

Efficacy and Safety of Daridorexant in patients with Insomnia: Systematic review & Meta-analysis of randomized controlled trials

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Background and objectives

- Insomnia is a common disorder defined by difficulties in initiating or maintaining sleep. It not only affect the sleep but is also associated with distress or impaired daytime functioning.^{1,2}
- Current guidelines recommend the use of cognitive behavioral therapy as first-line treatment for insomnia. Additionally, a wide variety of pharmaceutical treatments are offered to alleviate insomnia. However, these are not adequately efficient and associated with common side effects of somnolence and drowsiness.^{1,2}
- The objective of this systematic review was to determine the clinical efficacy of daridorexant in people with insomnia disorder.

Methodology

- A literature search was conducted in Medline®, Embase® and Cochrane via Ovid platform. In addition, clinicaltrials.gov and bibliographic searches were also performed to identify relevant English studies.
- All the identified studies were screened based on the title/abstracts and followed by full-texts screening against the eligibility criteria (Table 1) and data extraction by two reviewers independently. Randomized controlled trials (RCTs) including adults with insomnia, treated with daridorexant were included.
- A meta-analysis using fixed-effects model was conducted to calculate pooled effect estimates with 95% confidence intervals (CI) for sleep-related outcomes
- The quality assessment of the included RCTs was performed using the revised Cochrane (RoB 2.0) for RCTs.³

Table 1: Study eligibility criteria

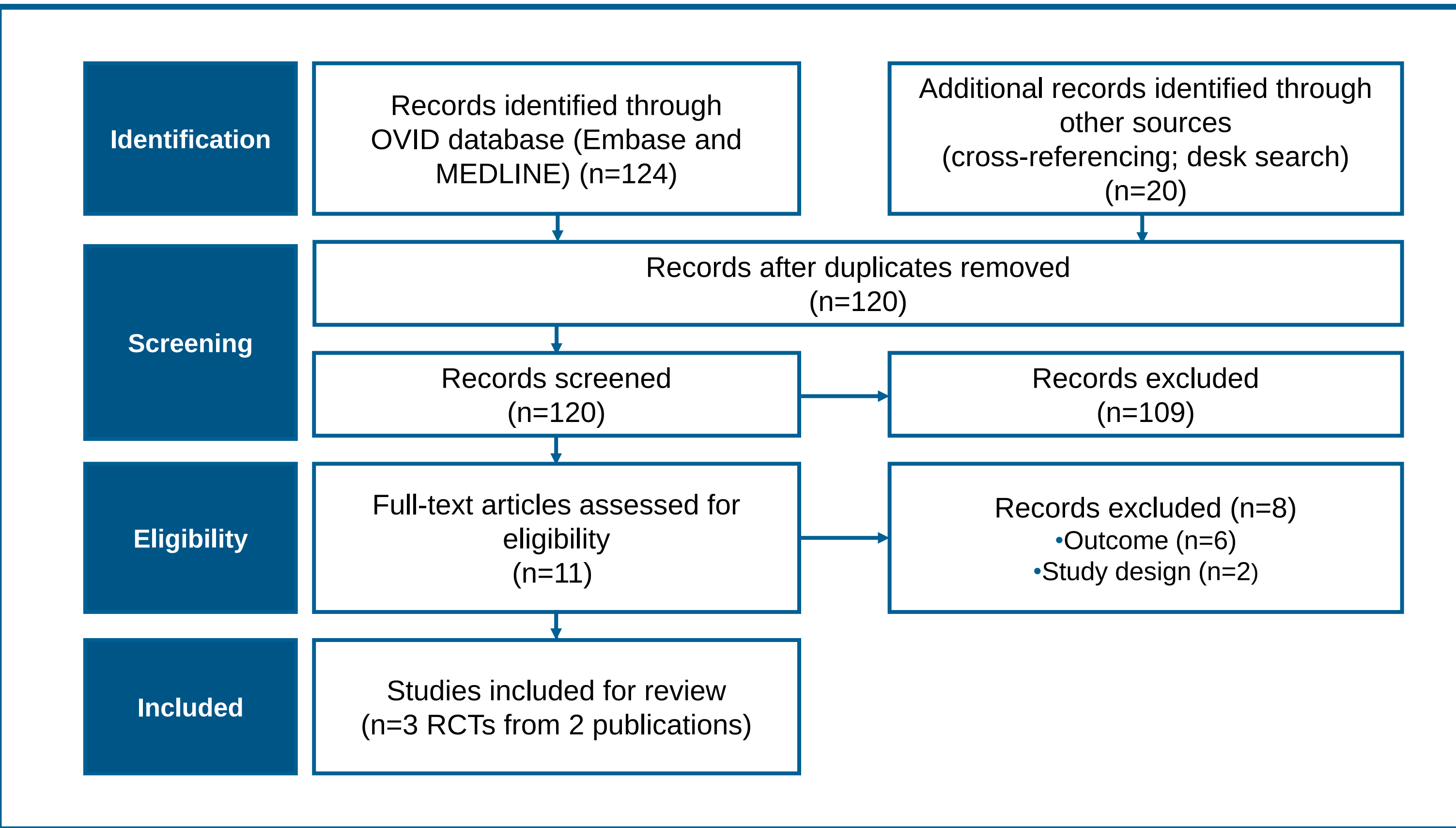
PICOS	Inclusion criteria	Exclusion criteria
Populations	Adult patients with insomnia; sleep initiation and maintenance disorders)	Patients below <18 years of age
Interventions	Daridorexant	Interventions not listed in the inclusion criteria
Comparators	No restrictions	None
Outcomes	Efficacy & Safety	None
Study designs	RCTs	Other studies not listed in the inclusion criteria

Results

Study Selection:

- After removing the duplicates, 144 records were obtained through databases and additional searches.
- A total of 3 RCTs (2 publications)^{1,2} were included (Figure 1).

Figure 1: PRISMA chart of included studies



Results

Outcomes:

- Pooled analysis of RCTs reported that a significant dose-response relationship was found in the reduction of wake after sleep onset with daridorexant 25mg (mean difference [MD] -11.2, 95%CI -15 to -7.45, three RCTs), daridorexant 50mg (MD -21.37, 95%CI -26.06 to -16.68, two RCTs) (Figure 2) and latency to persistent sleep with daridorexant 25mg (MD -7.75, 95%CI -11.25 to -4.25, three RCTs), daridorexant 50mg (MD -10.77, 95%CI -15.15 to -6.40, two RCTs) from baseline to 1 month, when compared to placebo (See Supplementary Figure 1).^{1,2}
- Similar favourable results were reported for total sleep time daridorexant 10mg (MD 14.23, 95%CI 7.08 to 21.39, two RCTs), daridorexant 25mg (MD 14.42, 95%CI 9.17 to 19.68, three RCTs), and daridorexant 50mg (MD 21.92, 95%CI 14.99 to 28.85, two RCTs) (See Supplementary Figure 2).^{1,2}
- No significant differences were observed in terms of treatment-emergent adverse events with daridorexant 10mg (risk ratio [RR] 1.18, 95%CI 0.97 to 1.44, two RCTs) and daridorexant 50mg (RR 1.12, 95%CI 0.92 to 1.36, two RCTs) when compared to placebo (Figure 3).^{1,2}
- The risk of bias was assessed in five distinct domains, with each answer leading to judgements of “low risk of bias,” “some concerns,” or “high risk of bias.” All the three studies reported correspond to low risk (See Supplementary Figure 3).

Figure 2: WASO plot of daridorexant

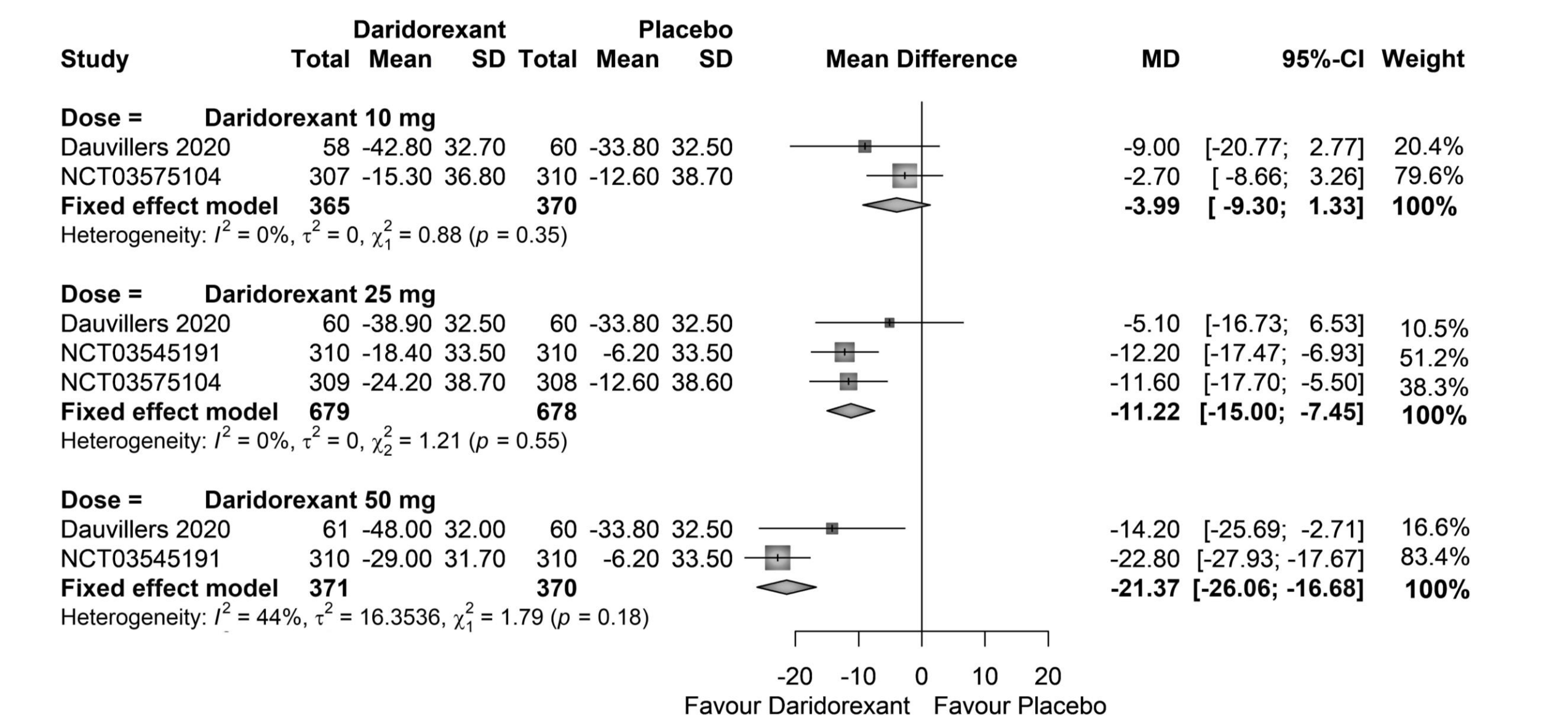
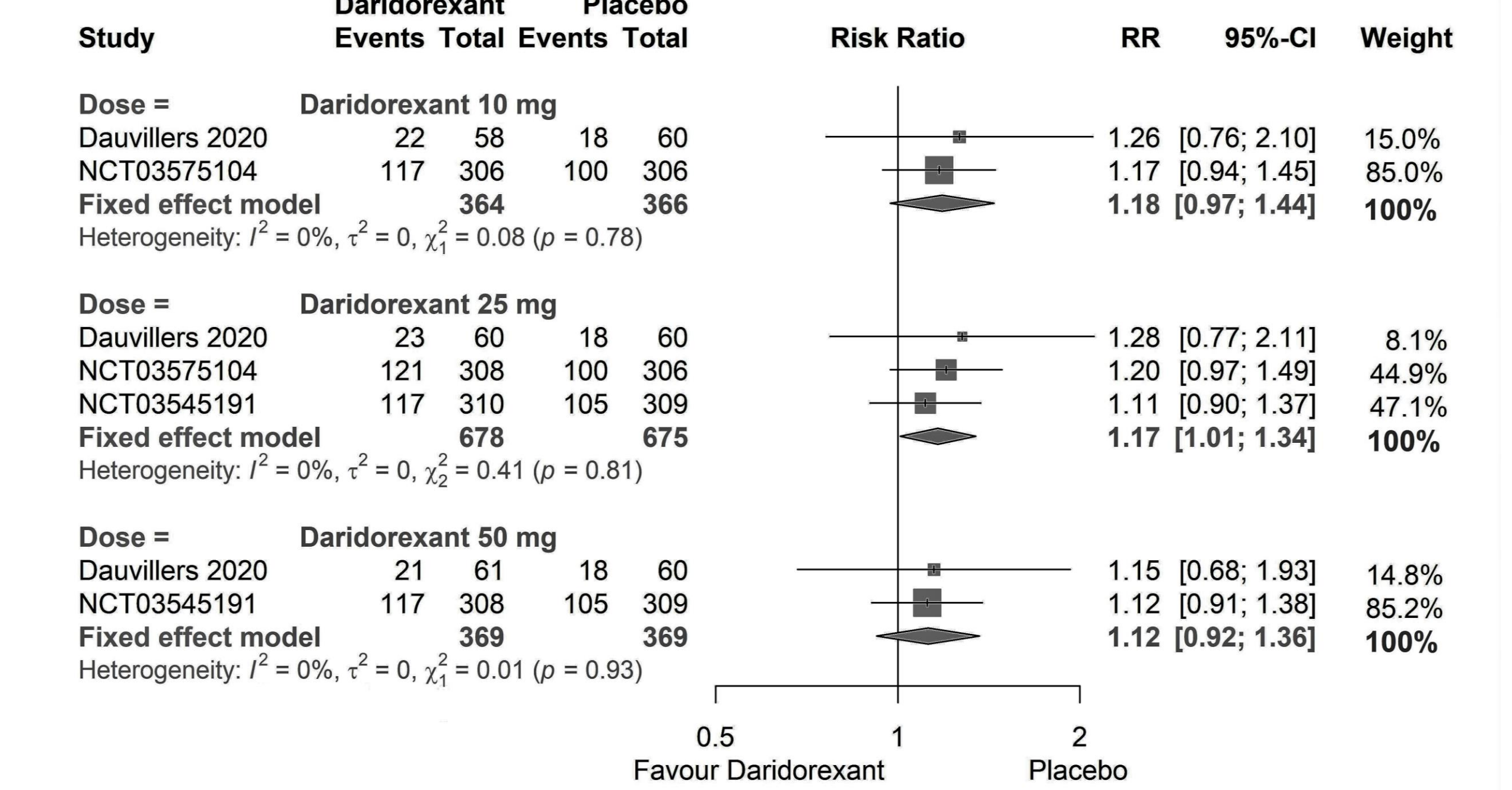


Figure 3: Forest plot of safety events



Conclusion

- Despite a smaller number of included studies; this Meta-analysis provides up-to-date evidence that daridorexant is effective in reduction of wake after sleep onset and latency to persistent sleep with daridorexant 25mg and 50mg as well as total sleep time with daridorexant 10mg, 25mg and 50mg.
- There was no difference observed in treatment-emergent adverse events between the groups.

References:

1. Emmanuel M et., Lancet Neurol 2022; 21: 125–39;
2. Dauvilliers Y et al., ANN NEUROL 2020;87:347–356;
3. Sterne et al., BMJ 366 (2019).