



# Thirteen Years of Immediate Lymphatic Reconstruction (ILR) for the Prevention of Lymphedema: A Meta-analysis of Prospective Clinical Trials

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## Background

Despite the growing use of immediate lymphatic reconstruction (ILR) for preventing lymphedema, prospective long-term data on its efficacy remain limited. This study aims to analyze long-term, prospective outcomes of ILR, utilizing all available outcome measures.

## Methods

A systematic review was conducted on PubMed, Embase, and Web of Science to search for studies on ILR to prevent or reduce the incidence of lymphedema in patients undergoing axillary lymph node dissection in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. Outcome data included the pooled cumulative incidence of lymphedema (assessed by limb measurements), odds ratio (OR), and relative risk (RR) for lymphedema development in patients who underwent ILR versus those who did not. Only prospective clinical trials with a minimum of 12 months of follow-up were included.

## Results

Nine prospective studies (2011–2024) were included, totaling 791 patients, with 460 undergoing ILR and an average follow-up of  $20.6 \pm 4.8$  months. On average,  $1.9 \pm 0.4$  anastomoses were performed per patient. ILR was associated with a significantly lower incidence of lymphedema: 9% (95% CI: 1% – 16%) compared to 29% (95% CI: 11% – 46%) in the non-ILR group. Patients who received ILR had 69% lower odds of developing lymphedema compared to those without ILR (OR = 0.31, 95% CI: 0.19 – 0.51). A 58% reduction in lymphedema risk was also observed among ILR recipients (RR = 0.42, 95% CI: 0.26 – 0.68).

## Conclusion

This meta-analysis is the largest study to evaluate the long-term efficacy of ILR in lymphedema prevention. The findings demonstrate that ILR significantly reduces the incidence, odds, and risk of lymphedema, supporting its role as an effective preventive strategy in at-risk patients.

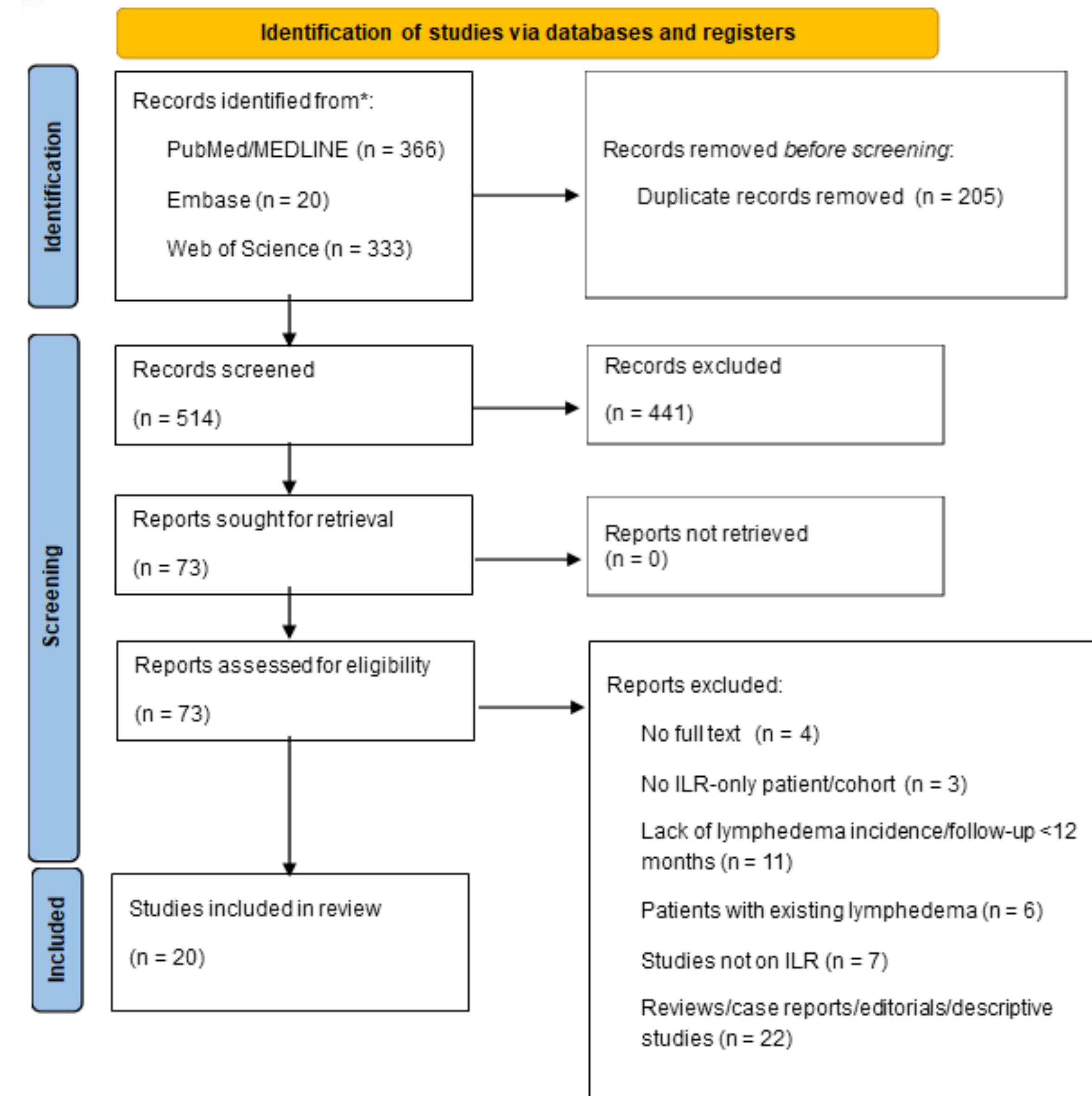


**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow chart

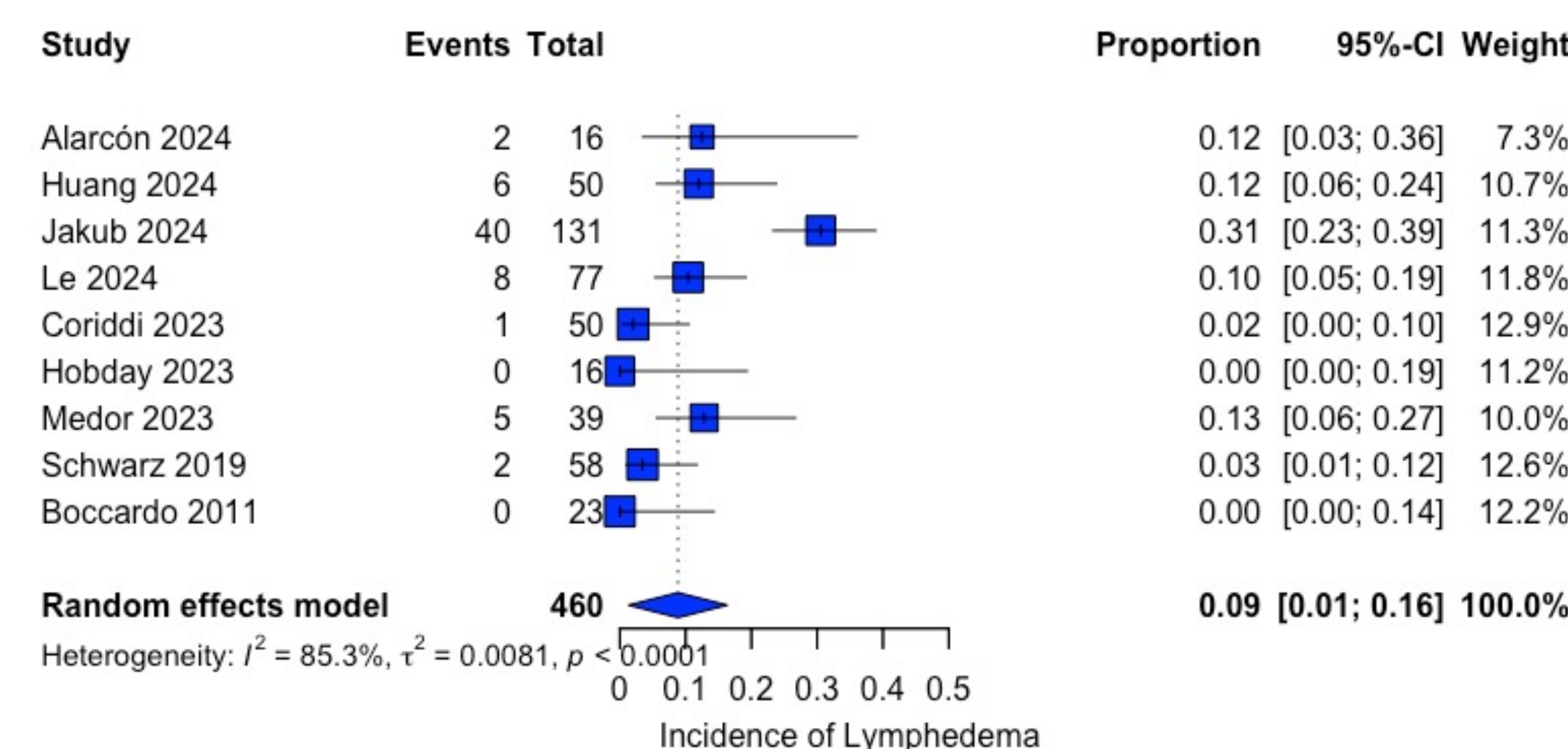


**Figure 2.** Cumulative Incidence of Lymphedema in Patients Who Received Immediate Lymphatic Reconstruction

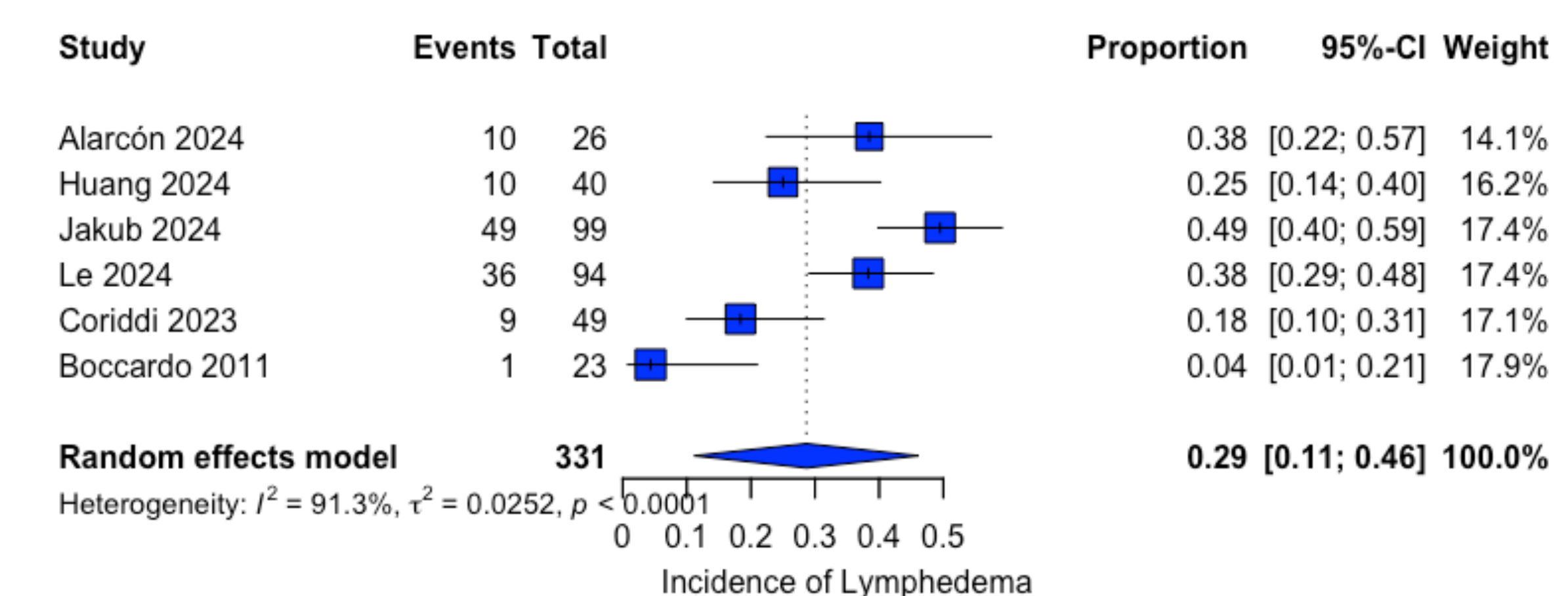


**Figure 3.** Cumulative Incidence of Lymphedema in Patients Who Did Not Receive ILR

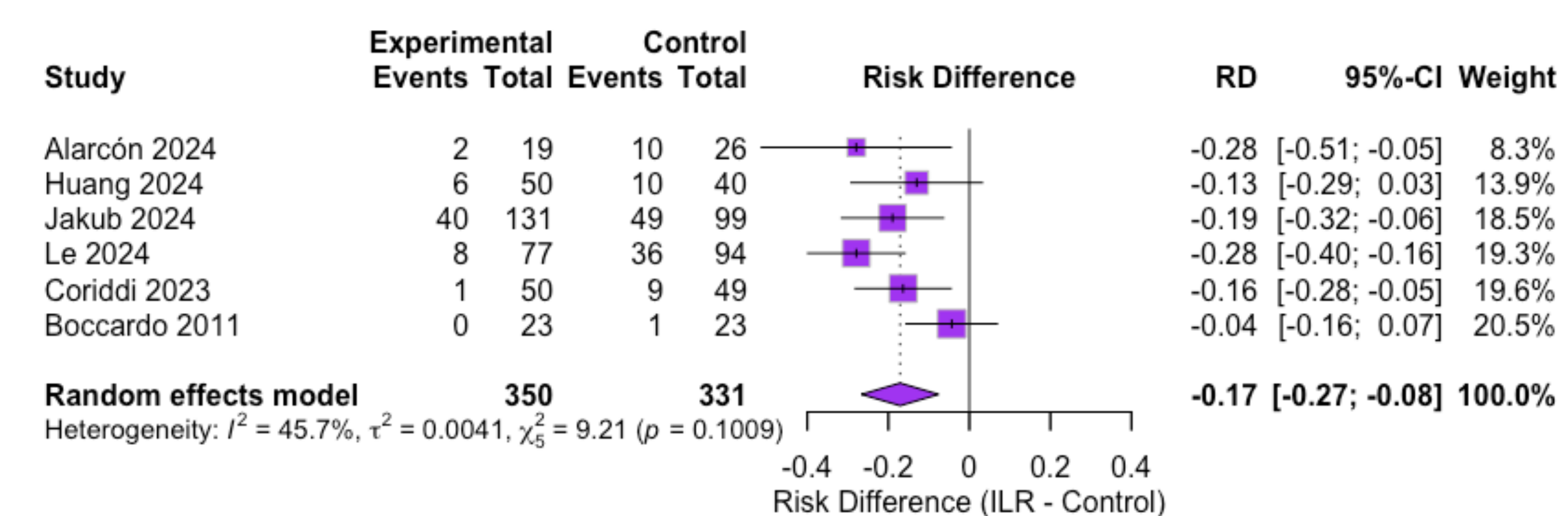
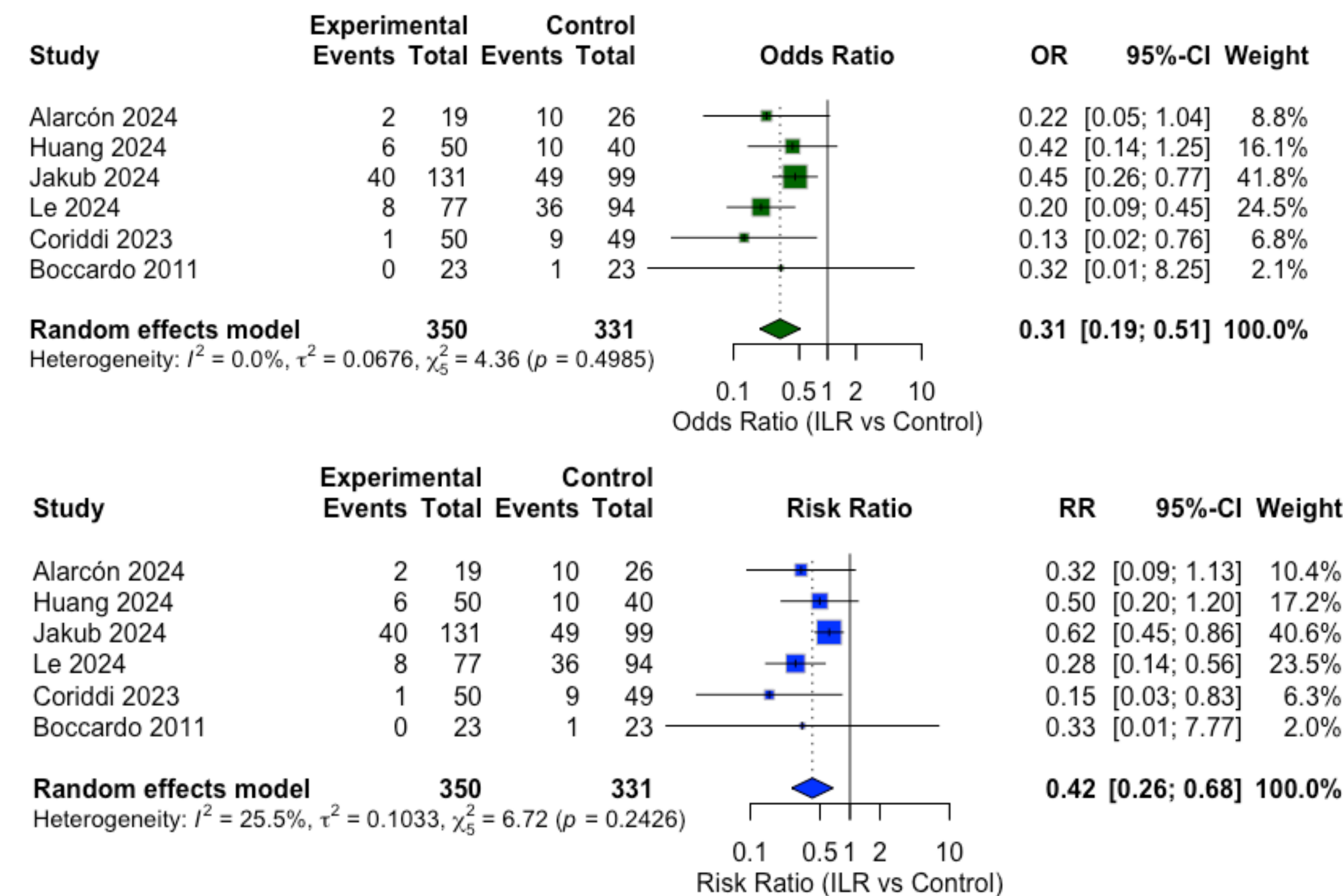


**Figure 4.** Odds Ratios (OR), Risk Ratio (RR), and Risk Difference (RD) with 95% Confidence Intervals (CI) for Lymphedema Development in Patients Who Received ILR Compared to Patients Who Did Not

|       |                                                                                                                                                                                                                                                                                                                             | Risk of bias domains |    |    |    |    |    |                                                 |
|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|----|----|----|----|----|-------------------------------------------------|
|       |                                                                                                                                                                                                                                                                                                                             | D1                   | D2 | D3 | D4 | D5 | D6 | D7                                              |
| Study | Alarcón et al., 2024                                                                                                                                                                                                                                                                                                        | ⊗                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊗  | ⊕                                               |
|       | Brahma et al., 2024                                                                                                                                                                                                                                                                                                         | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊖                                               |
|       | Huang et al., 2024                                                                                                                                                                                                                                                                                                          | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊖                                               |
|       | Le et al., 2024                                                                                                                                                                                                                                                                                                             | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊗  | ⊗                                               |
|       | Poskevicius et al., 2024                                                                                                                                                                                                                                                                                                    | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊖  | ⊖                                               |
|       | Uyulmaz et al., 2024                                                                                                                                                                                                                                                                                                        | ⊖                    | ⊕  | ⊕  | ⊕  | ⊖  | ⊕  | ⊖                                               |
|       | Chung et al., 2023                                                                                                                                                                                                                                                                                                          | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊗  | ⊗                                               |
|       | Hobday et al., 2023                                                                                                                                                                                                                                                                                                         | ⊗                    | ⊗  | ⊖  | ⊕  | ⊕  | ⊕  | ⊗                                               |
|       | Granoff et al., 2023                                                                                                                                                                                                                                                                                                        | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊖  | ⊖                                               |
|       | Levy et al., 2023                                                                                                                                                                                                                                                                                                           | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊕                                               |
| Study | Médor et al., 2024                                                                                                                                                                                                                                                                                                          | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊖                                               |
|       | Wong et al., 2024                                                                                                                                                                                                                                                                                                           | ⊗                    | ⊕  | ⊕  | ⊕  | ⊖  | ⊕  | ⊗                                               |
|       | Herremans et al., 2021                                                                                                                                                                                                                                                                                                      | ⊕                    | ⊕  | ⊖  | ⊕  | ⊕  | ⊕  | ⊖                                               |
|       | Gomberawalla et al., 2017                                                                                                                                                                                                                                                                                                   | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊖  | ⊗                                               |
|       | Boccardo et al., 2016                                                                                                                                                                                                                                                                                                       | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊖                                               |
|       | Boccardo et al., 2014                                                                                                                                                                                                                                                                                                       | ⊖                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊖                                               |
|       | Domains:<br>D1: Bias due to confounding.<br>D2: Bias due to selection of participants.<br>D3: Bias in classification of interventions.<br>D4: Bias due to deviations from intended interventions.<br>D5: Bias due to missing data.<br>D6: Bias in measurement of outcomes.<br>D7: Bias in selection of the reported result. |                      |    |    |    |    |    | Judgement<br>⊗ Serious<br>⊖ Moderate<br>⊕ Low   |
|       | Boccardo et al., 2011                                                                                                                                                                                                                                                                                                       | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊕                                               |
|       | Coriddi et al., 2023                                                                                                                                                                                                                                                                                                        | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊕                                               |
|       | Jakub et al., 2024                                                                                                                                                                                                                                                                                                          | ⊖                    | ⊕  | ⊖  | ⊖  | ⊖  | ⊖  | ⊗                                               |
| Study | Domains:<br>D1: Bias arising from the randomization process.<br>D2: Bias due to deviations from intended intervention.<br>D3: Bias due to missing outcome data.<br>D4: Bias in measurement of the outcome.<br>D5: Bias in selection of the reported result.                                                                 |                      |    |    |    |    |    | Judgement<br>⊗ High<br>⊖ Some concerns<br>⊕ Low |
|       | Boccardo et al., 2011                                                                                                                                                                                                                                                                                                       | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊕                                               |
|       | Coriddi et al., 2023                                                                                                                                                                                                                                                                                                        | ⊕                    | ⊕  | ⊕  | ⊕  | ⊕  | ⊕  | ⊕                                               |
|       | Jakub et al., 2024                                                                                                                                                                                                                                                                                                          | ⊖                    | ⊕  | ⊖  | ⊖  | ⊖  | ⊖  | ⊗                                               |
|       |                                                                                                                                                                                                                                                                                                                             |                      |    |    |    |    |    |                                                 |

**Figure 7.** Assessment of Risk of Bias Using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) and Risk of Bias 2 (ROB2) Tools