSION

This meta-analysis synthesizes randomized evidence evaluating PRE as a preventive strategy for BCRL after surgery. Overall, the findings support that PRE, when implemented after breast cancer surgery, is associated with a lower risk of developing BCRL and that this preventive signal is stable across a range of patient- and trial-level characteristics. These findings were generally similar across subgroup analyses, with no clear evidence of effect modification. The findings of this meta-analysis are consistent with previous evidence (11) and further support the potential role of PRE in reducing the risk of BCRL, with moderate-certainty evidence. Subgroup analyses did not identify clear evidence of effect modification according to factors such as timing of initiation. However, these findings should be interpreted cautiously given the limited number of studies and heterogeneity in intervention protocols.

Several plausible mechanisms may explain why PRE could reduce the risk of BCRL. First, rhythmic muscle contraction during resistance exercise enhances the “muscle

---

pump,” which can facilitate lymphatic and venous return from the upper limb, potentially mitigating postoperative lymphatic stasis (33, 34). Second, progressive loading may promote restoration of shoulder and arm function, improving range of motion and activity of daily living; improved mobility and functional use of the limb may prevent prolonged dependent positioning and disuse that could otherwise exacerbate fluid retention (35). Third, resistance training can favorably influence body composition and metabolic health, including reductions in adiposity and improvement in insulin sensitivity (36, 37). Excess adipose tissue is increasingly recognized as a pro-inflammatory milieu and a risk factor for lymphatic dysfunction, and weight control may therefore indirectly support lymphatic recovery (38). Finally, structured PRE may reduce chronic inflammation and fibrosis within subcutaneous tissues by improving local circulation and regulating inflammatory mediators, which is biologically relevant because BCRL progression is linked to inflammatory remodeling and tissue fibrosis over time (39, 40). Collectively, these pathways align with the concept that PRE is not merely safe but may be physiologically protective when delivered in a progressive, monitored manner.

Subgroup analyses showed broadly consistent point estimates across categories such as age and baseline BMI. However, no clear evidence of effect modification was observed, and accordingly, these findings should be interpreted cautiously. Consistent associations were observed in trials with all participants undergoing ALND as well as those with mixed axillary surgery profile, which may indicate that PRE can be incorporated even in higher-risk surgical contexts. However, residual confounding at the study level cannot be excluded. Similarly, no statistically significant differences were detected across subgroups defined by timing of initiation. However, these results do not provide clear evidence of differential effects and should be interpreted with caution. Similarly, comparable findings in shorter versus longer intervention duration categories may suggest that even relatively time-limited, structured PRE programs can be beneficial if they include appropriate progression and adherence support, though the optimal dose remains uncertain. However, because one trial contributed multiple comparisons and that several subgroup confidence intervals crossed the null value, these subgroup findings should be interpreted with caution.

Sensitivity analyses further strengthen confidence in the conclusions. Leave-one-out analyses retrieved consistent pooled estimates, indicating that the overall result was

---

not likely to be driven by any single trial. Excluding the two studies judged at high risk of bias (28, 31) did not substantially change the direction or statistical significance of the association, which suggests that the preventive effect is not solely attributable to lower-quality evidence. In addition, the absence of heterogeneity in the pooled effect estimates indicates a coherent evidence pattern across trials despite inevitable differences in exercise delivery and outcome ascertainment. Finally, the GRADE assessment rated the certainty of evidence as moderate, which reflects downgrading mainly because of the risk of bias inherent to open-label exercise trials and the presence of a small number of studies with contamination or unclear outcome assessment.

This review has several strengths. The literature search was up to date and comprehensive across major databases. Moreover, only RCTs were included, which improves internal validity compared with broader evidence syntheses that mix designs involving observational studies. The review applied contemporary methodological standards, including RoB 2.0 and GRADE, and conducted a set of prespecified subgroup analyses and multiple sensitivity analyses that consistently supported the primary finding. In addition, the inclusion of newer trials expands the evidence base beyond earlier meta-analyses (11-13) and better reflects modern surgical and survivorship care pathways.

Nevertheless, limitations should be acknowledged. There is unavoidable clinical heterogeneity in PRE protocols across trials, including differences in exercise selection, intensity progression rules, supervision level, adherence support, and whether programs were facility-based or home-based. In addition, BCRL definitions and measurement approaches varied (e.g., circumference-based thresholds, volumetric criteria, interlimb difference cutoffs, or clinician-defined diagnoses). Although lymphedema definitions and diagnostic thresholds varied across studies, subgroup analysis based on measurement method yielded generally similar results. However, further stratification was not feasible due to the heterogeneity of cutoff values, and these findings should be interpreted with caution. Besides, because this meta-analysis was based on study-level data, it could not address individual-level effect modifiers. The potential roles of surgical details (extent of axillary surgery, number of nodes removed), reconstruction procedures, radiotherapy fields, chemotherapy regimens, and postoperative complications (e.g., seroma, infection) could not be reliably

---

quantified due to inconsistent reporting and lack of individual participant data (IPD). Moreover, adherence and contamination are particularly relevant in exercise trials. Some control groups may have increased their activity or engaged in resistance exercise outside the protocol, which could dilute observed effects. Conversely, incomplete adherence in PRE arms could lead to conservative estimates of efficacy. Furthermore, although funnel plot inspection and Egger's test did not suggest publication bias, the number of included trials remains modest for definitive small-study effect assessment. Another limitation is that participants were considered free of lymphedema at baseline based on conventional clinical criteria. Subclinical lymphatic dysfunction (41), which may be detectable using imaging techniques such as indocyanine green lymphography but not captured by standard diagnostic thresholds, could not be identified. This may have led to misclassification of baseline status and potentially influenced the observed associations. Additionally, potential contamination in control groups and the open-label nature of exercise interventions may have introduced performance bias. Such bias is likely to attenuate between-group differences, potentially leading to an underestimation of the true effect. However, sensitivity analyses excluding studies at high risk of bias yielded consistent results, supporting the robustness of the findings. In addition, cellulitis (42), a clinically important and potentially severe complication of lymphedema, was inconsistently reported across the included studies, precluding quantitative synthesis. Future trials should incorporate standardized reporting of cellulitis outcomes to better evaluate the broader clinical impact of preventive interventions. Finally, the findings primarily address incident BCRL within typical trial follow-up periods. Longer-term durability, late-onset BCRL, and the optimal maintenance strategy beyond supervised phases warrant further study.

From a clinical perspective, these findings support incorporating PRE into postoperative rehabilitation and survivorship care with appropriate safeguards. For nursing practice in particular, PRE represents an actionable, patient-centered strategy that can be operationalized through education, monitoring, and coordinated survivorship pathways. Nurses are often the first point of contact for symptom surveillance and behavior coaching. Structured nursing-led programs could include early risk stratification, standardized arm measurement or symptom screening, individualized exercise counseling, and adherence support using check-ins, diaries, or

---

digital tools. Clear messaging is essential to counter persistent fear that upper-limb loading is harmful. Nurses can help patients initiate PRE gradually, reinforce safe progression principles (e.g., start low, progress slowly, monitor symptoms), and coordinate referrals to physiotherapists or accredited exercise physiologists when higher-risk patients require supervised initiation. Integration with compression guidance, skin care education, and early recognition of swelling or infection can further enhance preventive benefit while maintaining safety. Future research should prioritize several directions. Pragmatic multicenter RCTs with standardized PRE prescriptions and consistent BCRL definitions would improve comparability across studies. Trials should report key surgical and oncologic variables (axillary procedure details, radiotherapy, and systemic therapy) and systematically capture adherence, contamination, and adverse events using harmonized frameworks. IPD meta-analyses or large registry-linked trials could clarify whether PRE effects differ by baseline risk, such as ALND extent, obesity, or radiotherapy exposure. From a nursing and implementation perspective, studies should evaluate scalable delivery models (e.g., nurse-led education plus telehealth coaching, community-based supervised programs transitioning to home-based maintenance) and assess outcomes beyond BCRL incidence, including function, patient-reported symptoms, fear avoidance, self-efficacy, and cost-effectiveness. Additionally, longer follow-up is needed to determine whether early PRE translates into sustained protection against late-onset BCRL and whether continued maintenance exercise is necessary for durable benefit.

## **CONCLUSION**

This meta-analysis suggests that PRE may be associated with a reduced risk of BCRL. However, the findings should be interpreted with caution given the variability across studies. Resistance exercise may be considered as a supportive strategy in this context, but further high-quality trials are warranted to confirm its effectiveness and to define optimal intervention protocols.

**Conflicts of interest:** Authors declare no conflicts of interest.

**Funding:** Authors received no specific funding for this work.

---

Data availability: All data generated or analyzed during this study are included in this published article.

**Submitted:** January 9, 2026

**Accepted:** April 15, 2026

**Published online:** June 26, 2026

## REFERENCES

- 1.Sahbaz Pirincci C, Gercek H, Cihan E, Durmaz ED, Sari Z. From mobility to management: a scoping review on exercise in breast cancer–related lymphedema. *Clin Breast Cancer*. 2026;26(1):114–30. <https://doi.org/10.1016/j.clbc.2025.11.011>
- 2.Donahue PMC, MacKenzie A, Filipovic A, Koelmeyer L. Advances in the prevention and treatment of breast cancer–related lymphedema. *Breast Cancer Res Treat*. 2023;200(1):1–14. <https://doi.org/10.1007/s10549-023-06947-7>
- 3.Gillespie TC, Sayegh HE, Brunelle CL, Daniell KM, Taghian AG. Breast cancer–related lymphedema: risk factors, precautionary measures, and treatments. *Gland Surg*. 2018;7(4):379–403. <https://doi.org/10.21037/gs.2017.11.04>
- 4.Sharifi N, Ahmad S. Breast cancer–related lymphedema: a critical review on recent progress. *Surg Oncol*. 2024;56:102124. <https://doi.org/10.1016/j.suronc.2024.102124>
- 5.Ciamarra P, de Sire A, Aksoyler D, Paolino G, Cantisani C, Sabbatino F, et al. Surgical treatment, rehabilitative approaches and functioning assessment for patients affected by breast cancer–related lymphedema: a comprehensive review. *Medicina (Kaunas)*. 2025;61(8):1327. <https://doi.org/10.3390/medicina61081327>
- 6.Tendero-Ruiz L, Palomo-Carrión R, Megía-García-Carpintero Á, Pérez-Nombela S, López-Muñoz P, Bravo-Esteban E. The effect of therapeutic exercise in the prevention of lymphoedema secondary to breast cancer: a systematic review. *Arch Med Sci*. 2023;19(6):1684–92.
- 7.Park YJ, Na SJ, Kim MK. Effect of progressive resistance exercise using Thera-band on edema volume, upper limb function, and quality of life in patients with breast

---

cancer-related lymphedema. *J Exerc Rehabil.* 2023;19(2):105–13. <https://doi.org/10.12965/jer.2346046.023>

8.Zhang Z, Guo L, Zhou L, Hao X, Fan Y, Li H, et al. Preventive effects of progressive resistance training of different intensities on breast cancer-related lymphedema. *Support Care Cancer.* 2025;33(3):194. <https://doi.org/10.1007/s00520-025-09256-5>

9.García-Chico C, López-Ortiz S, Pinto-Fraga J, Ceci C, Valenzuela PL, Peñín-Grandes S, et al. Physical exercise and breast cancer-related lymphedema: an umbrella review, systematic review and meta-analysis. *Disabil Rehabil.* 2026;48(2):259–75. <https://doi.org/10.1080/09638288.2025.2536722>

10.Shamesfandabadi P, Shams Esfand Abadi M, Yin Y, Carpenter DJ, Peluso C, Hilton C, et al. Resistance training and lymphedema in breast cancer survivors. *JAMA Netw Open.* 2025;8(6):e2514765. <https://doi.org/10.1001/jamanetworkopen.2025.14765>

11.Cheema BS, Kilbreath SL, Fahey PP, Delaney GP, Atlantis E. Safety and efficacy of progressive resistance training in breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat.* 2014;148(2):249–68. <https://doi.org/10.1007/s10549-014-3162-9>

12.Hasenoehrl T, Palma S, Ramazanov D, Kölbl H, Dorner TE, Keilani M, et al. Resistance exercise and breast cancer-related lymphedema – a systematic review update and meta-analysis. *Support Care Cancer.* 2020;28(8):3593–603. <https://doi.org/10.1007/s00520-020-05521-x>

13.Lin Y, Chen Y, Liu R, Cao B. Effect of exercise on rehabilitation of breast cancer surgery patients: a systematic review and meta-analysis of randomized controlled trials. *Nurs Open.* 2023;10(4):2030–43. <https://doi.org/10.1002/nop2.1518>

14.Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.

15.Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al., editors. *Cochrane handbook for systematic reviews of interventions.* Version 6.2. London:

---

The Cochrane Collaboration; 2021. Available from:  
[www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook)

16.Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21(11):1539–58. <https://doi.org/10.1002/sim.1186>

17.Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ.* 1997;315(7109):629–34. <https://doi.org/10.1136/bmj.315.7109.629>

18.Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction–GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol.* 2011;64(4):383–94. <https://doi.org/10.1016/j.jclinepi.2010.04.026>

19.Speck RM, Gross CR, Hormes JM, Ahmed RL, Lytle LA, Hwang WT, et al. Changes in the Body Image and Relationship Scale following a one-year strength training trial for breast cancer survivors with or at risk for lymphedema. *Breast Cancer Res Treat.* 2010;121(2):421–30. <https://doi.org/10.1007/s10549-009-0550-7>

20.Winters-Stone KM, Laudermilk M, Woo K, Brown JC, Schmitz KH. Influence of weight training on skeletal health of breast cancer survivors with or at risk for breast cancer–related lymphedema. *J Cancer Surviv.* 2014;8(2):260–8. <https://doi.org/10.1007/s11764-013-0337-z>

21.Brown JC, Schmitz KH. Weight lifting and appendicular skeletal muscle mass among breast cancer survivors: a randomized controlled trial. *Breast Cancer Res Treat.* 2015;151(2):385–92. <https://doi.org/10.1007/s10549-015-3409-0>

22.Schmitz KH, Ahmed RL, Troxel AB, Cheville A, Lewis-Grant L, Smith R, et al. Weight lifting for women at risk for breast cancer–related lymphedema: a randomized trial. *JAMA.* 2010;304(24):2699–705. <https://doi.org/10.1001/jama.2010.1837>

23.Ahmed RL, Thomas W, Yee D, Schmitz KH. Randomized controlled trial of weight training and lymphedema in breast cancer survivors. *J Clin Oncol.* 2006;24(18):2765–72. <https://doi.org/10.1200/JCO.2005.03.6749>

24.Courneya KS, Segal RJ, Mackey JR, Gelmon K, Reid RD, Friedenreich CM, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant

---

chemotherapy: a multicenter randomized controlled trial. *J Clin Oncol.* 2007;25(28):4396–404. <https://doi.org/10.1200/JCO.2006.08.2024>

25.Sagen A, Karesen R, Risberg MA. Physical activity for the affected limb and arm lymphedema after breast cancer surgery. A prospective, randomized controlled trial with two years follow-up. *Acta Oncol.* 2009;48(8):1102–10. <https://doi.org/10.3109/02841860903061683>

26.Kilbreath SL, Refshauge KM, Beith JM, Ward LC, Lee M, Simpson JM, et al. Upper limb progressive resistance training and stretching exercises following surgery for early breast cancer: a randomized controlled trial. *Breast Cancer Res Treat.* 2012;133(2):667–76. <https://doi.org/10.1007/s10549-012-1964-1>

27.Ammitzbøll G, Johansen C, Lanng C, Andersen EW, Kroman N, Zerahn B, et al. Progressive resistance training to prevent arm lymphedema in the first year after breast cancer surgery: results of a randomized controlled trial. *Cancer.* 2019;125(10):1683–92. <https://doi.org/10.1002/cncr.31962>

28.Bloomquist K, Adamsen L, Hayes SC, Lillelund C, Andersen C, Christensen KB, et al. Heavy-load resistance exercise during chemotherapy in physically inactive breast cancer survivors at risk for lymphedema: a randomized trial. *Acta Oncol.* 2019;58(12):1667–75. <https://doi.org/10.1080/0284186X.2019.1643916>

29.Owusu C, Margevicius S, Nock NL, Austin K, Bennet E, Cerne S, et al. A randomized controlled trial of the effect of supervised exercise on functional outcomes in older African American and non-Hispanic White breast cancer survivors: Are there racial differences in the effects of exercise on functional outcomes? *Cancer.* 2022;128(12):2320–38. <https://doi.org/10.1002/cncr.34184>

30.Lin Y, Wu C, He C, Yan J, Chen Y, Gao L, et al. Effectiveness of three exercise programs and intensive follow-up in improving quality of life, pain, and lymphedema among breast cancer survivors: a randomized, controlled 6-month trial. *Support Care Cancer.* 2023;31(1):9. <https://doi.org/10.1007/s00520-022-07494-5>

31.Min J, Kim JY, Ryu J, Park S, Courneya KS, Ligibel J, et al. Early implementation of exercise to facilitate recovery after breast cancer surgery: a randomized clinical trial. *JAMA Surg.* 2024;159(8):872–80. <https://doi.org/10.1001/jamasurg.2024.1633>

- 
- 32.Fan YJ, Xu HQ, Li H, Zhang ZR, Zhang SF, Du AJ, et al. Effects of resistance training at different intensities on preventing breast cancer–related lymphedema: a 1-year randomized controlled trial. *Clin Breast Cancer*. 2026;26(1):204–12. <https://doi.org/10.1016/j.clbc.2025.07.012>
- 33.Shariq A, Shaikh HA, Usmani SUR. Resistance training: an overlooked tool in breast cancer recovery. *Crit Rev Oncol Hematol*. 2026;217:105077. <https://doi.org/10.1016/j.critrevonc.2025.105077>
- 34.Wang L, Shi YX, Wang TT, Chen KX, Shang SM. Breast cancer–related lymphoedema and resistance exercise: an evidence-based review of guidelines, consensus statements and systematic reviews. *J Clin Nurs*. 2023;32(9–10):2208–27. <https://doi.org/10.1111/jocn.16437>
- 35.Ellis MD, Sukal-Moulton T, Dewald JP. Progressive shoulder abduction loading is a crucial element of arm rehabilitation in chronic stroke. *Neurorehabil Neural Repair*. 2009;23(8):862–9. <https://doi.org/10.1177/1545968309332927>
- 36.Warner SO, Linden MA, Liu Y, Harvey BR, Thyfault JP, Whaley-Connell AT, et al. The effects of resistance training on metabolic health with weight regain. *J Clin Hypertens (Greenwich)*. 2010;12(1):64–72. <https://doi.org/10.1111/j.1751-7176.2009.00209.x>
- 37.Lopez P, Taaffe DR, Galvão DA, Newton RU, Nonemacher ER, Wendt VM, et al. Resistance training effectiveness on body composition and body weight outcomes in individuals with overweight and obesity across the lifespan: a systematic review and meta-analysis. *Obes Rev*. 2022;23(5):e13428. <https://doi.org/10.1111/obr.13428>
- 38.Nitti MD, Hespe GE, Kataru RP, García Nores GD, Savetsky IL, Torrisi JS, et al. Obesity-induced lymphatic dysfunction is reversible with weight loss. *J Physiol*. 2016;594(23):7073–87. <https://doi.org/10.1113/JP273061>
- 39.Brown S, Dayan JH, Kataru RP, Mehrara BJ. The vicious circle of stasis, inflammation, and fibrosis in lymphedema. *Plast Reconstr Surg*. 2023;151(2):330e–41e. <https://doi.org/10.1097/PRS.00000000000009866>

---

40. Bowman C, Rockson SG. The role of inflammation in lymphedema: a narrative review of pathogenesis and opportunities for therapeutic intervention. *Int J Mol Sci.* 2024;25(7):3907. <https://doi.org/10.3390/ijms25073907>

41. Tokumoto H, Akita S, Nakamura R, Yamamoto N, Kubota Y, Mitsukawa N. Lymphatic dysfunction on indocyanine green lymphography in breast cancer patients undergoing sentinel lymph node biopsy. *J Plast Reconstr Aesthet Surg.* 2021;74(8):1931–71. <https://doi.org/10.1016/j.bjps.2021.05.029>

42. Burian EA, Franks PJ, Borman P, Quéré I, Karlsmark T, Keeley V, et al. Factors associated with cellulitis in lymphoedema of the arm – an international cross-sectional study (LIMPRINT). *BMC Infect Dis.* 2024;24(1):102. <https://doi.org/10.1186/s12879-023-08839-z>

EARLY ACCESS

## TABLES AND FIGURES WITH LEGENDS

**Table 1. Characteristics of the included studies**

Study	Country	Design	No. of patients	Mean age (years)	Baseline mean BMI	Tumor stage	ALND (%)	RT (%)	Timing of PRE	Details of PRE	Duration of PRE treatment (months)	Details of control	Follow-up duration (months)	Diagnostic criteria for BCRL
Ahmed 2006	USA	R, OL	45	52.0	26.8	I–III	100	75.6	Mean: 13.4 months post-treatment	Supervised weight training, 2×/week, 9 exercises (upper & lower body), progressive load increase, at university recreation center	6	Usual care/no structured exercise	6	Arm circumference difference $\geq 2$ cm, self-reported clinical diagnosis
Courne	Canada	R,	164	49.0	26.6	I–	100	N	Started	Supervised	4	Usual	4	$\geq 200$ mL

ya 2007	da	OL				III A		R	1–2 weeks after beginning adjuvant chemothe rapy (2-4 weeks after surgery)	resistance exercise, 3×/week, 9 exercises, progressive load increase, in fitness facility		care/no structure d exercise		increase in arm volume differenc e (water displace ment)
Sagen 2009	Norw ay	R, OL	204	55.0	24.5	I– III	100	75	Started 2 days post- surgery	Supervised moderate progressive resistance training, 2–3×/week, low weight/high reps (≥15), outpatient clinic	6	Activity restrictio ns (AR) + usual care (passive manual therapy, no PRE)	24	≥ 10% volume increase
Schmit z 2010	USA	R, OL	146	55.0	28	I– III	100	76	Mean: 3 years	Supervised progressive weight	12	Usual care and	12	≥ 5% increase

									post treatment	lifting 2×/week for 13 weeks, then unsupervised to 1 year; community fitness centers		no exercise		in interlimb volume difference (water displacement) & clinician-defined
Kilbreath 2012	Australia	R, OL	160	52.5	26.3	I–III	60	78	Started 4–6 weeks post-surgery	Supervised weekly resistance training + stretching, plus home program with Thera-bands, 8 weeks	2	Usual care and no exercise	8	Interlimb volume difference $\geq 10\%$
Bloomquist 2019	Denmark	R, OL	99	51.7	26.1	I–III	39.9	N R	Started 6–9 weeks post-surgery	Supervised, group-based multimodal program (resistance + aerobic); machine-based resistance exercises	3	Usual care plus a home-based walking program	9	Inter-arm volume % difference $> 5\%$

										(e.g., chest press) at 80–90% 1RM, 3 sets × 5–8 reps; loads progressed every 3 weeks based on repeat 1RM testing; weekly frequency not explicitly reported		using a pedometer		
Ammitzboell 2019	Denmark	R, OL	158	52.5	26.5	I–III	100	100	Started week 3 post-surgery	Method: Supervised (Phase 1, 20 weeks) + Self-administered (Phase 2, 30 weeks). Progression: Load started at <60% 1RM, progressed based on monthly 7-RM tests to lifting to fatigue.	12	Usual care. Allowed to exercise and participate in municipal rehabilitation	12	Inter-arm volume % difference > 3%

										Frequency: 3x/week (2 supervised, 1 home-based) for 20 weeks, then 3x/week self-administered for 30 wks. Exercises: Major muscle groups of upper limb, lower limb, and core.		ation without restrictions		
Owusu 2022	USA	R, OL	213	71.9	30.1	I–III	NR	65	Mean: 28.5 months after diagnosis	Supervised, group-based moderate-intensity aerobic plus progressive resistance training at a community cancer support center; supervised for 20 weeks with 3 sessions/week (60	5	Usual care and support group (one 60-min session/week) focused on	5	Estimated volume increase of >3% in arm girth measurements

										min: 30 min aerobics + 30 min resistance) plus 60 min/week unsupervised walking; resistance began at 40–60% 1RM and progressed from 1– 2 to 3 sets of 10 reps, with loads increased after two consecutive symptom-free sessions.		psychos ocial topics		
Lin 2023	China	R, OL	95	51.6	23.4	I– III	45.3	N R	Interventi on started immediat ely after surgery	PRE consisted of 8 movements with gradually increasing intensity, using elastic bands. Exercise interval for	6	Usual care and JME	6	≥ 5% volume increase

									the same muscle group was 48h. Supervision: Likely unsupervised/home-based with remote monitoring via WeChat video uploads. Setting: Home-based. Frequency: Not explicitly stated for PRE alone, but within the combined program. Combined with JME				
Min 2024	South Korea	R, OL	56	50.3	23.4	I–III	25	82.1	Initiated 1 day after surgery Tailored, home-based stretching and resistance exercises using body weight. Intensity progressively	1	Usual care without personalized exercise	6	Clinically diagnosed BCRL

									<p>increased across a 4-stage program based on individual shoulder function recovery.</p> <p>Supervision: Hybrid. 4 supervised sessions (post-op days 1-2, 7-10, 14-20, 21-30) with a certified exercise specialist.</p> <p>Setting: Home-based with supervised sessions at clinic. Frequency: Daily home-based exercise for the first post-op month.</p> <p>Supervised sessions as above.</p>	<p>education or training</p>		
--	--	--	--	--	--	--	--	--	--	------------------------------	--	--

Fan 2026 Low	China	R, OL	54	49.9	25.6	I– III	100	59 .3	Initiated postopera tively during hospitaliz ation	Progressive resistance exercise for upper limbs (7 movements) using water bottles/dumbbells. Intensity: 40%-70% 1-RM. Progression: Every 4 weeks, increase 2%-10% of 1-RM, not exceeding 70%. Supervision: Hybrid. Initial instruction in hospital, then independent home- based training with weekly video submission via WeChat for remote	3	Usual care with routine postoper ative exercise guidance	12	Arm circumfe rence differenc e $\geq$ 2 cm differenc e
--------------------	-------	----------	----	------	------	-----------	-----	----------	---	--	---	---	----	--

										guidance. Setting: Home-based. Frequency: 2-3 times per week.				
Fan 2026 High	China	R, OL	56	48.3	26	I- III	100	73 .2	Initiated postopera tively during hospitaliz ation	Progressive resistance exercise for upper limbs (7 movements) using water bottles/dumbbells. Intensity: 60%-85% 1-RM. Progression: Every 4 weeks, increase 2%-10% of 1-RM, not exceeding 85%. Supervision/Setting/ Frequency: Same as L-MIEG.	3	Usual care with routine postoper ative exercise guidance	12	Arm circumfe rence differenc e $\geq$ 2 cm differenc e

Abbreviations: 1RM, one-repetition maximum; 7-RM, seven-repetition maximum; ALND, axillary lymph node dissection; AR, activity restriction; BCRL, breast cancer-related lymphedema; BMI, body mass index; JME, joint mobilization exercise; L-MIEG, low-to-

---

moderate intensity exercise group; NR, not reported; OL, open-label; PRE, progressive resistance exercise; R, randomized; RT, radiotherapy.

EARLY ACCESS

**Table 2. Evaluation of study quality using the RoB 2.0 tool**

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Ahmed 2006	Low risk (Block randomization used, balanced by age and body fat percentage. Baseline characteristics similar between groups)	Low risk (Intervention protocol clearly described; adherence high (>80% attendance); no co-interventions reported)	Low risk (45/78 with axillary dissection included; losses explained; no differential attrition between groups)	Some concerns (Objective circumference measures used, but self-report also included; outcome assessors blinded to allocation)	Low risk (Pre-specified outcomes reported; no evidence of selective reporting)	Some concerns
Courneya 2007	Low risk (Computer-generated, stratified by center and chemo protocol, concealed)	Low risk (Supervised exercise, high adherence, no major co-interventions reported)	Low risk (92.1% follow-up for patient-rated outcomes; lymphedema data available for most)	Some concerns (Objective volumetric measurement used, but assessors not blinded to group assignment)	Low risk (Pre-specified outcomes reported; no evidence of selective reporting)	Some concerns

	allocation)					
Sagen 2009	Low risk (Computer-generated block randomization, baseline balanced)	Some concerns (Intervention clearly defined, but adherence moderate (83–89%); control group also received usual care)	Some concerns (52/204 lost to 2-year follow-up (~25%), but ITT with LOCF used; baseline characteristics similar between completers and dropouts)	Low risk (Objective volumetric measurement (water displacement), assessor blinded)	Low risk (Pre-specified outcomes reported; no evidence of selective reporting)	Some concerns
Schmitz 2010	Low risk (Computerized minimization, balanced prognostic factors, concealed allocation)	Some concerns (Supervised initially, then unsupervised; adherence moderate (79%); control group non-exercise, no major co-intervention)	Low risk (134/154 completed follow-up (13% loss); ITT with imputation used)	Low risk (Objective volumetric measurement (water displacement); assessors blinded)	Low risk (Pre-specified outcomes reported; equivalence design clearly described)	Some concerns
Kilbreath 2012	Low risk (Computer-	Some concerns (Supervised weekly +	Low risk (Low attrition; ITT	Low risk (Blinded assessor; multiple	Low risk (Pre-specified outcomes	Some concerns

	generated, block randomization, stratified by axillary surgery and hospital, concealed allocation)	home program; adherence good (78–90%); control group had regular contact (fortnightly assessments)	analysis with complete data)	objective measures: BIS, circumferences)	reported; no evidence of selective reporting)	
Bloomquist 2019	Low risk (Computer-generated random sequence by Copenhagen Trial Unit, stratified by age and hospital. Baseline table shows balanced groups)	High risk (Usual care includes municipality low-moderate intensity resistance programs, likely accessible to the control group. This dilutes the contrast between PRE and non-PRE. Adherence in HIGH group was 66%. ITT analysis used)	Some concerns (Attrition: 85% at 12 weeks, 79% at 39 weeks. Dropouts were higher in the LOW group. Analysis used linear mixed models with all available data, but missingness may not be	Low risk (Outcome assessors were blinded to group allocation. Objective measures are robust. Self-reported symptoms could be influenced but are not the primary extraction target)	Low risk (Trial was registered. Pre-specified secondary outcomes are reported. No evident selective reporting)	High risk

			completely random)			
Ammitzbøll 2019	Low risk (Computer randomization, stratified by site and BMI >30. Baseline table shows well-balanced groups)	Some concerns (Potential contamination: 39% of the control group self-reported engaging in strength training during the study. This could dilute the treatment effect. Authors acknowledge this likely diluted difference. Intervention adherence was good (79% in Phase 1). ITT analysis was used)	Low risk (Attrition was 12% (19/158) at 12 months. Missing data were addressed with multiple imputation for primary analysis, and sensitivity analyses (complete case, worst/best scenario) did not change interpretation)	Low risk (Outcome assessors (physiotherapists for water displacement, DXA technician, statistician) were blinded to group allocation. The primary outcome (water displacement) is an objective, robust measure)	Low risk (Trial was registered. Pre-specified primary outcome (arm volume/lymphedema) and secondary outcomes are reported. Analysis plan appears consistent)	Some concerns
Owusu 2022	Low Risk	Some concerns	Low risk (High	Low risk	Low risk (The trial	Some

	<p>( Computer-generated randomization lists were created by a biostatistician, stratified by SES, race, and chemotherapy. Allocation was concealed (research coordinators saw assignment only at randomization)</p>	<p>(open-label (participants and personnel were aware of the intervention). While the control was designed as an attention-control, the provision of a Fitbit to all participants may have inadvertently increased physical activity in the control group, blurring the difference between groups. The authors acknowledge this as a limitation)</p>	<p>retention (90% at 20 weeks). Analysis was modified intention-to-treat, including all randomized participants with baseline and 20-week data)</p>	<p>(Lymphedema was assessed objectively by a certified specialist using a standardized method (girth measurement, &gt;3% volume increase). It is unlikely the outcome assessor was blinded due to the study design, but the objective nature of the measurement minimizes bias)</p>	<p>was pre-registered. The reported outcomes (including lymphedema incidence) match those described in the methods)</p>	<p>concerns</p>
Lin 2023	<p>Low risk (Computer-generated block</p>	<p>Some concerns (The trial was assessor-blinded, with</p>	<p>Low risk (192 of 200 randomized</p>	<p>Low risk (The outcome was measured</p>	<p>Low risk (The trial was registered prospectively. The</p>	<p>Some concerns</p>

	<p>randomization, baseline balanced)</p>	<p>participants instructed not to disclose group allocation, reducing detection bias. However, blinding of participants and intervention staff was not feasible due to the exercise nature, introducing potential performance bias. Adherence was monitored via daily WeChat check-ins and video uploads, which helped limit non-adherence and contamination, and no major protocol deviations were</p>	<p>participants completed the study (96% retention). Attrition was low and balanced across groups. Reasons for dropout (withdrawal, lost to follow-up, condition change) are provided and appear unrelated to the outcome. The proportion of missing data is unlikely to bias</p>	<p>objectively using the Relative Volume Change (RVC) calculated from arm circumference measurements, a standardized method. Outcome assessors were blinded to group allocation)</p>	<p>outcomes and time points specified in the Methods section are reported in the Results. There is no suggestion of selective reporting from the provided manuscript)</p>	
--	--	---	---	--	---	--

		reported)	the result)			
Min 2024	Low risk (Randomization used a permuted block design with stratification by age and surgery type. Allocation concealment was achieved using sequentially numbered, sealed, opaque envelopes. Baseline characteristics appear balanced between groups)	Some concerns (open label, the exercise group had high compliance (100% supervised, 96.7% home-based). There is no mention of contamination. The effect of non-blinding on the outcome (lymphedema incidence) is likely low as it's an objective measure, but knowledge of allocation could influence patient reporting or clinical detection)	Low risk (54 of 56 randomized participants (96%) completed the trial. Two participants in the exercise group were lost to follow-up at the 6-month assessment. Attrition is low, balanced, and unlikely to bias the lymphedema outcome)	High risk (The method of diagnosis of BCRL is not specified. Critically, outcome assessors were not blinded, and it is unclear if those assessing complications including BCRL were blinded)	Low risk (The trial was prospectively registered. Lymphedema is reported as a secondary/safety outcome. No evidence of selective reporting for this outcome within the manuscript)	High risk
Fan 2026	Low risk	Some concerns (Due	Low risk (Low	Low risk (The	Some concerns (No	Some

	<p>(Computer-generated block randomization, baseline balanced)</p>	<p>to the exercise nature, blinding of participants/personnel was not possible. However, the control group received only routine care, minimizing contamination. Adherence was monitored (weekly videos) and was high (&gt;80% in both exercise groups). No major deviations reported)</p>	<p>attrition: 110/114 (96.5%) completed. Dropouts: CG:1, L-MIEG:2, M-HIEG:1. Reasons: muscle soreness/fear (2 in exercise groups) and unspecified (2). Proportion is low, balanced, and unlikely to bias the lymphedema incidence outcome)</p>	<p>outcome was measured objectively using standardized circumference measurements at 6 anatomical sites. Although unblinded, the use of a tape measure and predefined criteria reduces the risk of bias. The measurement is unlikely to be influenced by knowledge of intervention)</p>	<p>trial registration number is mentioned. The outcomes reported align with the methods described. However, without a protocol or registration, the risk of selective reporting cannot be fully assessed)</p>	<p>concerns</p>
--	--	--	--	---	---	-----------------

---

Abbreviations: BCRL, breast cancer-related lymphedema; BIS, bioimpedance spectroscopy; BMI, body mass index; CG, control group; DXA, dual-energy X-ray absorptiometry; ITT, intention-to-treat; L-MIEG, low-to-moderate intensity exercise group; LOCF, last observation carried forward; M-HIEG, moderate-to-high intensity exercise group; NR, not reported; PRE, progressive resistance exercise; RoB, risk of bias; RVC, relative volume change; SES, socioeconomic status.

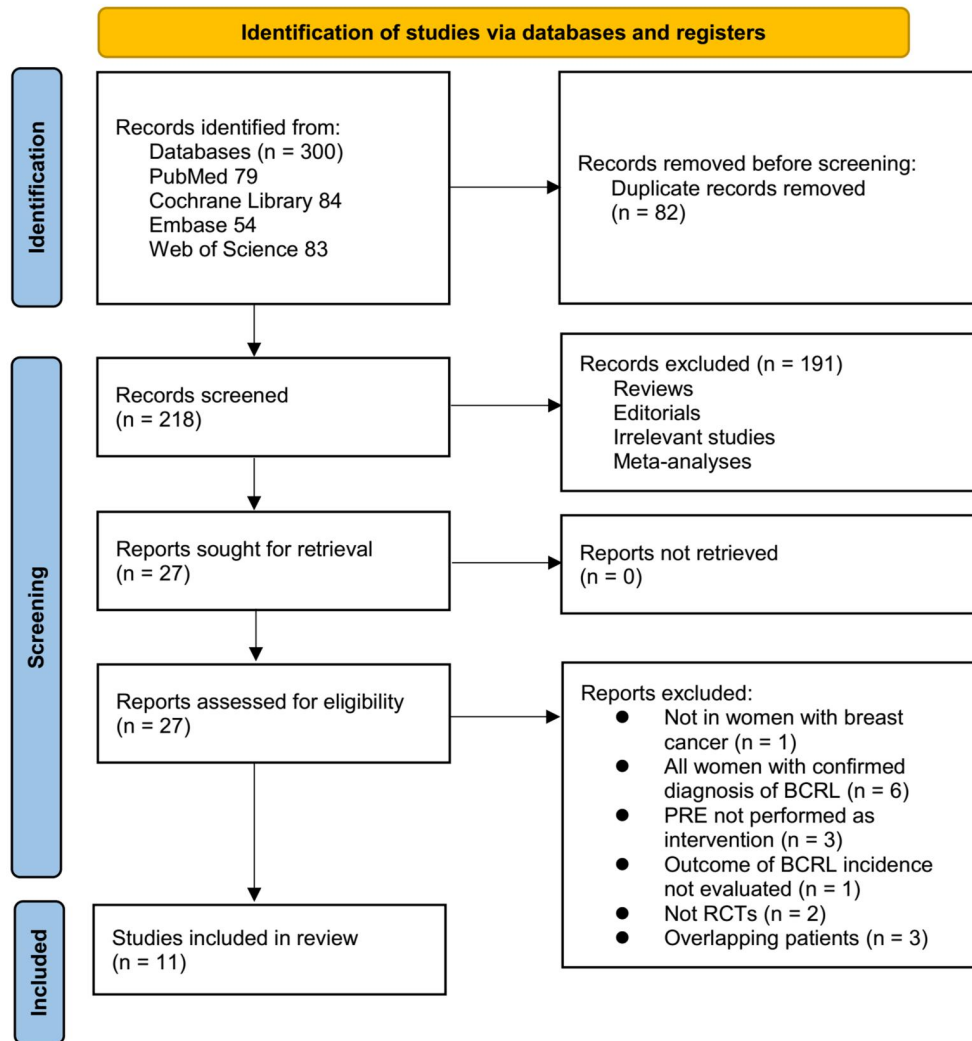
EARLY ACCESS

**Table 3. Summary of findings and certainty of evidence (GRADE)**

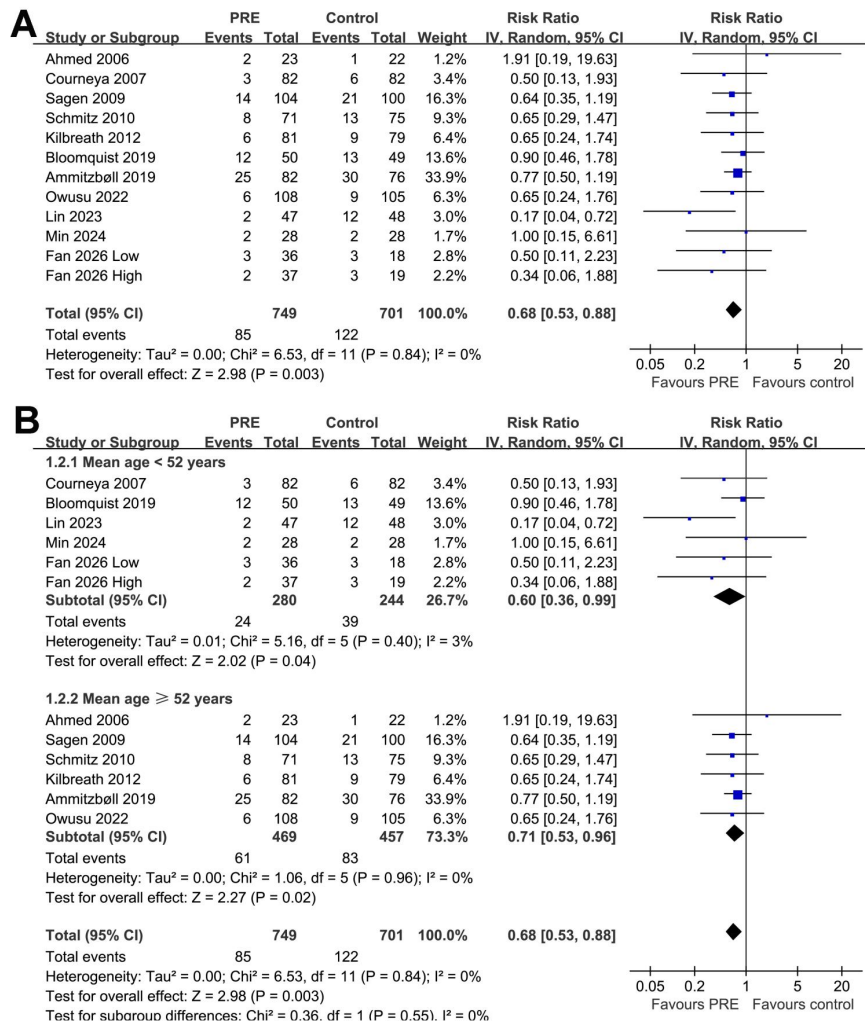
Outcome	No. of participants (studies)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relative effect: RR (95% CI),	Certainty of evidence (GRADE)	Comments
Incidence of BCRL	1,450 (11 RCTs, 12 datasets)	RCTs	Serious – all trials were open-label; two studies were at high overall risk of bias (e.g., contamination or unclear outcome assessment)	Not serious – direction of effect consistent across studies; low heterogeneity ( $I^2 = 0\%$ )	Not serious – intervention populations, and outcomes directly aligned with the review question	Not serious – pooled CI excludes no effect; total sample >1,000 provides adequate information size	None	0.68 (0.53 to 0.88)	⊕⊕⊕○ Moderate	PRE may reduce the risk of BCRL.

---

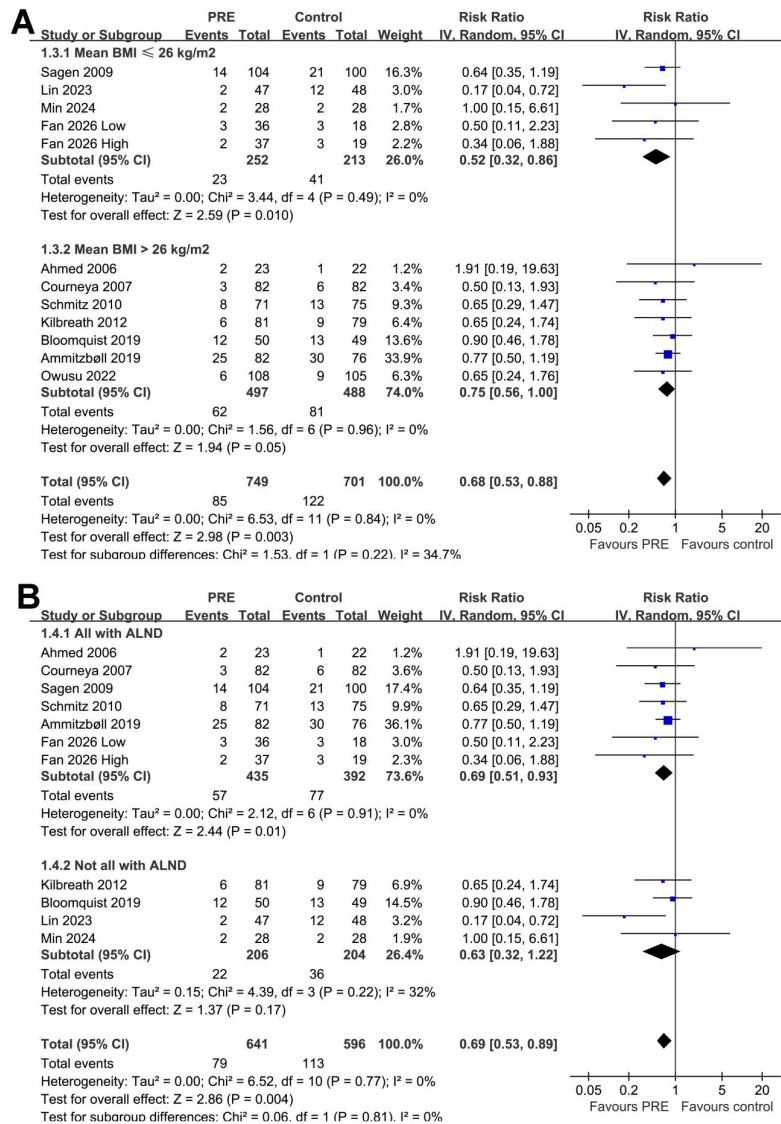
Specific reasons for each GRADE domain include: **1. Risk of bias:** The rating was downgraded when a significant proportion of studies exhibited unclear or high risk of bias in critical areas, such as random sequence generation, allocation concealment, or selective reporting. **2. Inconsistency:** The rating was downgraded in cases where substantial heterogeneity ( $I^2 > 50\%$ ) was observed and could not be accounted for by subgroup analyses or meta-regression. **3. Indirectness:** This domain was evaluated but not downgraded, as all included studies directly assessed the relevant population and outcomes. **4. Imprecision:** The rating was downgraded if confidence intervals were wide, overlapped with no effect, or if the overall sample size was small. **5. Publication bias:** This was assessed using funnel plots and Egger's test; the rating was downgraded if significant asymmetry indicated potential bias. **Abbreviations:** BCRL, breast cancer-related lymphedema; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; PRE, progressive resistance exercise; RCT, randomized controlled trial; RR, risk ratio.



**Figure 1. Flowchart for literature search and study inclusion**



**Figure 2. Forest plots of the effect of PRE on the incidence of BCRL after breast cancer surgery. (A)** Overall meta-analysis of 12 comparisons from 11 randomized controlled trials showed that PRE was associated with a significantly lower risk of BCRL than control conditions without PRE (RR = 0.68, 95% CI: 0.53–0.88;  $p = 0.003$ ), with no evidence of between-study heterogeneity ( $I^2 = 0\%$ ). **(B)** Subgroup analysis stratified by study-level mean age (<52 vs.  $\geq 52$  years) showed similar associations in both strata (<52 years: RR = 0.60, 95% CI: 0.36–0.99;  $\geq 52$  years: RR = 0.71, 95% CI: 0.53–0.96), with no significant difference between subgroups ( $p$  for subgroup difference = 0.55). Squares represent study-specific effect estimates weighted by inverse variance, horizontal lines indicate 95% confidence intervals, and diamonds indicate pooled effect estimates. Values <1 favor PRE. **Abbreviations:** BCRL, breast cancer-related lymphedema; CI, confidence interval; PRE, progressive resistance exercise; RR, risk ratio.

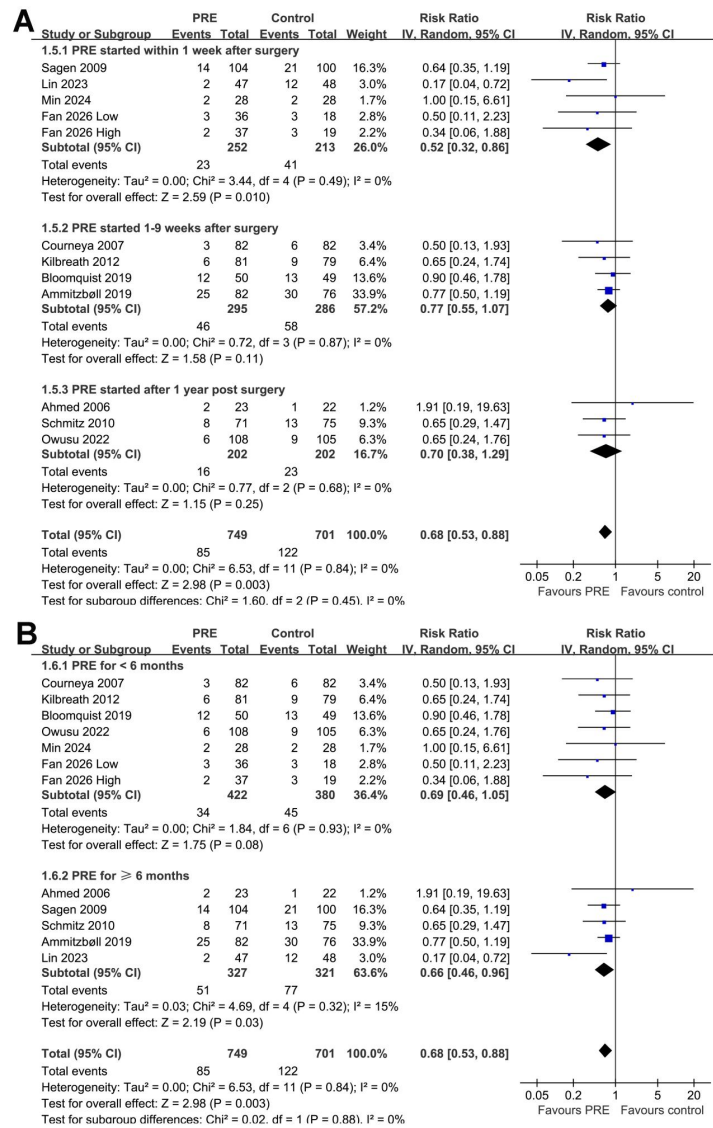


**Figure 3. Forest plots of subgroup analyses evaluating the association of PRE with the incidence of BCRL after breast cancer surgery. (A)** Subgroup analysis according to study-level mean baseline BMI showed a pooled RR of 0.52 (95% CI: 0.32–0.86) in studies with mean BMI  $\leq 26$  kg/m<sup>2</sup> and 0.75 (95% CI: 0.56–1.00) in studies with mean BMI  $> 26$  kg/m<sup>2</sup>, with no statistically significant difference between subgroups ( $p$  for subgroup difference = 0.22). **(B)** Subgroup analysis according to ALND status showed a pooled RR of 0.69 (95% CI: 0.51–0.93) in studies in which all participants underwent ALND and 0.63 (95% CI: 0.32–1.22) in studies in which not all participants underwent ALND, with no evidence of a subgroup effect ( $p$  for subgroup difference = 0.81). Panel B includes only studies that could be classified according to ALND status. Squares represent study-specific effect estimates weighted by inverse variance, horizontal lines indicate 95% CIs, and diamonds indicate pooled

---

effect estimates from random-effects models. Values  $<1$  favor PRE. **Abbreviations:** ALND, axillary lymph node dissection; BCRL, breast cancer-related lymphedema; BMI, body mass index; CI, confidence interval; PRE, progressive resistance exercise; RR, risk ratio.

EARLY ACCESS

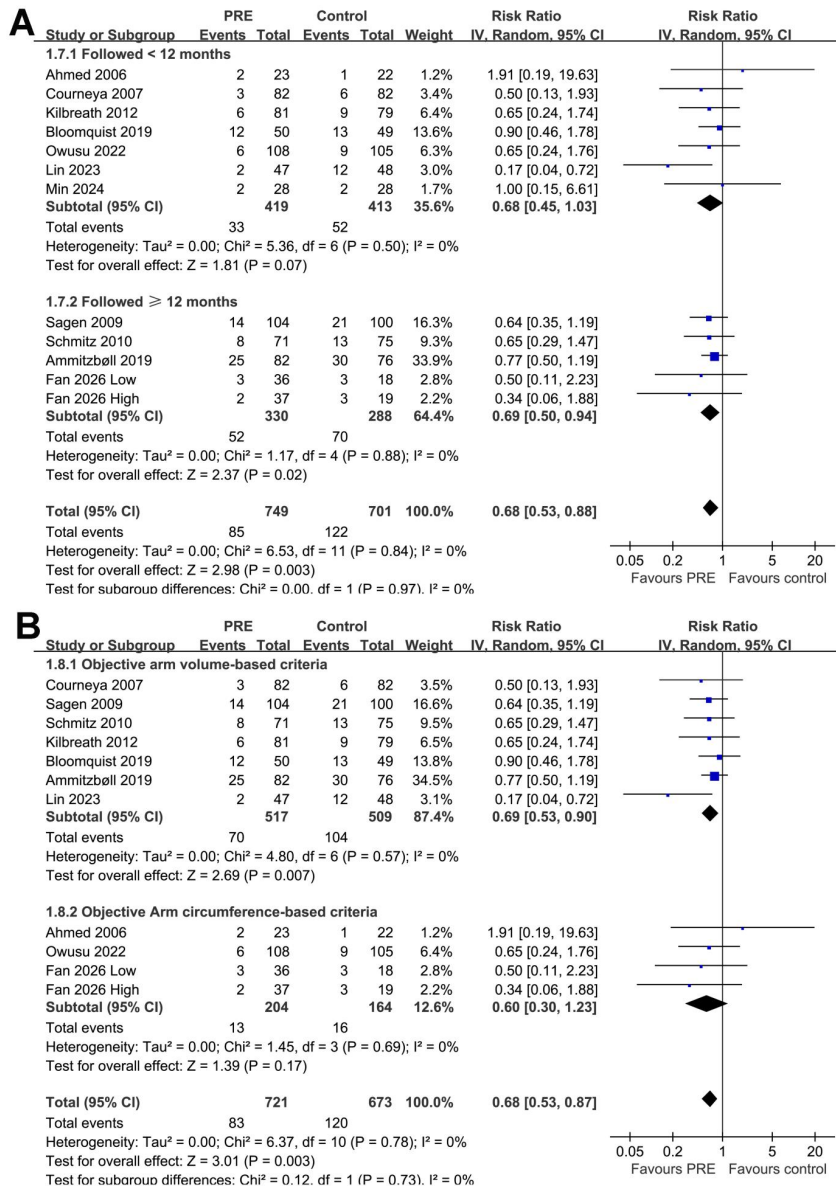


**Figure 4. Forest plots of subgroup analyses evaluating whether timing of initiation and intervention duration modify the association between PRE and the incidence of BCRL after breast cancer surgery. (A)** When studies were stratified according to the timing of PRE initiation, the pooled RRs were 0.52 (95% CI: 0.32–0.86) for programs started within 1 week after surgery, 0.77 (95% CI: 0.55–1.07) for programs started 1–9 weeks after surgery, and 0.70 (95% CI: 0.38–1.29) for programs initiated more than 1 year postoperatively, with no significant difference between subgroups ( $p$  for subgroup difference = 0.45). **(B)** When studies were stratified according to PRE duration, the pooled RRs were 0.69 (95% CI: 0.46–1.05) for interventions lasting <6 months and 0.66 (95% CI: 0.46–0.96) for interventions lasting  $\geq$ 6 months, again with no evidence of a subgroup effect ( $p$  for subgroup difference = 0.88). The overall pooled estimate favored PRE (RR = 0.68, 95% CI:

---

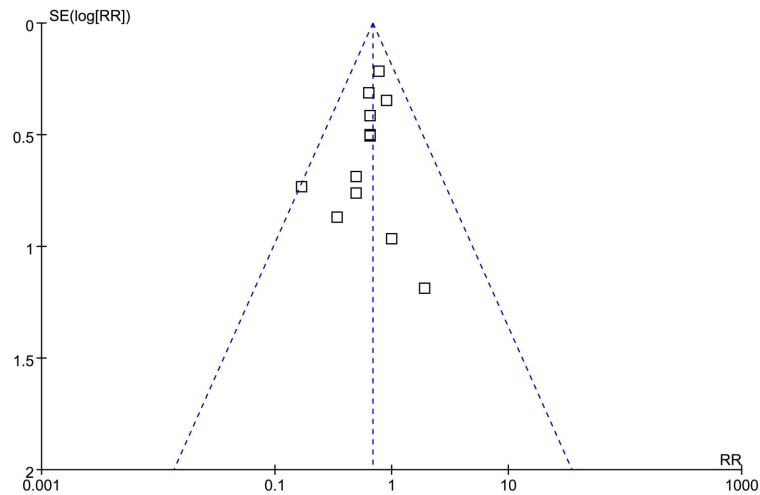
0.53–0.88). Squares represent study-specific effect estimates weighted by inverse variance, horizontal lines indicate 95% CIs, and diamonds indicate pooled effect estimates from random-effects models. Values <1 favor PRE. **Abbreviations:** BCRL, breast cancer–related lymphedema; CI, confidence interval; PRE, progressive resistance exercise; RR, risk ratio.

EARLY ACCESS



**Figure 5. Forest plots of subgroup analyses evaluating whether follow-up duration and diagnostic approach modify the association between PRE and the incidence of BCRL after breast cancer surgery. (A)** When studies were stratified according to follow-up duration, the pooled RRs were 0.68 (95% CI: 0.45–1.03) for follow-up <12 months and 0.69 (95% CI: 0.50–0.94) for follow-up ≥12 months, with no evidence of a subgroup effect ( $p$  for subgroup difference = 0.97). **(B)** When studies were stratified according to the diagnostic criteria used for incident BCRL, the pooled RRs were 0.69 (95% CI: 0.53–0.90) for studies using objective arm volume-based criteria and 0.60 (95% CI: 0.30–1.23) for studies using objective arm circumference-based criteria, again with no significant difference between subgroups ( $p$  for subgroup difference = 0.73). In panel B, only studies that could be classified according to

objective diagnostic approach were included. Squares represent study-specific effect estimates weighted by inverse variance, horizontal lines indicate 95% CIs, and diamonds indicate pooled effect estimates from random-effects models. Values <1 favor PRE. **Abbreviations:** BCRL, breast cancer-related lymphedema; CI, confidence interval; PRE, progressive resistance exercise; RR, risk ratio.



**Figure 6. Funnel plot assessing potential publication bias for the meta-analysis of PRE and BCRL risk. Each square represents an individual comparison. The plot appears approximately symmetrical, suggesting a low risk of publication bias. Abbreviations:** BCRL, breast cancer-related lymphedema; PRE, progressive resistance exercise.

---

## SUPPLEMENTAL DATA

### Supplemental File 1. Detailed search strategy for each database

#### PubMed

((("Breast Neoplasms"[Mesh] OR breast cancer[tiab] OR breast tumor\*[tiab] OR breast tumour\*[tiab] OR breast neoplasm\*[tiab] OR breast carcinoma\*[tiab]) AND ("Lymphedema"[Mesh] OR lymphedema[tiab] OR lymphoedema[tiab] OR secondary lymphedema[tiab] OR arm lymphedema[tiab] OR arm swelling[tiab] OR upper extremity edema[tiab]) AND ("Resistance Training"[Mesh] OR resistance exercise\*[tiab] OR progressive resistance exercise\*[tiab] OR progressive resistance training[tiab] OR strength exercise\*[tiab] OR strength training[tiab] OR weight lifting[tiab] OR weight training[tiab]) AND ("Randomized Controlled Trial"[Publication Type] OR randomized[tiab] OR randomised[tiab] OR randomly[tiab] OR trial[tiab] OR control\*[tiab] OR allocated[tiab] OR placebo[tiab]))

#### Cochrane Library

(breast cancer OR breast tumor\* OR breast tumour\* OR breast neoplasm\* OR breast carcinoma\*) AND (lymphedema OR lymphoedema OR secondary lymphedema OR arm lymphedema OR arm swelling OR upper extremity edema) AND (resistance exercise OR progressive resistance exercise OR progressive resistance training OR strength exercise OR strength training OR weight lifting OR weight training) AND (random\* OR trial OR control\* OR allocated OR placebo)

#### Embase

('breast cancer'/exp OR 'breast tumor\*':ti,ab OR 'breast tumour\*':ti,ab OR 'breast neoplasm\*':ti,ab OR 'breast carcinoma\*':ti,ab) AND ('lymphedema'/exp OR lymphedema:ti,ab OR lymphoedema:ti,ab OR 'secondary lymphedema':ti,ab OR 'arm

---

swelling':ti,ab OR 'upper extremity edema':ti,ab) AND ('resistance training'/exp OR 'progressive resistance exercise':ti,ab OR 'progressive resistance training':ti,ab OR 'strength training':ti,ab OR 'weight lifting':ti,ab OR 'weight training':ti,ab) AND ('randomized controlled trial'/exp OR random\*:ti,ab OR placebo:ti,ab OR control\*:ti,ab OR allocated:ti,ab)

### **Web of Science**

TS=(("breast cancer" OR "breast tumor\*" OR "breast tumour\*" OR "breast neoplasm\*" OR "breast carcinoma\*") AND ("lymphedema" OR "lymphoedema" OR "secondary lymphedema" OR "arm lymphedema" OR "arm swelling" OR "upper extremity edema") AND ("resistance exercise" OR "progressive resistance exercise" OR "progressive resistance training" OR "strength exercise" OR "strength training" OR "weight lifting" OR "weight training") AND (random\* OR randomized OR randomised OR trial OR control\* OR allocated OR placebo))