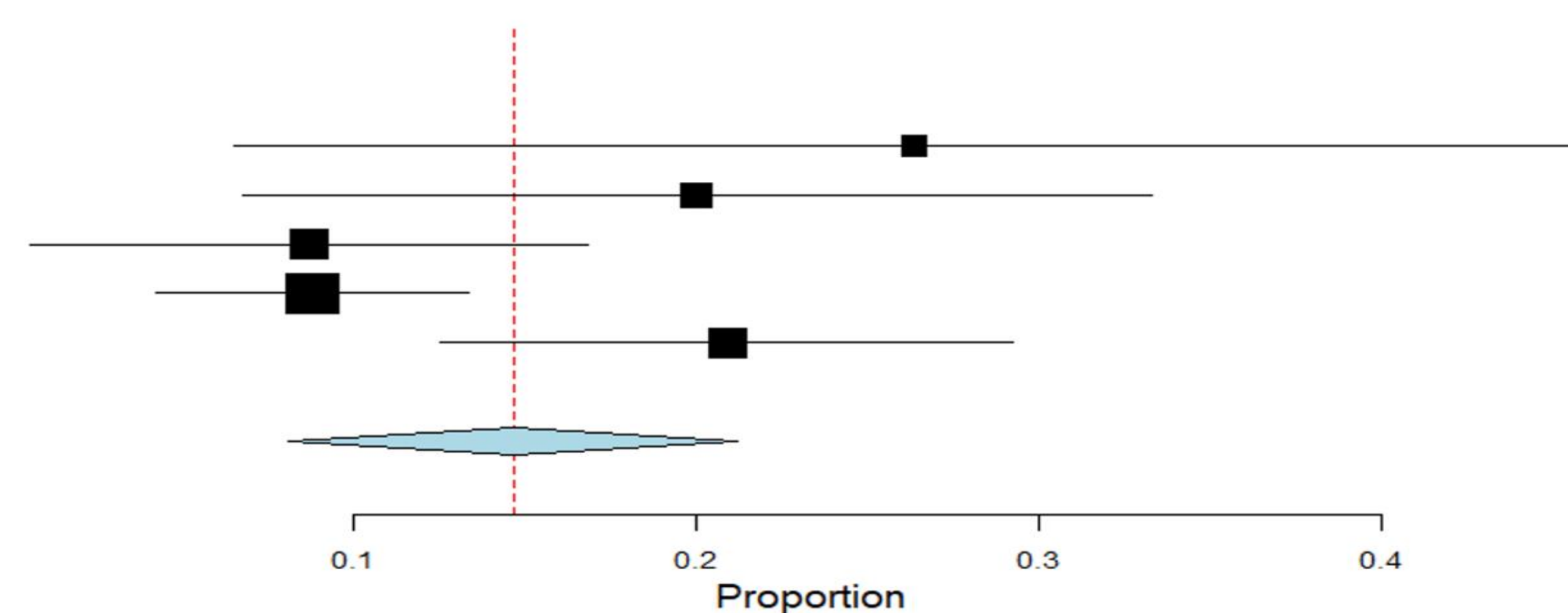


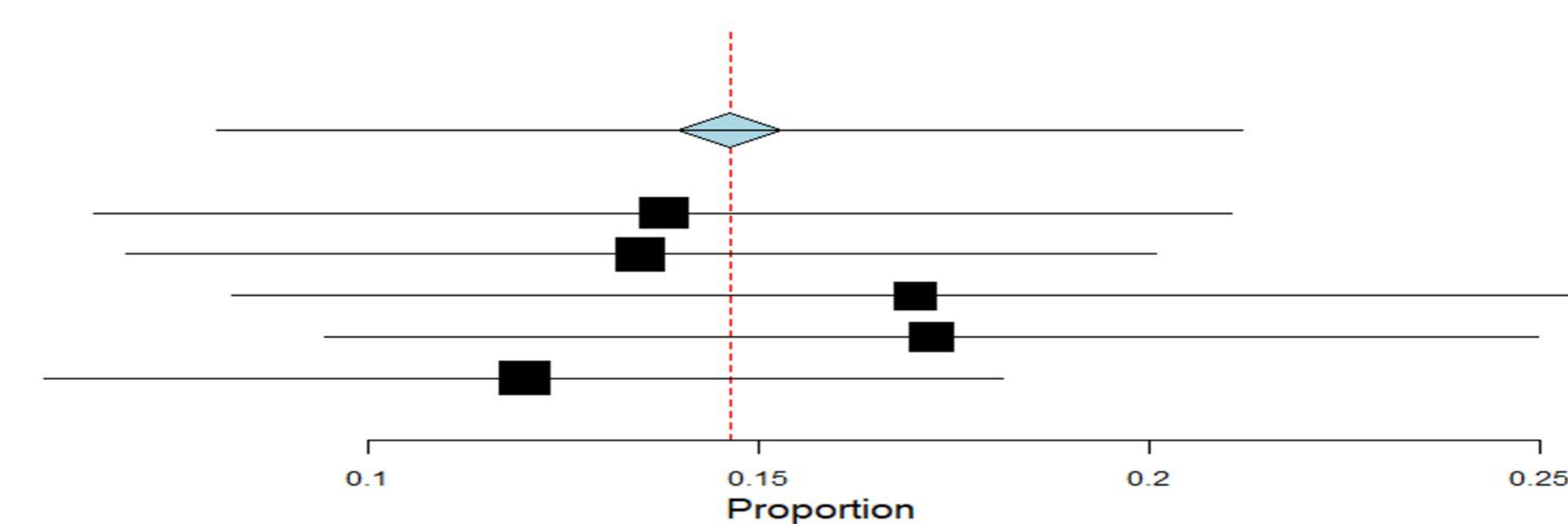
(A) Studies

| Study | Estimate (95% C.I.) | Ev/Trt |
|--|-----------------------------|---------------|
| Ito, 2017 | 0.263 (0.065, 0.461) | 5/19 |
| Nyuzuki, 2013 | 0.200 (0.067, 0.333) | 7/35 |
| Shimada, 2015 | 0.087 (0.006, 0.168) | 4/46 |
| Tajima, 2020 | 0.088 (0.042, 0.133) | 13/148 |
| Toya, 2016 | 0.209 (0.125, 0.292) | 19/91 |
| Overall (I²=61.14 % , P=0.036) | 0.146 (0.081, 0.212) | 48/339 |



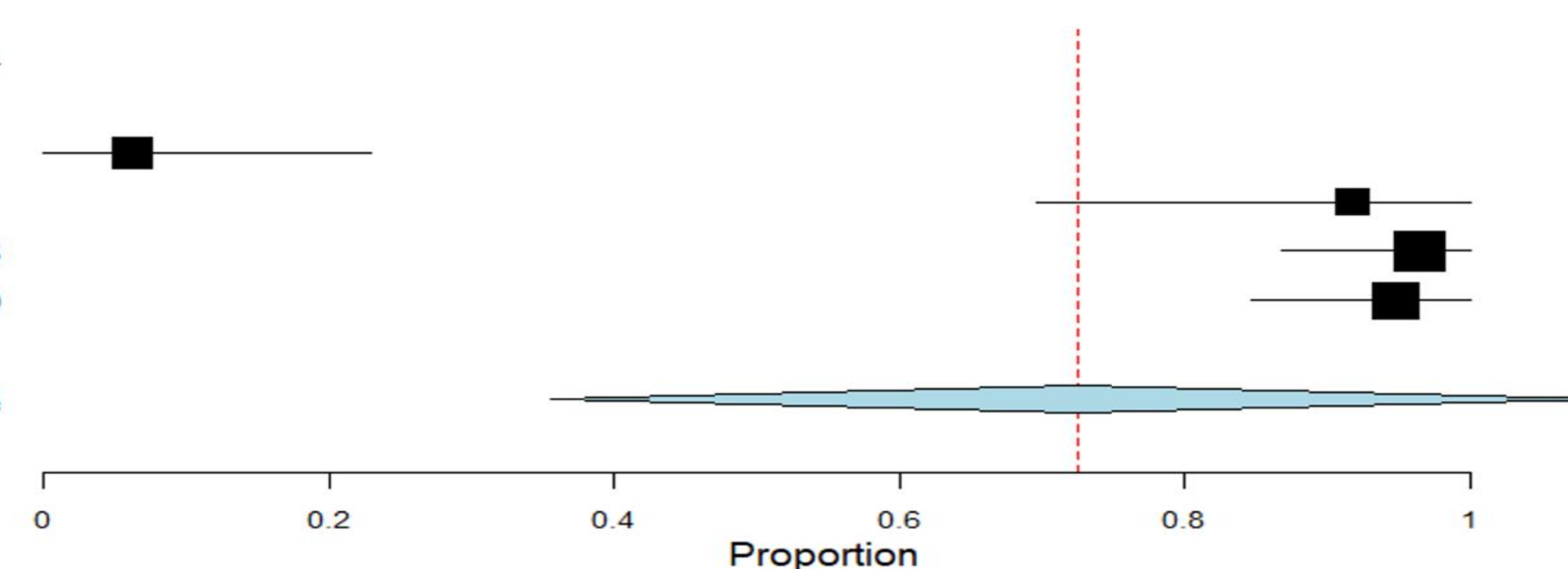
(B) Studies

| Study | Estimate (95% C.I.) |
|-----------------|-----------------------------|
| Overall | 0.146 (0.081, 0.212) |
| - Nyuzuki, 2013 | 0.138 (0.065, 0.211) |
| - Ito, 2017 | 0.135 (0.069, 0.201) |
| - Shimada, 2015 | 0.170 (0.083, 0.257) |
| - Tajima, 2020 | 0.172 (0.095, 0.250) |
| - Toya, 2016 | 0.120 (0.059, 0.181) |



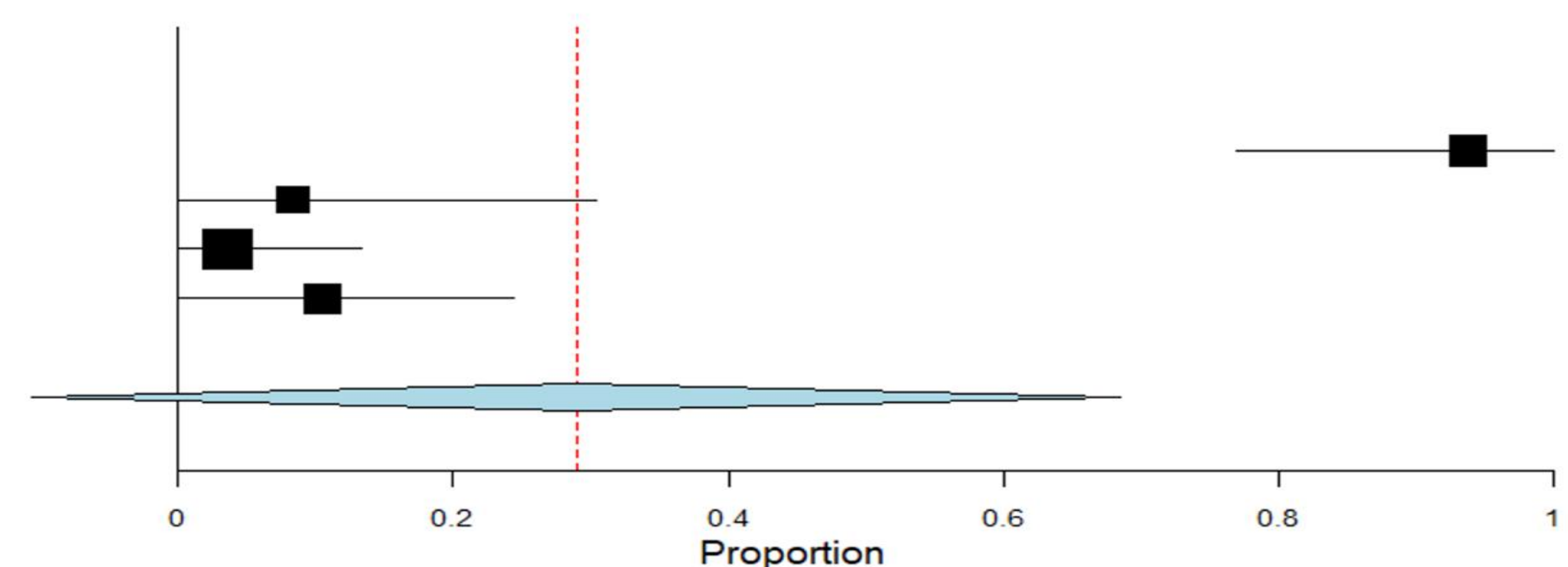
(C) Studies

| Study | Estimate (95% C.I.) | Ev/Trt |
|--|-----------------------------|--------------|
| Nyuzuki, 2013 | 0.062 (0.000, 0.230) | 0/7 |
| Ito, 2017 | 0.917 (0.696, 1.000) | 5/5 |
| Tajima, 2020 | 0.964 (0.867, 1.000) | 13/13 |
| Toya, 2016 | 0.947 (0.847, 1.000) | 18/19 |
| Overall (I²=96.79 % , P< 0.001) | 0.725 (0.356, 1.094) | 36/44 |



(D) Studies

| Study | Estimate (95% C.I.) | Ev/Trt |
|--|------------------------------|-------------|
| Nyuzuki, 2013 | 0.938 (0.770, 1.000) | 7/7 |
| Ito, 2017 | 0.083 (0.000, 0.304) | 0/5 |
| Tajima, 2020 | 0.036 (0.000, 0.133) | 0/13 |
| Toya, 2016 | 0.105 (0.000, 0.243) | 2/19 |
| Overall (I²=96.59 % , P< 0.001) | 0.289 (-0.107, 0.686) | 9/44 |



Introduction

- Dabigatran-induced esophagitis (DIE) has been reported increasingly recently in the literature.
- However, the exact prevalence of DIE is uncertain.
- Therefore, we performed a systematic review and meta-analysis to define and provide a quantitative assessment of the prevalence of DIE on endoscopy.

Methods and Materials

- A comprehensive literature search of PubMed/Medline, Embase, and Web of Science was conducted on April 01, 2022, to include all studies that reported the prevalence of DIE among patients undergoing upper endoscopy.
- Two independent reviewers (AB and RM) screened and shortlisted articles and performed data extraction.
- Any discrepancy was resolved by consensus.
- The statistical analysis was performed using Open Meta Analyst (CEBM, Oxford, UK).
- Pooled event rate and corresponding 95% confidence intervals (CI) were calculated using the random-effects model and DerSimonian Laird method.
- Heterogeneity was assessed using the Higgins I² index (I² values >50% implied the presence of significant heterogeneity).

Results

- Five retrospective cohort studies with 339 patients were included.
- All studies originated from Japan.
- The pooled prevalence rate of DIE was 15.5% (95% CI 0.096-0.239, I²=62.4%, Figure 1A).
- A leave-one-out sensitivity analysis showed similar results (Figure 1B).
- Four studies reported the detailed endoscopic features of DIE.
- All DIE occurred in the mid and/or lower esophagus.
- Longitudinal mucosal casts were the most common endoscopic feature, with a pooled rate of 82.2% (95% CI 0.254-0.984, I²=74.8%, Figure 1C).
- The pooled rate of mucosal erosions was 20.5% (95% CI 0.025-0.725, I²=72.5%, Figure 1D).

Conclusions

- Nearly 15% of patients receiving dabigatran were found to have dabigatran-induced esophagitis on endoscopy.
- Physicians should be cautious about using dabigatran in patients with a history of esophagitis or gastroesophageal reflux disease.
- Patients who receive dabigatran should undergo an upper endoscopy to evaluate for DIE if they develop gastrointestinal symptoms.
- Prospective, large-scale, multicenter studies are needed to further understand DIE.