

E-cigarettes in smoking cessation: A systematic review and network meta-analysis of randomised controlled trials

Daniel Stjepanović¹, Gary C. K. Chan¹, Carmen Lim¹, Tianze Sun¹, Aathavan Shanmuga Anandan¹, Jason P. Connor^{1,2}, Coral Gartner³, Wayne D. Hall¹, Janni Leung¹

¹National Centre for Youth Substance Use Research, The University of Queensland; ²Discipline of Psychiatry, The University of Queensland; ³School of Public Health, The University of Queensland

Introduction

Combustible cigarettes are responsible for more deaths than any other consumer product in history. Over 8 million people die prematurely each year due to smoking-related diseases

Nicotine replacement therapy products (NRTs) increase smoking cessation by providing users with nicotine, thereby reducing cravings.

Nicotine containing electronic cigarettes (“e-cigarettes”) may be a more effective aid than existing NRTs because they provide a similar behavioural and sensory experience to cigarette smoking in addition to nicotine delivery.

E-cigarettes and NRTs have been shown to be effective cessation tools, but much of this evidence is drawn from observational and cohort studies.

Evidence from randomised controlled trials (RCTs) is necessary to evaluate the effectiveness of e-cigarettes.

The aims of the present work are to:

- Systematically synthesise evidence from existing RCTs on the effectiveness of e-cigarettes in promoting smoking cessation
- Utilise network meta-analysis to contrast effectiveness of e-cigarettes against existing NRTs and nicotine-free control conditions

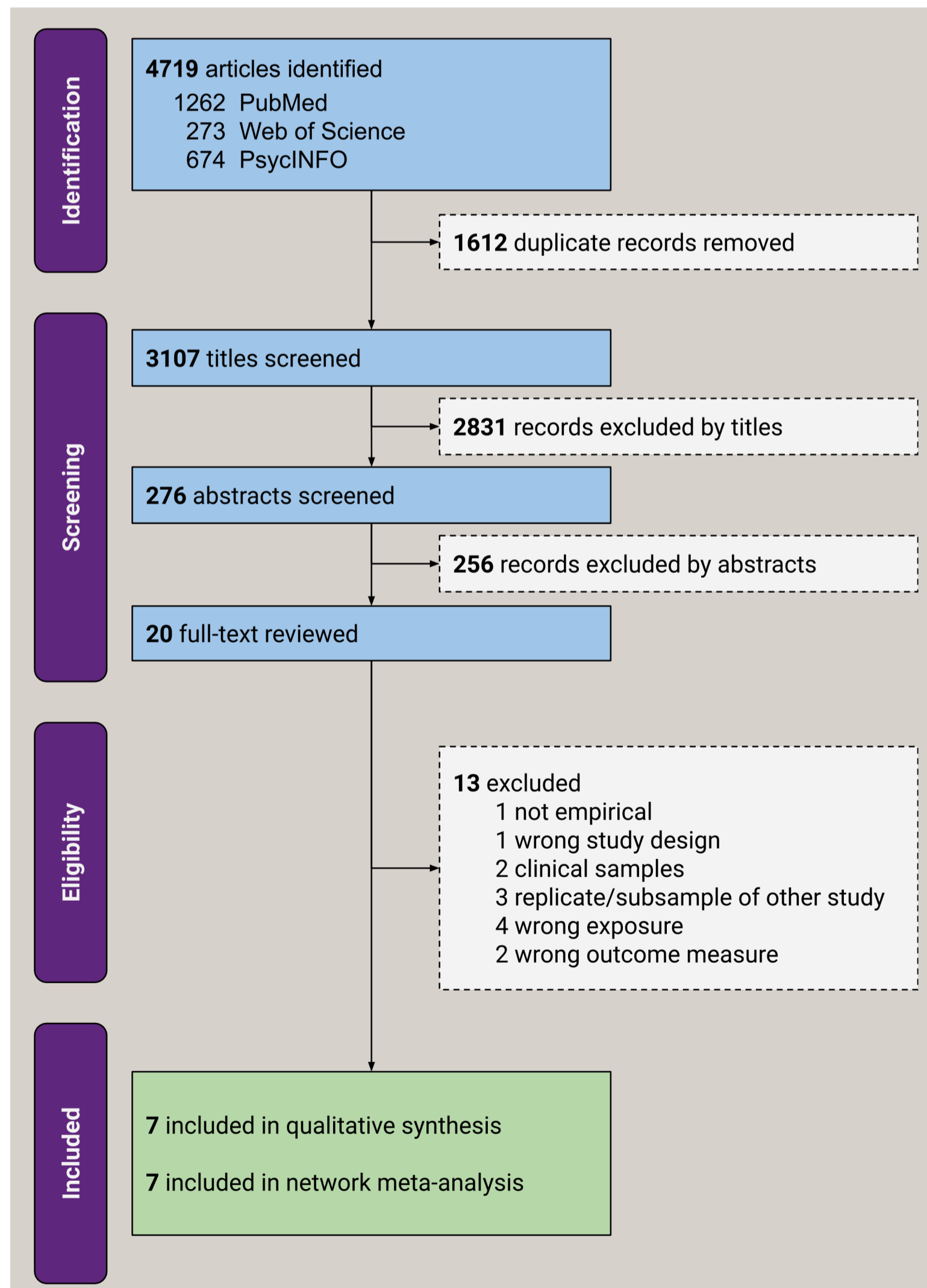


Figure 1. PRISMA flowchart of search results and inclusion of RCTs on e-cigarette effectiveness.

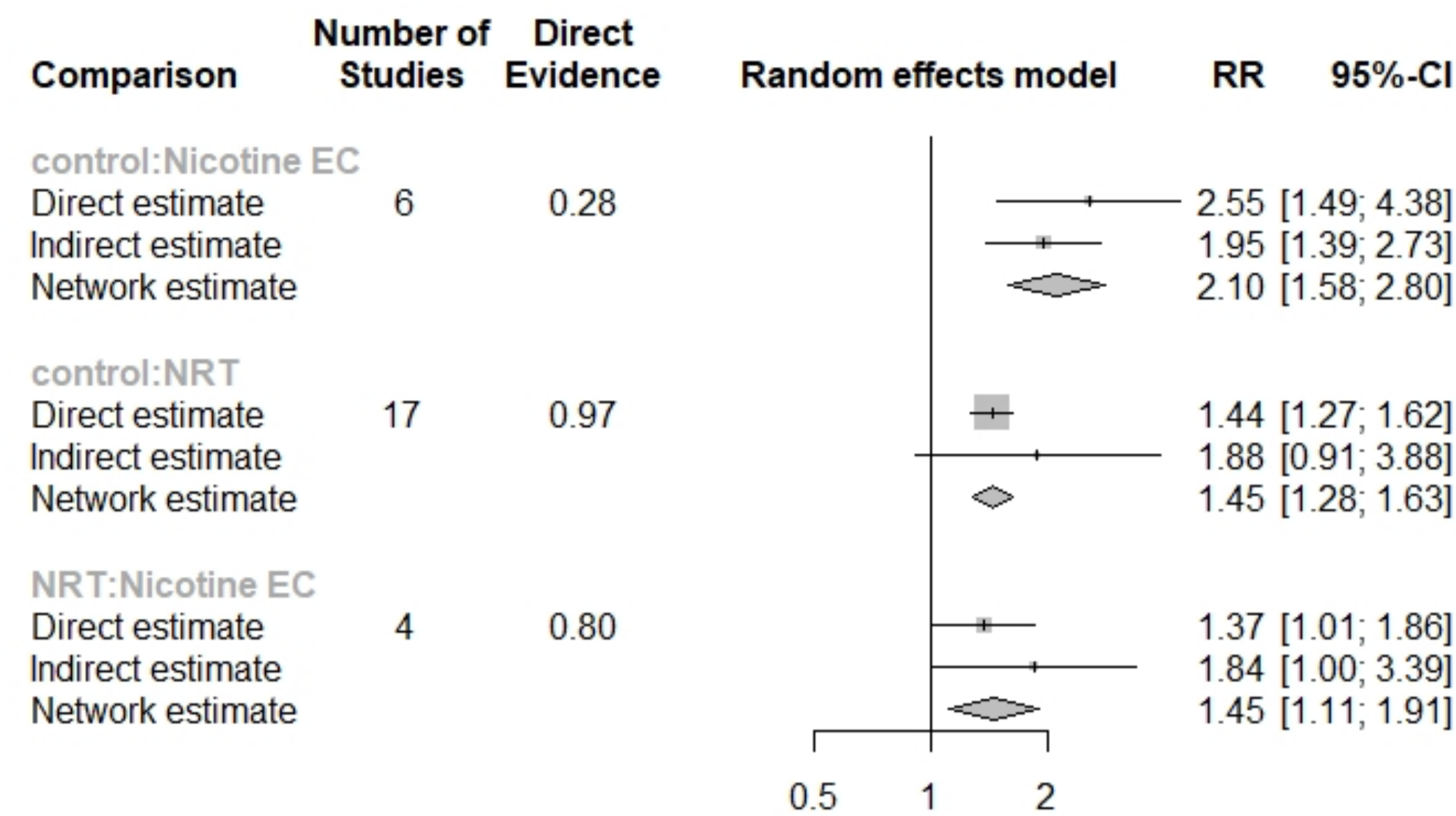


Figure 2. Forest plot of the decomposition of estimates computed from the direct and indirect comparison. All the direct and indirect estimates were largely consistent, and Z-tests indicated that these effects were not significantly different in the three comparisons (all p-values > 0.30).

Methods

Pre-registered systematic review and network meta-analysis in accordance with PRISMA guidelines (PROSPERO registration CRD42020169165). Two separate searches were undertaken:

- To identify studies of **e-cigarette** effectiveness in cessation we searched PubMed, Web of Science and PsycINFO for RCTs matching e-cigarette and smoking keywords. Search flowchart shown in **Figure 1**.
- To identify studies of **NRT** effectiveness in smoking cessation we utilised a three-step approach: (i) identify most recent review of NRTs in smoking cessation within Cochrane Database of Systematic Reviews; (ii) search for articles published following this review using Google Scholar and PubMed; and (iii) identify articles citing this Cochrane review using Google Scholar.

Study inclusion criteria:

- Study design: RCT.
- Sample population: Healthy individuals who smoke tobacco.
- Exposure and comparison:
 - NRT: NRT compared with nicotine-free control conditions;
 - E-cigarette: Nicotine e-cigarettes compared to nicotine-free control or NRT.
- Outcome: Smoking abstinence at end of study.
- Only studies published post-2013 were included to align with earliest RCT on e-cigarette effectiveness in smoking cessation.

A total of 7 e-cigarette and 9 NRT studies met inclusion criteria.

Random-effects network meta-analysis was used to assess three comparisons:

- Nicotine e-cigarette vs NRT
- Nicotine e-cigarette vs control
- NRT vs control

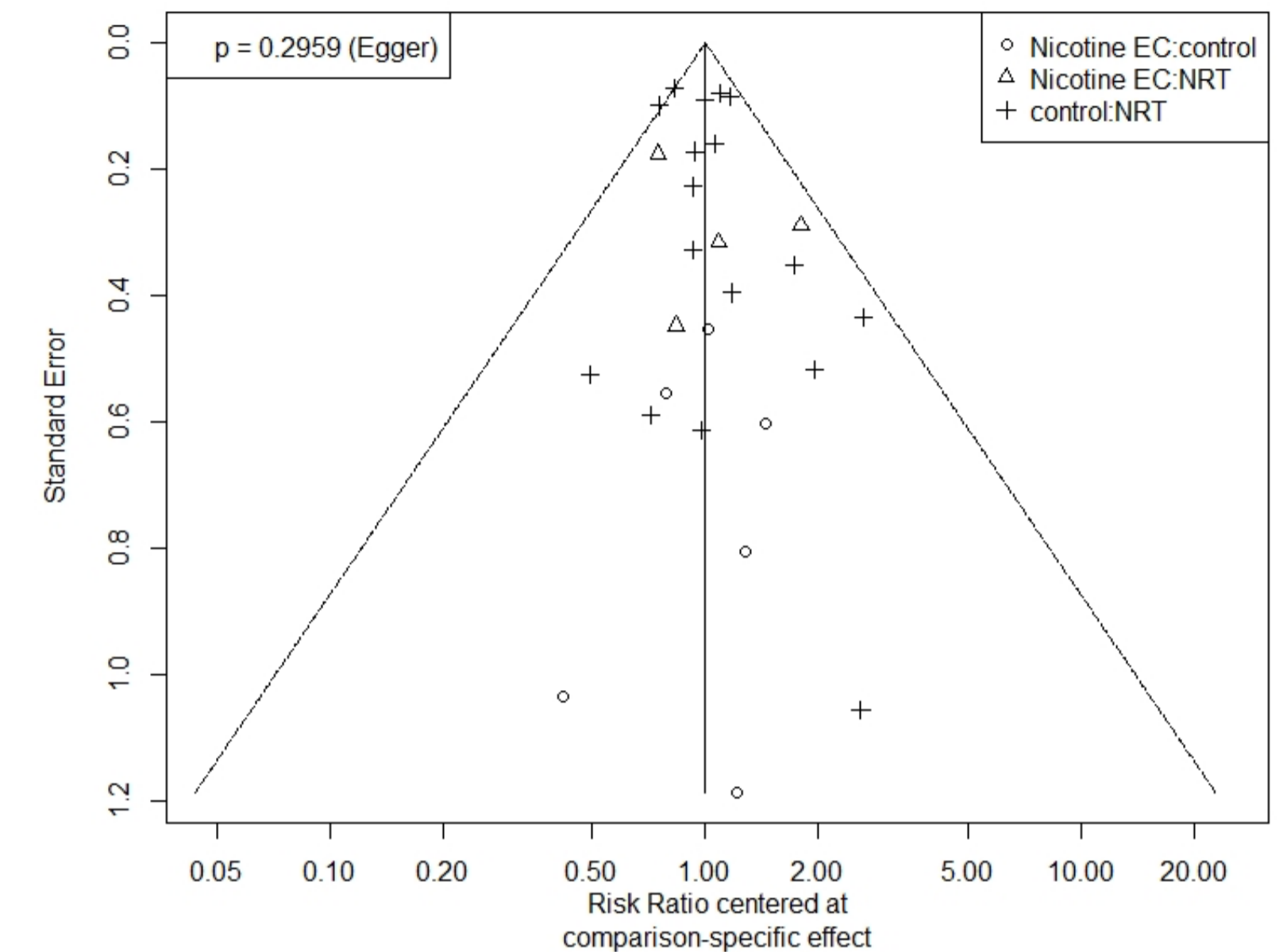


Figure 3. Comparison-adjusted funnel plots. Publication scatter is largely symmetrical, with Egger's test additionally indicating lack of evidence of asymmetry.

Findings

Results from the network meta-analysis (shown in **Figure 2**) indicated:

- Individuals randomised to **e-cigarette** conditions were more likely to be abstinent than those in control conditions, RR = 2.10, 95% CI = [1.58, 2.80].
- Individuals randomised to **NRT** conditions were more likely to be abstinent than those in control conditions, RR = 1.45, 95% CI = [1.28, 1.63].
- Individuals randomised to **e-cigarette** conditions were more likely to be abstinent than those in **NRT** conditions, RR = 1.45, 95% CI = [1.11, 1.91].

Sensitivity analyses excluding pilot studies and studies with short follow-up periods yielded similar results with no change in conclusions drawn.

Conclusions

Participants randomised to receive nicotine e-cigarettes were 45% more likely to remain abstinent from smoking than those who received NRTs.

Those randomised to receive nicotine e-cigarettes were 110% more likely to remain abstinent from smoking than those in control conditions where no nicotine was supplied.

These findings are consistent with evidence from observational studies that nicotine e-cigarettes are effective in facilitating smoking cessation.

Most trials included in meta-analysis were assessed as moderate or high risk of bias. Furthermore, studies were frequently pilot studies with small samples or short follow-up durations.

A further limitation is the moderate level of heterogeneity of included studies, possibly due to considerable variation in the e-cigarette and NRT products used.

More high quality studies are needed to ascertain the effectiveness of e-cigarettes in promoting smoking cessation.