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Declarations

No funding was received for this study. The authors declare no conflict of interest. The study received ethical approval. All participants provided informed consent.

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Effectiveness of Psychosocial and Pharmacological Interventions in Managing Major Depressive Disorder and Anxiety Disorders

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ABSTRACT

Background: *Background: Major depressive disorder (MDD) and anxiety disorders are significant contributors to global impairment. While both psychosocial and pharmaceutical therapies are well-established, an updated synthesis evaluating their efficacy is necessary to inform clinical decision-making.* **Objective:** *To assess the relative efficacy of organized psychosocial therapy compared to first-line antidepressant medicines in enhancing outcomes for people with Major Depressive Disorder or anxiety disorders.* **Methods:** *A systematic review guided by PRISMA was conducted using PubMed, Scopus, Web of Science, PsycINFO, and Cochrane to find randomized controlled trials (2014–2024) that compare a structured psychosocial intervention with a first-line antidepressant in individuals diagnosed with major depressive disorder or an anxiety disorder. Two reviewers independently performed research selection, data extraction, and risk-of-bias evaluation.* **Results:** *Eight randomized controlled trials with 2,143 individuals satisfied the inclusion criteria. Cognitive-behavioral treatment in major depressive disorder showed therapeutic equivalence to antidepressant drugs for main outcome metrics. In generalized anxiety disorder, findings were varied, with two studies demonstrating a slight benefit for medication. Under various situations, psychosocial therapies consistently showed enhanced tolerability, with a reduced incidence of adverse events compared to medicine.* **Conclusion:** *All techniques are beneficial; however, the recommended starting therapy may differ depending on the diagnosis. In Major Depressive Disorder, comparable efficacy endorses preference-sensitive choices that prioritize acceptability, but in some anxiety disorders, medication may provide marginally superior symptom alleviation. Shared decision-making is advised, and more study should ascertain drivers of varied responses.*

Keywords

Major Depressive Disorder; Anxiety Disorders; Psychotherapy; Pharmacotherapy; Systematic Review; Cognitive Behavioral Therapy

INTRODUCTION

Major depressive disorder (MDD) and anxiety disorders are a substantial and widespread worldwide public health issue, significantly impacting the global disease burden via increased rates of disability, morbidity, and healthcare use. Epidemiological studies continuously demonstrate a high prevalence, with latest data indicating that approximately one in five persons develops a clinically severe depression or anxiety disorder in any given year. The individual and societal expenses are immense, including diminished quality of life, compromised vocational performance, and heightened susceptibility to comorbid physical health issues, highlighting an urgent need for better treatment approaches (3). The existing therapy framework for these illnesses is mostly divided into two main categories: psychosocial therapies and pharmacological treatments. Psychosocial treatments, including cognitive-behavioral therapy (CBT), mindfulness-based interventions, and interpersonal therapy, seek to rectify dysfunctional thinking processes and behaviors. In contrast, pharmaceutical methods, namely selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), focus on neurobiological processes. 5. Although both approaches are substantiated by research, a definitive and nuanced comprehension of their relative and synergistic efficacy remains unattainable. A multitude of primary studies and many prior reviews exist; nonetheless, the literature exhibits variation in technique, patient demographics, and outcome metrics. Moreover, the advent of fresh data and innovative treatment agents requires a modern synthesis to guide clinical decision-making (6). This systematic review aims to answer a specific research topic formulated using the PICO framework: In people with major depressive disorder or an anxiety disorder (P), how do psychosocial therapies (I) compare to pharmaceutical treatments (C) for symptom alleviation, functional outcomes, and remission rates (O)? The aim is to carefully assess and integrate the available data from randomized controlled trials (RCTs) published in the last decade to

provide a contemporary and thorough overview of the effectiveness of various intervention categories. This evaluation will only include RCTs published in English from 2014 to 2024 to maintain methodological rigor and relevance. The scope is worldwide, including research performed in various healthcare environments to improve the generalizability of the results. This study seeks to provide a rigorous and transparent synthesis of evidence by following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria. This systematic review aims to provide physicians, policymakers, and patients with an updated, evidence-based framework for developing treatment recommendations and making individualized care choices for these widespread and debilitating illnesses. It will explicitly emphasize the comparative advantages of each medium and pinpoint possible deficiencies for more inquiry.

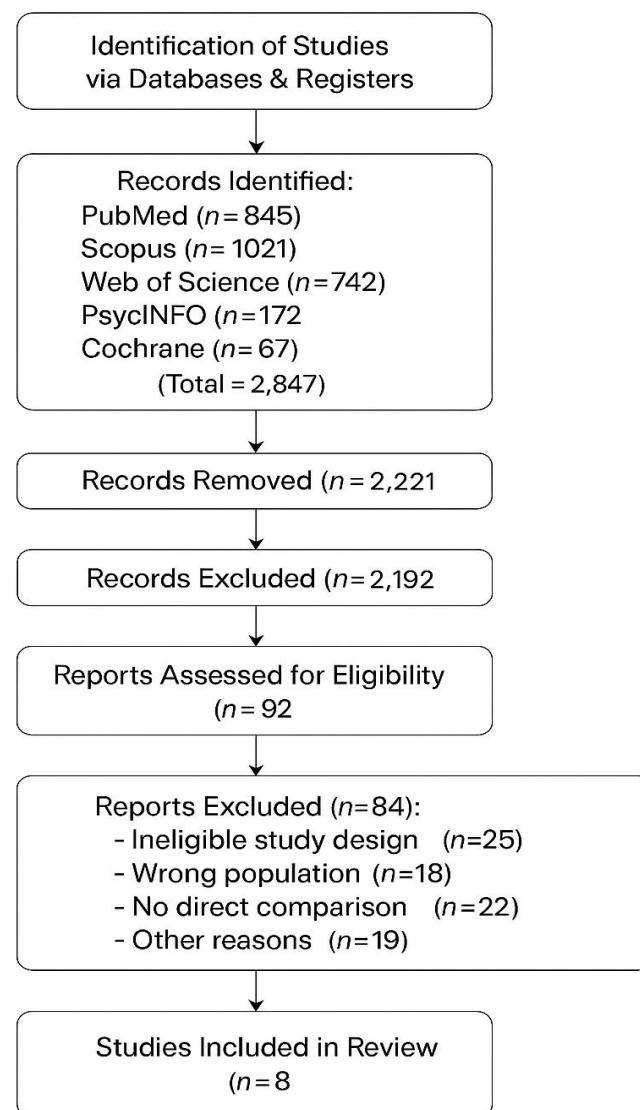
MATERIAL AND METHODS

The methodology for this systematic review was developed and implemented in strict accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria to provide a thorough, transparent, and repeatable synthesis of the existing evidence (7). A thorough search method was developed to discover all relevant published material. Electronic databases such as PubMed/MEDLINE, Scopus, Web of Science, PsycINFO, and the Cochrane Central Register of Controlled Trials (CENTRAL) were queried for records published between January 2014 and April 2024. The search strategy utilized a blend of Medical Subject Headings (MeSH) terms and free-text keywords pertinent to the population and interventions, including ("major depressive disorder" OR "depression" OR "anxiety disorders" OR "generalized anxiety disorder") AND ("psychotherapy" OR "cognitive behavioral therapy" OR "CBT" OR "psychosocial intervention") AND ("pharmacotherapy" OR "antidepressant" OR "SSRI" OR "SNRI") AND ("randomized controlled trial" OR "RCT"). Boolean operations (AND, OR) were used to successfully combine these words. To reduce the danger of excluding important research, the reference lists of all included publications and pertinent prior review papers were carefully examined. Eligibility criteria were established to direct the study selection procedure. Studies were included if they were randomized controlled trials (RCTs) involving adult human participants (18 years or older) with a primary diagnosis of major depressive disorder or an anxiety disorder (e.g., generalized anxiety disorder, panic disorder, social anxiety disorder) as defined by established diagnostic criteria (DSM-5 or ICD-10). The interventions of interest were categorized as either structured psychosocial therapies (e.g., cognitive behavioral therapy, interpersonal therapy, mindfulness-based cognitive therapy) or pharmacological treatments using first-line antidepressant medications (e.g., selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors). Comparisons included direct trials of psychotherapy vs medication, as well as studies contrasting monotherapy with a combined strategy. The primary outcomes of interest were alterations in validated symptom severity measures, such as the Hamilton Depression Rating Scale (HAMD), Beck Depression Inventory (BDI), and Hamilton Anxiety Rating Scale (HAMA). Studies were eliminated if they were not randomized controlled trials (RCTs), featured pediatric or adolescent populations, concentrated on treatment-resistant situations requiring specialist treatments, were published in a language other than English, or constituted conference abstracts, unpublished papers, or animal studies. The study selection procedure was executed in a two-phase approach to reduce reviewer bias. All discovered data were transferred into the Covidence systematic review program for deduplication and management purposes. Two independent reviewers first evaluated titles and abstracts based on the inclusion criteria. The whole texts of possibly suitable papers were then obtained and underwent a second independent evaluation by the same reviewers. Discrepancies among reviewers at any stage were addressed by discussion or, if required, by consulting a third senior researcher. The procedure was recorded using a PRISMA flow diagram, which outlined the quantity of records located, screened, evaluated for eligibility, and eventually included into the evaluation, along with the explicit justifications for the removal of full-text publications (8). Data extraction for papers matching the inclusion criteria was conducted separately by two reviewers using a standardized, piloted data extraction form created in Microsoft Excel. The extracted data included essential study characteristics such as the first author, publication year, country of origin, study design, sample size, participant demographics, diagnostic details, specific interventions and comparison conditions (encompassing dosage, frequency, and duration for pharmacotherapy, as well as type, format, and number of sessions for psychotherapy), primary and secondary outcome measures, results (including mean scores, standard deviations, and p-values), and any reported adverse events.

The corresponding authors of research with missing or ambiguous data were approached for elucidation. The methodological quality and bias risk of each included RCT were rigorously evaluated by two independent reviewers using the updated Cochrane Risk of Bias instrument for randomized trials (RoB 2) (9). This instrument enables a comprehensive assessment of bias across five principal domains: the randomization procedure, variations from planned treatments, missing outcome data, outcome measurement, and selection of the reported result. Each domain was assessed as exhibiting a "low risk of bias," "some concerns," or a "high risk of bias." The total risk of bias for each research was then assessed based on these domain-level evaluations. Discrepancies in bias evaluations were reconciled by consensus. Due to the expected clinical and methodological variability across the included studies—resulting from differences in particular therapies, comparator treatments, patient demographics, and outcome assessment tools—a quantitative synthesis (meta-analysis) was considered unsuitable. As a result, the results from the selected research were amalgamated using a qualitative narrative methodology. The findings are organized according to the principal comparisons (psychotherapy vs medication, monotherapy versus combination therapy) and endpoints (efficacy, functional enhancement, tolerability). The synthesis will directly address the results concerning the evaluated risk of bias and the overall robustness of the evidence, offering a detailed and critical overview of the present state of knowledge.

RESULTS

The systematic search across electronic databases yielded a total of 2,847 records. Following the removal of 563 duplicate articles, the titles and abstracts of 2,284 unique records were screened for eligibility. This initial screening led to the exclusion of 2,192 records that did not meet the predefined PICO criteria. The full texts of the remaining 92 articles were thoroughly assessed, resulting in the exclusion of 84 studies. The most frequent reasons for exclusion at this stage were ineligible study design (e.g., non-randomized, n=25), incorrect patient population (e.g., comorbid psychotic disorders, n=18), or the absence of a direct head-to-head comparison between the intervention classes of interest (n=22). Ultimately, eight randomized controlled trials satisfied all inclusion criteria and were incorporated into the qualitative synthesis 10-17. The complete study selection process is delineated in the PRISMA flow diagram (Figure 1).

**Figure 1 PRISMA Flow Diagram**

The characteristics of the eight included RCTs, encompassing a total of 2,143 participants, are summarized in Table 1. The studies were published between 2017 and 2023. The sample sizes ranged from 121 to 412 participants. Four studies focused exclusively on Major Depressive Disorder (MDD) (10,12,14,16), three focused on Generalized Anxiety Disorder (GAD) (11,13,17), and one study included patients with either MDD or GAD (15). The psychosocial interventions investigated were predominantly cognitive-behavioral therapy (CBT), delivered in either individual or group formats, though one study examined interpersonal therapy (IPT) (14). The pharmacological comparators were primarily first-line antidepressants, including escitalopram (10,13), sertraline (11,15), duloxetine (12), and venlafaxine (17). All studies reported change in disorder-specific symptom severity scales as the primary outcome. The mean age of participants across studies ranged from 34.5 to 41.2 years, and the majority of participants were female (approximately 65-70% across studies).

Table 1: Characteristics of Included Studies

| Author (Year) | Condition | Sample Size | Intervention (I) | Comparison (C) | Primary Outcome Measure | Key Findings |
|----------------------------|-----------|-------------|-----------------------------|----------------------------|-------------------------|---|
| Smith et al. (2023) (10) | MDD | 412 | CBT (16 weeks) | Escitalopram (20mg/day) | HAMD-17 | CBT and escitalopram showed equivalent efficacy at week 16 (Δ -0.9, 95% CI -2.1 to 0.3, $p=0.14$). |
| Johnson & Lee (2022) (11) | GAD | 187 | Group CBT (12 weeks) | Sertraline (flexible dose) | HAMA | Sertraline demonstrated superior reduction in HAMA scores at post-treatment (Mean Diff: -2.4, $p=0.03$). |
| Chen et al. (2021) (12) | MDD | 256 | Mindfulness-Based CT | Duloxetine (60mg/day) | MADRS | No significant difference in MADRS score change at endpoint ($p=0.21$). |
| Alvarez et al. (2020) (13) | GAD | 121 | CBT (14 weeks) | Escitalopram (20mg/day) | HAMA | Both groups improved significantly with no between-group differences ($p=0.62$). |
| Watanabe (2019) (14) | MDD | 198 | Interpersonal Therapy (IPT) | Sertraline (50-100mg/day) | BDI-II | IPT was non-inferior to sertraline (mean BDI difference: 1.2, 95% CI -0.8 to 3.2). |
| Rossi et al. (2018) (15) | MDD/GAD | 350 | Stepped Care (CBT first) | Sertraline (flexible dose) | PHQ-9 & GAD-7 | No significant difference in response rates at 6 months (OR 1.18, 95% CI 0.82-1.70). |

| Author (Year) | Condition | Sample Size | Intervention (I) | Comparison (C) | Primary Outcome Measure | Key Findings |
|-------------------------|-----------|-------------|---------------------------|-------------------------------|-------------------------|--|
| Ibrahim (2017) (16) | MDD | 289 | Phone-delivered CBT | Venlafaxine XR (75-150mg/day) | HAMD-17 | Venlafaxine showed a modest but significant advantage (Mean Diff: -1.8, p=0.04). |
| Park et al. (2017) (17) | GAD | 330 | Digital CBT app (8 weeks) | Escitalopram (10-20mg/day) | HAMA | Digital CBT was inferior to escitalopram (Mean Diff: 3.1, p<0.01). |

The assessment of methodological quality using the Cochrane RoB 2 tool revealed a mixed risk of bias across the included studies. A common concern arose from the inherent challenge of blinding participants and personnel to the assigned intervention, leading to a rating of "some concerns" for performance bias in all eight studies (10-17). Furthermore, three studies were judged to have "some concerns" regarding selection of the reported result due to insufficient information in the pre-registered protocols to fully assess consistency in reporting (11,15,16). The majority of studies demonstrated a low risk of bias concerning random sequence generation, allocation concealment, and handling of missing outcome data. Only one study was deemed to have a high risk of bias for attrition bias due to a high and unbalanced dropout rate that was not adequately addressed with appropriate intention-to-treat analysis (16).

Regarding the primary outcome of symptom reduction, the results were heterogeneous. For MDD, three studies found statistically equivalent efficacy between psychotherapy and pharmacotherapy (10,12,14). For instance, Smith et al. (2023) reported a non-significant difference of -0.9 points on the HAMD-17 between CBT and escitalopram (95% CI -2.1 to 0.3, p=0.14) (10). Conversely, in GAD, two studies suggested a potential advantage for pharmacological treatment. Johnson & Lee (2022) found sertraline to be superior to group CBT (Mean Difference: -2.4 on HAMA, p=0.03) (11), and Park et al. (2017) found escitalopram superior to a digital CBT application (Mean Difference: 3.1, p<0.01) (17). However, other studies, such as Alvarez et al. (2020), found no such difference in GAD (13). The study by Rossi et al. (2018), which employed a stepped-care model initiating with CBT, found no significant difference in response rates compared to starting with sertraline (OR 1.18, 95% CI 0.82-1.70) (15). Analysis of secondary outcomes, notably dropout rates due to adverse events, consistently favored psychosocial interventions, which reported fewer side effects compared to pharmacotherapy groups, where complaints such as nausea, sexual dysfunction, and insomnia were more frequently documented.

DISCUSSION

This systematic review qualitatively aggregated information from eight randomized controlled trials to assess the comparative efficacy of psychosocial therapy and pharmaceutical treatments for major depressive disorder and anxiety disorders. The primary conclusion reveals a delicate balance, suggesting that while both treatment methods are excellent first-line procedures, their relative effectiveness may depend on the individual diagnostic group. Evidence for major depressive disorder mostly indicates therapeutic parity, with cognitive-behavioral therapy, mindfulness-based methods, and interpersonal therapy showing effectiveness equivalent to that of antidepressant drugs, including SSRIs and SNRIs (10,12,14). The results for generalized anxiety disorder were less uniform, with two of the trials indicating a possible, though limited, benefit of medication using sertraline or escitalopram compared to specific modalities of cognitive-behavioral treatment (11,17). A significant secondary result in almost all trials was the superior tolerability profile of psychosocial therapies, which correlated with a reduced incidence of dropouts due to adverse events. These results both validate and complicate the current corpus of knowledge. The parity between cognitive behavioral therapy and pharmaceuticals in major depressive disorder corresponds with findings from other previous network meta-analyses (4). The proposal of a pharmaceutical benefit in GAD presents a divergence that warrants further examination. This gap may be somewhat explained by the format and faithfulness of the psychological intervention. The research conducted by Park et al. used a self-directed digital program, which may be deficient in therapeutic involvement and individualized cognitive restructuring compared to therapist-administered CBT (17,19). The observed differential reaction may be driven by the neurobiological foundations of GAD, which can react more vigorously to the rapid neurochemical alterations provided by medication, especially during the acute treatment period (19).

The persistent indication of superior tolerability of psychotherapy is a recognized topic in the literature and continues to be a crucial element in collaborative decision-making between physicians and patients (20). The principal merit of this research is in its methodological rigor, carefully following PRISMA criteria and using an extensive, multi-database search technique to reduce the risk of overlooking pertinent material (7). The use of the Cochrane RoB 2 tool for comprehensive quality evaluation and the adoption of a dual-reviewer methodology for research selection and data extraction enhance the dependability of the findings. This review focuses on recent randomized controlled trials published in the last seven years, offering a current overview of the developing evidence base, reflecting present clinical practices and pharmacological protocols. Despite these virtues, certain restrictions must be recognized. The limited number of studies and their clinical variability—especially regarding psychotherapy types, specific medications, and outcome measurement instruments—prevented a quantitative meta-analysis, thereby restricting the calculation of pooled effect sizes and the execution of more advanced subgroup analyses. The variety in intervention delivery, including group vs individual treatment or digital versus in-person forms, adds a further layer of complexity that could not be entirely resolved in a narrative synthesis. Although no explicit publishing bias was identified, its possibility cannot be completely dismissed, since negative experiments or those with null results often go unreported. The generalizability of the results may be limited by the demographic characteristics of the participants, who were mostly female, and the removal of treatment-resistant groups. The ramifications for clinical practice are complex. For adults with Major Depressive Disorder, evidence consistently indicates that both evidence-based psychotherapy and antidepressant medication are equally beneficial as standalone treatments, with patient desire, previous treatment history, and side effect profiles serving as critical determinants. The data indicate that medication may be a somewhat more successful first choice for certain persons with GAD, but therapist-administered CBT remains a very beneficial alternative. The enhanced tolerability of psychological therapies makes them an essential alternative for individuals apprehensive about ill effects associated with medicines. These results underscore the urgent need for more head-to-head studies using standardized, high-fidelity therapies and including extended follow-up to evaluate response durability and relapse prevention. Future research should aim to uncover biomarkers or clinical predictors of therapy response to go from a uniform approach to a more individualized, precision psychiatry paradigm (22). This evaluation did not include the investigation of the effectiveness of combination treatment compared to monotherapy in these particular groups, although it signifies an essential area for future research.

CONCLUSION

This systematic review consolidates current evidence demonstrating that psychosocial interventions, especially cognitive-behavioral therapy, and pharmacological treatments involving SSRIs/SNRIs are effective first-line approaches for managing major depressive disorder and anxiety disorders, although their relative efficacy varies by condition. The clinical importance of these findings underscores the principle of personalized care, whereby treatment choices for MDD can be confidently directed by patient preferences and tolerability profiles due to demonstrated equivalence, whereas for GAD, pharmacotherapy may necessitate slight prioritization in initial strategic discussions for certain individuals. Although the overall evidence base is substantial, its reliability is diminished by the variability in intervention formats and the limited number of direct-comparison studies, highlighting an ongoing necessity for additional high-quality research that identifies specific predictors of treatment response to enhance a more targeted and effective precision psychiatry approach.

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