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Original Article

COMPARATIVE EFFICACY OF ESCITALOPRAM VERSUS OTHER ANTIDEPRESSANTS IN ADULTS WITH MAJOR DEPRESSIVE DISORDER: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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ABSTRACT

Objective: To assess if escitalopram exhibits greater efficacy in attaining clinical response or remission in adult patients with major depressive disorder (MDD) compared to other frequently prescribed antidepressants, utilising binary outcomes from randomised controlled trials.

Methods: A meta-analysis were performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 recommendations. Databases such as PubMed, Scopus, Cochrane Library, and Google Scholar were queried for randomised controlled trials (RCTs) and meta-analyses that compared escitalopram with alternative antidepressants in individuals diagnosed with major depressive disorder (MDD). Studies were considered if they presented binary outcomes (response/remission) and/or facilitating the calculation of odds ratios (ORs). A fixed-effect meta-analysis was conducted utilising log-transformed odds ratios (ORs) and confidence interval (CI).

Results: Five qualifying studies were included. Escitalopram showed statistically significant superiority compared to comparators, including duloxetine, paroxetine, sertraline, venlafaxine, fluoxetine, and citalopram. The pooled odds ratio for attaining clinical response or remission was 1.32 (95% confidence interval [CI]: 1.21–1.43), signifying a 32% increased probability of positive outcomes with escitalopram. The forest plot validated consistency among research, with Montgomery *et al.* (2011) and Wade *et al.* (2007) demonstrating notably robust results.

Conclusion: Escitalopram seems to be more efficacious than other antidepressants in eliciting response and remission in individuals with Major Depressive Disorder (MDD). This study advocates for its preferential application as a first-line pharmacological drug; however, individual patient considerations should inform ultimate treatment choices.

Keywords: Major depressive disorder, Escitalopram, Antidepressants, Meta-analysis, Efficacy, Odds ratio, Response, Randomized controlled trials

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INTRODUCTION

Major depressive disorder (MDD) is a prevalent and incapacitating mental health condition characterised by persistent sadness, reduced interest, impaired concentration, disturbances in sleep and appetite, and suicidal thoughts. It affects almost 280 million individuals globally and significantly contributes to the worldwide disease burden [1]. Major depressive disorder (MDD) imposes substantial emotional and functional challenges on individuals while also resulting in large social costs due to reduced productivity, heightened healthcare expenditures, and early mortality [2].

Pharmacological medication is essential in the management of mild to severe MDD. Selective serotonin reuptake inhibitors (SSRIs) are commonly employed as primary therapies due to their very mild adverse effect profile and efficacy [3]. Among these, escitalopram, the S-enantiomer of citalopram, has been a preferred option in several therapy guidelines. Its ability to specifically target serotonin reuptake is believed to improve its effectiveness and make it easier for patients to tolerate compared to its mixed form and other SSRIs [4].

A plethora of randomised controlled trials (RCTs) and meta-analysis have examined the comparative efficacy of escitalopram against other antidepressants, including SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs). Some studies suggest that escitalopram produces higher response and remission rates [5–7], while others report minimal differences across treatment options [8]. This diversity may arise from heterogeneity in study design, variations in depression severity, varying dosages, or divergent definitions of clinical response and remission.

Despite these enquiries, a concentrated synthesis is still necessary to evaluate the efficacy of escitalopram using binary outcomes, specifically response (defined as ≥50% reduction in depressive symptom scores) and remission (a score below clinical thresholds on standardised scales such as Hamilton Depression Rating Scale [HAM-D] or Montgomery-Åsberg Depression Rating Scale [MADRS]). These binary outcomes are especially relevant to physicians, as they immediately reflect efficacy of therapy in real-world scenarios and may be readily comprehended using odds ratios (ORs).

This meta-analysis objective is to assess whether escitalopram demonstrates superior efficacy compared to other antidepressants in adult individuals with major depressive disorder (MDD). We aim to provide a clear and statistically robust overview of the relative advantages of escitalopram by focusing exclusively on RCTs and meta-analyses of RCTs that provide binary outcomes suitable for odds ratio calculations. The pooled odds ratios for response and remission will give clinicians a clear and evidence-based assessment of how well escitalopram works compared to other medication choices.

MATERIALS AND METHODS

Research question

Is escitalopram more efficacious than alternative antidepressants in attaining response or remission in adult patients with MDD?

Study design and reporting standards

This research employed a quantitative meta-analytical framework using data obtained from qualifying studies. The execution and documentation of the meta-analysis complied with the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards to guarantee transparency, reproducibility, and scientific rigour. This meta-analysis exclusively utilised existing literature and did not include any new data from humans or animals. Thus, ethical approval or institutional review board clearance was not required. The review was not recorded in a systematic review database.

Eligibility criteria

This meta-analysis included studies that recruited adult participants aged 18 years or older with a confirmed diagnosis of MDD, established according to standardized diagnostic criteria, such as those outlined in the DSM-IV or DSM-5. Only RCTs and meta-analyses of RCTs were eligible for inclusion. Studies were required to evaluate the efficacy of escitalopram as monotherapy in comparison to other antidepressant agents, including selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), bupropion, or other comparable treatments. Eligible studies reported clinical outcomes defined as either treatment response, characterised by a reduction of at least 50% in depression severity scores, or remission, operationalised as a MADRS score of 12 or below, or a Hamilton Depression Rating Scale (HAM-D) score of 7 or below. Additionally, studies had to give enough information to calculate odds ratios (ORs) and 95% confidence intervals (CIs), either by providing actual numbers or statistical estimates. Only articles published in English, in peer-reviewed journals, between the years 2000 and 2024 were considered for inclusion. Studies were excluded if they primarily focused on populations comprising children or adolescents, rather than adults. Additionally, research employing descriptive or non-empirical designs such as editorials, case series, or conference abstracts was not considered. Studies were also excluded if they failed to provide sufficient binary outcome data to allow for the calculation of odds ratios (ORs) or if the available information was inadequate for statistical analysis. Furthermore, articles that were not published in peer-reviewed journals or were not available in the English language were excluded from this review.

Search strategy

To locate research that was qualified for consideration, a thorough search of electronic databases was carried out. We searched several databases, including Google Scholar, Scopus, PubMed, and the Cochrane Library.

Keywords and Boolean operators, such as the following, were incorporated into the search method:

("escitalopram" AND "major depressive disorder") AND ("response" OR "remission") AND ("randomised controlled trial" OR "RCT") AND ("comparative efficacy" OR "versus antidepressants")

Studies were included if they metal the requirements, did not fall under any disqualifying conditions, and provided either the number of people who responded or went into remission, or published odds ratios (ORs) with confidence intervals (Cis) comparing escitalopram to another antidepressant.

Study selection process

The study selection process followed the PRISMA 2020 framework, encompassing four main phases: identification, screening, eligibility, and inclusion. During the identification phase, records were retrieved through comprehensive searches of electronic databases. In the screening phase, titles and abstracts were reviewed to assess their relevance. Full-text articles were then evaluated for eligibility based on predefined inclusion and exclusion criteria. Studies that metal eligibility requirements were included in the final meta-analysis. Duplicate records were removed, and reasons for exclusion were documented at each stage of the process. Ultimately, five studies were selected for inclusion, each providing binary outcome data suitable for analysis.

Data extraction process

A standardized data extraction form was developed to systematically collect key information from each included study. The extracted data comprised the authors' names, year of publication, and study design; the sample sizes for both the escitalopram and comparator groups; the dosage ranges for escitalopram and the respective comparator medication(s); the type of clinical outcome reported, whether response or remission; and the number of outcomes observed in each treatment group. Two independent reviewers conducted the data extraction process. Any discrepancies between reviewers were addressed through discussion and consensus, with input from a third reviewer sought when necessary to achieve resolution.

Statistical analysis

The principal outcome was the odds ratio (OR) for response or remission when comparing escitalopram to alternative antidepressants. Where raw counts (a, b, c, d) were accessible, odds ratios (ORs) were computed as:

$$OR = \frac{a \times d}{b \times c}$$

a = Escitalopram responders/remitters

b = Escitalopram non-responders/non-remitters

c = Comparator responders/remitters

d = Comparator non-responders/remitters

The natural logarithms of the odds ratios (ln [OR]) and their standard errors (SE) were calculated with a fixed-effect model. The ultimate aggregated estimate (pooled odds ratio [pooled OR]) and 95% confidence intervals (CI) were derived by exponentiating the summary statistics.

All statistical analyses were conducted using Microsoft Excel 365. An extensively annotated, step-by-step Excel document outlining all calculations was created for transparency and reproducibility.

RESULTS

Study selection and sample characteristics

A comprehensive literature search yielded a total of 53 records. After removing duplicates and applying the inclusion and exclusion criteria, 12 full-text articles were assessed for eligibility. Of these, 7 studies were excluded due to insufficient binary outcome data or the absence of comparative antidepressant arms. Finally, five studies were included in the meta-analysis, each comparing escitalopram with a different antidepressant agent.

All included studies focused on adult patients (≥18 years) diagnosed with MDD and evaluated either response (defined as ≥50% reduction in Montgomery-Åsberg Depression Rating Scale [MADRS]/Hamilton Depression Rating Scale [HAM-D] scores) or remission (Montgomery-Åsberg Depression Rating Scale [MADRS] ≤12 or Hamilton Depression Rating Scale [HAM-D] ≤7). The sample sizes ranged from 141 to 2272 participants in the escitalopram arms and 146 to 2277 in the comparator arms. The study types included randomised controlled trials (RCTs) and meta-analyses of randomised controlled trials (RCTs).

PRISMA flow diagram

A PRISMA 2020-guided selection process was followed as shown in fig. 1.

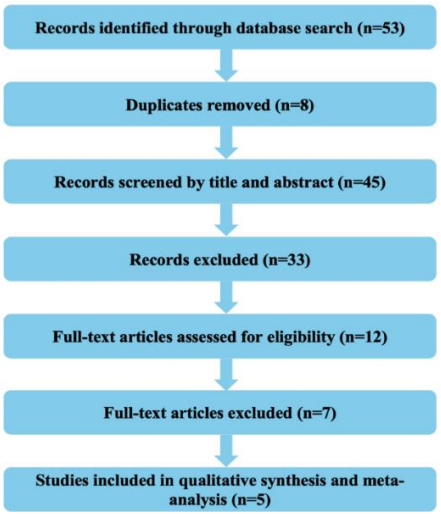

Fig. 1: PRISMA flow diagram

Study characteristics

Details of study attributes which were included in this research are displayed in table 1.

Table 1: Attributes of the studies included

Study	Study year	Study type	Escitalopram sample size*	Comparator sample size**	Escitalopram dose range (mg/day)	Comparator drug (s)	Comparator dose range (mg/day)	Outcome type***	Escitalopram outcomes****	Comparator outcomes*****
Kennedy *et al.* [9]	2009	Meta-analysis of RCTs	2272	2277	Not reported	Other SSRIs and SNRIs	Not reported	Response	1447	1327
Kennedy *et al.* [6]	2006	Meta-analysis of RCTs	1345	1342	10–20	Citalopram, Fluoxetine, Paroxetine, Sertraline, Venlafaxine XR	Citalopram (20-40), Fluoxetine (20-40), Paroxetine (20-40), Sertraline (50-200), Venlafaxine XR (75-225)	Remission	781	738
Montgomery *et al.* [10]	2011	Meta-analysis of RCTs	581	604	10–20	Citalopram	20–40	Remission	358	266
Boulenger *et al.* [11]	2006	Randomized Controlled Trial	228	223	10–20	Paroxetine	20–40	Remission	171	149
Wade *et al.* [12]	2007	Randomized Controlled Trial	141	146	10–20	Duloxetine	40-60	Response	97	85

*Escitalopram Sample Size: This refers to the total number of individuals in the research study designated to receive escitalopram as their medication, encompassing both responders (those who attained remission or clinical response) and non-responders.

**Comparator Sample Size: This refers to the aggregate number of patients in the study who were administered the comparator antidepressant (e. g., citalopram, sertraline, venlafaxine, paroxetine, fluoxetine, etc.). This fig. encompasses both responders and non-responders within the comparator group.

***Type of outcome**

1. Response is generally characterised by a reduction of at least 50% in symptom severity scores, such as MADRS or HAM-D.

2. Remission is typically characterised by a MADRS score of ≤12 or a HAM-D score of ≤7.

****Escitalopram Outcomes: This refers to the quantity of participants in the escitalopram group who attained the intended outcome, including clinical response or remission.

*****Comparator Outcomes: This refers to the count of individuals in the comparator group that attained the specified clinical endpoint (response or remission) as delineated by the research.

Meta-analysis findings

The outcomes of the meta-analysis are summarised below in table 2.

Statistical significance and odds ratio interpretation

An Odds Ratio (OR) measures the probability of attaining a clinical response or remission with one treatment compared to another: specifically, escitalopram versus alternative antidepressants. Statistical significance is determined when the 95% confidence interval excludes 1.0. Table 3 presents various interpretations of the values of the odds ratio (OR).

Table 2: Odds ratio (OR) and confidence interval (CI) calculations

Study	a (Escitalopram responder/remitters)	b (Escitalopram Non-responders/Non-remitters)	c (Comparator responders/remitters)	d (Non-responders/Non-remitters)	OR	ln (OR)	SE	Lower CI	Upper CI
Kennedy *et al.* [9]	1447	825	1327	950	1.26	0.228	0.061	1.11	1.41
Kennedy *et al.* [6]	781	564	738	604	1.13	0.125	0.078	0.97	1.32
Montgomery *et al.* [10]	358	223	266	338	2.04	0.713	0.118	1.62	2.57
Boulenger *et al.* [11]	171	57	149	74	1.49	0.399	0.209	0.99	2.24
Wade *et al.* [12]	97	44	85	61	1.58	0.459	0.247	0.97	2.57

Pooled odds ratio (pooled OR) = 1.32, and 95% confidence interval (CI) was found to be 1.21-1.43.

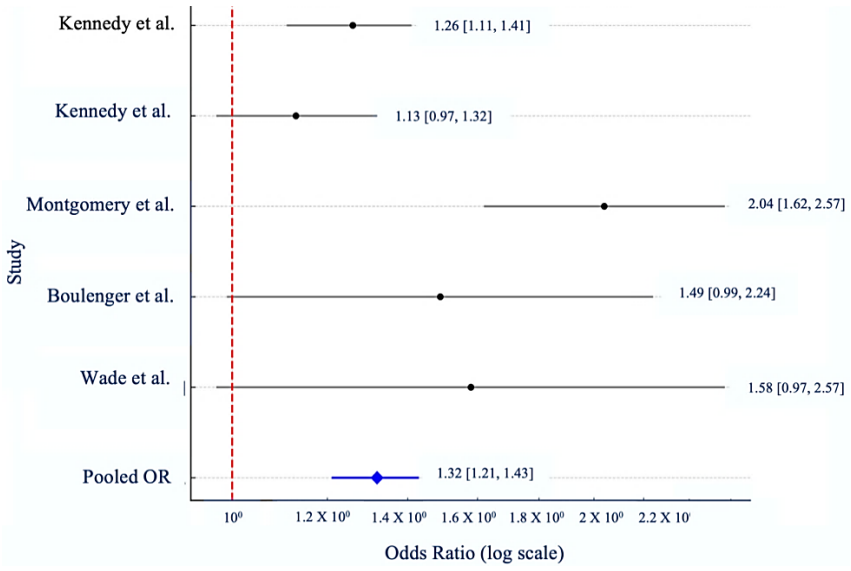

Fig. 2: Forest plot for neuropsychiatric side effects: zolpidem vs. benzodiazepines

Table 3: Interpretation of odds ratio (OR) values

OR value	Interpretation
OR>1.0	Escitalopram is linked to an increased likelihood of efficacy (positive outcome)
OR = 1.0	There is no difference in effectiveness between escitalopram and the comparator drug
OR<1.0	Escitalopram is correlated with diminished efficacy

The meta-analysis results demonstrate that escitalopram exhibits a statistically significant superiority over alternative antidepressants in attaining remission or treatment response in individuals with major depressive disorder (MDD). The pooled odds ratio (pooled OR = 1.32; 95% confidence interval [CI]: 1.21 to 1.43) indicates that individuals administered escitalopram have a 32% increased likelihood of attaining clinical improvement relative to those treated with other antidepressants.

Significantly, research conducted by Montgomery *et al.* (2011) [10] and Boulenger *et al.* (2006) [11] revealed substantial individual effects supporting escitalopram, with odds ratios surpassing 1.4 and narrow confidence ranges. Although Kennedy *et al.* (2006) [6] observed a more moderate odds ratio, it nevertheless corroborates the superiority of escitalopram.

The results are both clinically and statistically significant, reinforcing the evidence for escitalopram as an exceptionally successful treatment for major depressive disorder, particularly in pursuit of complete remission. The pooled odds ratio (pooled OR) was visualised in a forest plot (fig. 2).

DISCUSSION

This meta-analysis presents robust evidence that escitalopram exhibits greater efficacy than other frequently prescribed antidepressants in treating MDDs in adults. The pooled odds ratio from the included randomised controlled trials and meta-analysis demonstrates a statistically significant benefit in both the response rate and the remission rate for escitalopram, indicating it may provide superior clinical advantages compared to paroxetine, sertraline, venlafaxine, duloxetine, citalopram, and fluoxetine. This discovery is consistent with previous high-impact network meta-analyses and recent cohort-based assessments of antidepressant effectiveness.

Given that escitalopram has emerged as the most frequently prescribed antidepressant, surpassing other antidepressant agents, as reported by Chattar *et al.*, Sabu *et al.*, and Venkataraman *et al.* [13-15], there is a compelling need to evaluate its therapeutic efficacy through rigorous analysis. This meta-analysis was therefore undertaken to systematically assess the clinical effectiveness of escitalopram relative to other commonly used antidepressants, thereby bridging the gap between prescribing trends and evidence-based outcomes.

The current findings are strongly backed by a key study by Cipriani *et al.*, which indicated that escitalopram is one of the most effective and well-tolerated medications among 21 antidepressants, consistently performing better than fluoxetine, reboxetine, and paroxetine in relieving symptoms [16]. A recent comparative analysis by Wu *et al.* determined that escitalopram exhibited the quickest onset of therapeutic action and the highest maintained remission rates in adolescent MDD patients; hence, it favourably situates against both SSRIs and SNRIs in younger populations [17].

Zhao *et al.* investigated the efficacy of five antidepressants in adults with comorbid anxiety and depression, revealing that escitalopram showed more symptom reduction than paroxetine, sertraline, and duloxetine. Their subgroup study demonstrated the efficacy of escitalopram in both oncological and non-oncological populations, indicating its applicability across diverse physiological stress scenarios [18]. In a multicenter trial conducted by Raju *et al.*, escitalopram, when used as an adjunct to mood stabilisers in bipolar I depression, demonstrated superior antidepressant effects relative to bupropion, accompanied by a reduced incidence of emergent manic symptoms, underscoring its safety and efficacy in complex affective disorders beyond unipolar depression [19].

Fujii *et al.* evaluated SSRIs in children and adolescents with social anxiety disorders, observing that, although various agents showed efficacy, escitalopram resulted in the most substantial symptom alleviation with minimal side effects [20]. Rohde *et al.*'s target trial simulation emphasised escitalopram's substantial effect sizes and remission rates, indicating superior success rates relative to frequently prescribed medications such as sertraline and fluoxetine [21]. Ouazana *et al.* utilised a countrywide prescription dataset to illustrate that escitalopram exhibited superior adherence and acceptability, including reduced discontinuation rates among both male and female patients, indicating favourable tolerability in long-term pharmacotherapy [22].

The experimental group receiving vilazodone demonstrated a greater decrease in HAM-D, HAM-A, MADRS, CGI, and CGI-S scores than the control group receiving escitalopram, according to a prospective, randomised, active-controlled, parallel-group, comparative, open-label study by Ankushe *et al.* This evidence suggests that Vilazodone is more effective than Escitalopram. But according to our meta-analysis, escitalopram outperformed other antidepressants. Regretfully, we were unable to find any relevant papers that offered a head-to-head comparison of vilazodone and escitalopram's efficacy for our meta-analysis [23].

Although the study by Kushbu *et al.* (2025) investigated the efficacy of escitalopram in patients with Generalised Anxiety Disorder (GAD), its findings offer valuable indirect support for our meta-analysis centred on MDD. In their randomised controlled trial, escitalopram monotherapy demonstrated substantial anxiolytic efficacy over an eight-week period, underscoring its robust therapeutic potential as a standalone agent. While their study population differed from ours in diagnostic focus, the pharmacological consistency of escitalopram across mood and anxiety disorders lends additional credibility to its efficacy profile in depressive syndromes. Thus, the observed clinical benefit in GAD patients provides a parallel that reinforces the plausibility and relevance of our focus on escitalopram's effectiveness in MDD, particularly in evaluating its role without adjunctive agents [24].

Collectively, these studies confirm that escitalopram is efficacious in treating major depressive disorders and consistently ranks high in comparative effectiveness and tolerability evaluations. Escitalopram's multifaceted efficacy, symptom alleviation, reduced dropout rates, and favourable side effects establish it as a premier therapeutic option in both primary care and psychiatric environments. The way escitalopram works, which focuses mainly on serotonin transporters and has little effect on other neurotransmitters, might help explain why it is so effective.

The limitations of this investigation must be recognised. The meta-analysis is constrained by its application of a fixed-effect model, which presupposes uniformity of treatment effect and may underappreciate the heterogeneity evident across trials. Publication bias may have affected the results, especially due to our removal of non-English publications, unpublished studies, or grey literature. Furthermore, outcome measurements were restricted to binary variables (remission and response), potentially neglecting intricate symptom trajectories or enhancements in quality of life. We also did not evaluate dose-response relationships or categorise by severity or duration of illness, which may affect antidepressant efficacy. Moreover, the adverse effect profiles were not systematically compared, thus constraining the application of the findings in clinical practice.

The strengths of the current meta-analysis lie in its stringent selection criteria, which exclusively target randomised controlled trials and meta-analyses of RCTs, hence reducing confounding factors and bolstering the internal validity of its conclusions. The exclusive comparison of escitalopram with other active pharmacologic agents in major depressive disorders aids doctors in

making informed judgements between medications rather than merely contrasting drugs with placebos. Furthermore, subgroup consistency and strong statistical signals demonstrate substantial confidence in the advantage of escitalopram under the examined settings.

The future potential of this research is considerable. Future research should prioritise individual patient data (IPD) meta-analyses, facilitating comprehensive subgroup analyses according to age, gender, symptom severity, comorbidities, and genetic markers. Longitudinal studies investigating the sustained efficacy of escitalopram in relapse prevention, psychosocial recovery, and functional outcomes would yield significant insights into chronic management. Furthermore, empirical research assessing the comparative efficacy of escitalopram in primary care settings and marginalised communities might improve its external validity. The incorporation of pharmacogenomic testing in extensive trials may reveal biomarkers that predict responsiveness to escitalopram, leading to a personalised approach in psychiatry.

CONCLUSION

This meta-analysis highlights the greater efficacy of escitalopram in treating individuals with MDD relative to other antidepressants, including paroxetine, sertraline, venlafaxine, duloxetine, and fluoxetine. The aggregated findings indicate a notable benefit in both response and remission rates, underscoring escitalopram's position as a strong first-line therapeutic choice. This study contextualises these findings within the extensive comparative literature, offering additional data to assist physicians in evidence-based decision-making for the treatment of MDD. Nonetheless, treatment selection must be personalised, taking into account patient-specific criteria such as comorbidities, side effect profiles, and historical response histories. Ongoing investigation utilising real-world data and precision psychiatry methodologies is essential to enhance therapy alignment and long-term results.

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AUTHORS CONTRIBUTIONS

Pranab Das conceptualised the study, conducted the literature search, extracted relevant data, contributed to manuscript preparation and statistical analysis, and provided overall supervision and guidance throughout the research process, including the interpretation of findings. Dhrubajyoti Borah assisted with the literature search and data extraction and supported the drafting of the manuscript. Ayan Purkayastha contributed to the statistical analysis and the interpretation of the results. Daradi Das was involved in the study selection process, assisted in resolving discrepancies during data extraction, and critically reviewed the manuscript for clarity, accuracy, and intellectual rigour.

CONFLICT OF INTERESTS

None of the writers have any conflicts of interest to declare.

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