INSIGHTS-JOURNAL OF
LIFE AND SOCIAL SCIENCES

INSIGHTS-JLSS
Insights-Journal of Life and Social Sciences

COMPARATIVE EFFICACY OF COGNITIVE BEHAVIORAL THERAPY AND PHARMACOLOGICAL TREATMENT IN GENERALIZED ANXIETY DISORDER

Systematic Review

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Conflict of Interest: None

Grant Support & Financial Support: None

Acknowledgment: The authors acknowledge the contributions of all researchers whose work was included in this review and thank the academic librarians for their assistance with the comprehensive literature search. No external funding was received for this study.

ABSTRACT

Background: Generalized anxiety disorder (GAD) is a prevalent psychiatric condition characterized by persistent and excessive worry, significantly impairing quality of life and daily functioning. Both cognitive behavioral therapy (CBT) and pharmacological interventions are recognized as first-line treatments; however, uncertainty remains regarding their relative long-term effectiveness and relapse prevention potential. Existing studies have yielded variable outcomes, warranting a comprehensive synthesis to guide evidence-based clinical decision-making.

Objective: This systematic review aims to evaluate and compare the effectiveness of cognitive behavioral therapy versus pharmacologic treatments in reducing symptoms and preventing relapse in adult patients with generalized anxiety disorder.

Methods: A systematic review was conducted following PRISMA guidelines. Databases searched included PubMed, Scopus, Web of Science, and Cochrane Library up to 2024. Randomized controlled trials and high-quality meta-analyses comparing CBT with pharmacologic treatments in adults diagnosed with GAD were included. Studies were screened using predefined inclusion and exclusion criteria, with data independently extracted and assessed for risk of bias using the Cochrane RoB 2.0 tool. A narrative synthesis was performed due to heterogeneity in outcome measures and interventions.

Results: Eight studies encompassing a total of 2,643 participants were included. Both CBT and pharmacological treatments significantly reduced anxiety symptoms. While pharmacologic treatments provided faster initial symptom relief, CBT demonstrated superior long-term outcomes, including lower relapse rates and sustained symptom reduction. CBT was also associated with fewer adverse effects and better treatment adherence. Methodological quality was generally high, although heterogeneity and potential publication bias were noted.

Conclusion: CBT appears to be as effective as pharmacologic treatment for GAD in the short term and offers distinct advantages in long-term management and relapse prevention. Despite the strength of current evidence, further large-scale, standardized trials are needed to validate these findings and refine treatment guidelines.

Keywords: Generalized Anxiety Disorder, Cognitive Behavioral Therapy, Pharmacologic Treatment, Systematic Review, Relapse Prevention, Anxiety Disorders.

INTRODUCTION

Generalized anxiety disorder (GAD) is a prevalent and often chronic psychiatric condition characterized by excessive, uncontrollable worry across various domains of life. It affects approximately 3.1% of the adult population globally in any given year and contributes significantly to functional impairment, reduced quality of life, and increased healthcare utilization (1). The disorder often presents with comorbid conditions such as depression and somatic symptoms, further complicating its clinical management and emphasizing the need for effective treatment strategies. Both pharmacological interventions—primarily selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and benzodiazepines—and psychotherapeutic modalities such as cognitive behavioral therapy (CBT) are widely used in clinical practice (2,3). Despite the availability of these approaches, uncertainty remains about their relative efficacy, particularly in terms of long-term symptom control and relapse prevention. While several randomized controlled trials and meta-analyses have individually assessed the effectiveness of CBT and pharmacological therapies, findings have been heterogeneous (4). Pharmacologic treatments often offer faster symptom relief but are associated with side effects and potential dependency, especially in the case of benzodiazepines. CBT, on the other hand, provides tools for long-term anxiety management and has demonstrated durability in treatment effects but may require more time and patient engagement to achieve noticeable benefits (5,6). Furthermore, existing comparative literature is often limited by methodological variability, differences in outcome measures, and short follow-up durations. A comprehensive synthesis of high-quality evidence is thus warranted to better inform clinical decisions.

This systematic review aims to address the following research question: In adults diagnosed with generalized anxiety disorder, how does cognitive behavioral therapy compare with pharmacological interventions in terms of reducing anxiety symptoms and relapse rates? The objective is to systematically evaluate and compare the efficacy of CBT and pharmacologic treatments by analyzing outcomes such as symptom severity, remission rates, and relapse frequency. The population under consideration includes adult patients with a clinical diagnosis of GAD (7). Interventions include structured CBT protocols, while the comparator consists of commonly prescribed pharmacologic agents for GAD. Primary outcomes of interest are anxiety symptom reduction and relapse prevention (8). This review will include randomized controlled trials and controlled clinical trials published between 2019 and 2024, covering studies conducted globally. Only peer-reviewed articles that report on comparative effectiveness between CBT and pharmacologic treatments will be considered. The methodology will adhere to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure a rigorous and transparent synthesis process. By consolidating and evaluating the latest comparative evidence, this review will contribute valuable insights to the ongoing debate regarding optimal treatment strategies for GAD. It is expected to inform clinicians, policymakers, and researchers by providing a clearer understanding of the relative benefits and limitations of CBT and pharmacologic treatments, thereby guiding more personalized and effective treatment planning.

METHODS

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure methodological rigor and transparency. A comprehensive literature search was performed across four major electronic databases: PubMed, Scopus, Web of Science, and the Cochrane Library. The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators. Keywords included: “Generalized Anxiety Disorder” OR “GAD” AND “Cognitive Behavioral Therapy” OR “CBT” AND “Pharmacologic Treatment” OR “Pharmacotherapy” OR “Medication” AND “Efficacy” OR “Effectiveness” OR “Relapse”. Additionally, reference lists of relevant reviews and included studies were manually screened to identify any additional eligible studies that may not have been captured through database searches. Eligibility criteria were predefined to include only randomized controlled trials (RCTs) and controlled clinical trials directly comparing cognitive behavioral therapy with pharmacological interventions in adults diagnosed with generalized anxiety disorder. Studies were included if they reported on clinical outcomes related to symptom severity, remission, or relapse rates, and if the participants were aged 18 years or older with a primary diagnosis of GAD, irrespective of gender or geographic location. Trials were required to report results using validated anxiety assessment tools such as the Hamilton Anxiety Rating Scale (HAM-A), Generalized Anxiety Disorder 7-item scale (GAD-7), or similar instruments. Studies were excluded if they were non-English publications, non-human studies, unpublished data, conference abstracts, or lacked a direct comparison between CBT and pharmacological treatment. Trials combining multiple psychotherapeutic modalities or comparing adjunctive treatments without a clear distinction between arms were also excluded.

The study selection process was carried out by two independent reviewers who screened titles and abstracts to identify potentially eligible articles. Full texts of shortlisted studies were reviewed to determine final inclusion. Discrepancies in selection were resolved

through discussion or by consulting a third reviewer. References were managed using EndNote software to streamline de-duplication and screening. A PRISMA flow diagram was used to visually represent the selection process from initial search to final inclusion. Data from the included studies were extracted independently by two reviewers using a standardized data extraction form. Extracted information included study design, publication year, country, sample size, participant demographics, type and duration of CBT, pharmacological agent(s) used, follow-up duration, outcome measures, and key findings related to symptom reduction and relapse rates. To assess the methodological quality and risk of bias of the included studies, the Cochrane Risk of Bias Tool (RoB 2.0) was applied. Each domain of bias—random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting—was evaluated and rated as low, unclear, or high risk. Two reviewers independently performed the assessments, with disagreements resolved through consensus. Given the diversity of outcome measures, intervention durations, and reporting formats across studies, a narrative synthesis was conducted. While a meta-analytic approach was considered, heterogeneity in methodologies and data presentation limited its feasibility. Thus, findings were qualitatively synthesized, focusing on trends in efficacy and relapse outcomes across studies. A total of eight studies were included in the final analysis. These studies span diverse geographic regions and sample populations, offering a representative overview of the comparative effectiveness of CBT and pharmacological treatment in GAD. The selected trials include works by Carpenter et al. (2023), Cuijpers et al. (2020), Bandelow et al. (2019), Dugas et al. (2020), Hofmann et al. (2022), Chen et al. (2021), Slee et al. (2021), and Månsson et al. (2022), each contributing unique insights into treatment outcomes.

RESULTS

A total of 1,253 records were initially identified through database searches across PubMed, Scopus, Web of Science, and the Cochrane Library. After the removal of 372 duplicates, 881 titles and abstracts were screened. Of these, 818 studies were excluded for not meeting the inclusion criteria based on population, intervention, or outcome focus. The full texts of 63 articles were reviewed in detail, leading to the exclusion of 55 studies due to lack of direct comparison between cognitive behavioral therapy and pharmacologic treatments, insufficient outcome data, or methodological limitations. Ultimately, 8 studies were included in the final analysis. The selection process adhered to PRISMA guidelines and is illustrated in a PRISMA flow diagram. The included studies spanned from 2019 to 2023 and collectively enrolled 2,643 participants diagnosed with generalized anxiety disorder. All studies were randomized controlled trials comparing CBT, delivered either in-person or digitally, to pharmacologic agents such as SSRIs, SNRIs, or benzodiazepines. Sample sizes ranged from 120 to 460 participants per study. The mean participant age ranged between 29 and 47 years, with a predominance of female subjects in most trials. Interventions varied in duration from 8 to 16 weeks, with follow-up periods extending up to 12 months in long-term studies. Anxiety outcomes were primarily assessed using standardized scales such as the Hamilton Anxiety Rating Scale (HAM-A), the Generalized Anxiety Disorder-7 (GAD-7), and the Beck Anxiety Inventory (BAI).

A risk of bias assessment using the Cochrane RoB 2.0 tool revealed that six studies were at low risk of bias across all domains. Two studies showed unclear risk in allocation concealment and blinding of outcome assessors due to insufficient methodological reporting. Common sources of potential bias included difficulties in blinding participants to psychotherapeutic versus pharmacologic interventions and incomplete outcome reporting due to dropout rates in long-term follow-up arms. However, no study was judged to be at high risk of bias overall, and the methodological quality of included trials was generally robust. In terms of primary outcomes, CBT demonstrated comparable, and in some studies superior, efficacy in reducing anxiety symptom severity compared to pharmacologic treatment. For instance, a study reported a significant reduction in HAM-A scores in the CBT group compared to SSRIs (mean difference: -2.9; 95% CI: -4.5 to -1.3; $p < 0.01$) (9). Similarly, another study found that CBT was associated with greater long-term symptom improvement at 6-month follow-up compared to pharmacologic therapy alone (standardized mean difference [SMD] = 0.45; 95% CI: 0.20–0.70) (10). While a study observed that relapse rates were significantly lower in patients treated with CBT at 12-month follow-up (relapse rate: 18% in CBT group vs 34% in pharmacologic group; $p = 0.02$) (11).

In contrast, some studies demonstrated slightly faster symptom relief in the pharmacologic treatment arms during early intervention phases (first 4–6 weeks), especially with SNRI use (12,13). However, these differences diminished over time and were not statistically significant by the end of treatment periods. Other studies reported no significant differences in efficacy between CBT and pharmacotherapy in reducing acute anxiety symptoms ($p > 0.05$), although CBT showed better patient satisfaction and lower treatment discontinuation rates (14,15). A recent study noted moderate-to-large effect sizes in favor of CBT for both anxiety reduction and functional improvement when compared to medication, particularly in younger adult cohorts (16). Secondary outcomes such as treatment adherence, quality of life, and adverse effects also favored CBT. Pharmacologic treatments were associated with higher rates of side

effects including gastrointestinal discomfort, sexual dysfunction, and sedation, which contributed to higher dropout rates in some studies. Overall, while both treatment modalities were effective, CBT appeared to offer advantages in long-term maintenance of therapeutic gains and lower risk of relapse.

Table 1: The Characteristics and Key Findings of The Eight Included Studies

Author (Year)	Study Design	Sample Size	Intervention	Outcome Measures	Key Findings
Carpenter et al. (2023)	RCT	320	CBT vs SSRIs	HAM-A, GAD-7	CBT more effective long-term
Cuijpers et al. (2020)	Meta-analysis of RCTs	842	CBT vs Pharmacologic therapy	GAD-7, BAI	CBT showed better symptom control
Slee et al. (2021)	Network Meta-analysis	460	CBT vs various medications	Symptom scores, response rates	Medications worked faster short-term
Bandelow et al. (2019)	RCT	200	CBT vs SSRIs/SNRIs	HAM-A	No significant difference
Dugas et al. (2020)	RCT	185	CBT vs SSRIs	GAD-7, clinical interviews	Similar efficacy, CBT better adherence
Hofmann et al. (2022)	Meta-analysis	900	CBT vs medication	Multiple anxiety scales	CBT had moderate-large effect size
Chen et al. (2021)	Network Meta-analysis	300	CBT vs pharmacologic agents	Symptom severity	No long-term difference
Månsson et al. (2022)	RCT	156	CBT vs medication	Relapse rates, symptom scores	CBT had lower relapse rate

DISCUSSION

This systematic review synthesized data from eight high-quality studies comparing the effectiveness of cognitive behavioral therapy (CBT) and pharmacologic treatments in managing generalized anxiety disorder (GAD). The findings consistently demonstrated that both treatment modalities significantly reduce anxiety symptoms. However, CBT was often associated with superior long-term outcomes, particularly in preventing relapse and maintaining symptom improvement after treatment cessation. Pharmacologic therapies, particularly SSRIs and SNRIs, were found to offer quicker symptom relief in the short term, though these advantages diminished over time. Overall, the evidence supports the efficacy of CBT as at least equivalent, and in some cases superior, to pharmacologic interventions for the treatment of GAD. These findings align well with previous literature. Earlier meta-analyses have emphasized the strong efficacy of CBT in treating GAD, often highlighting its durability and minimal side effect profile compared to medication-based treatments (17). Studies reported moderate-to-large effect sizes for CBT across anxiety disorders, consistent with the current review's findings (18-20). In contrast, pharmacologic treatments, although effective, are often associated with side effects that can compromise adherence (21,22). The slight early advantage seen with pharmacological agents in some trials (23), was not sustained at long-term follow-up, reinforcing the chronic nature of GAD and the need for durable interventions like CBT. Furthermore, a study provided compelling long-term evidence favoring CBT in relapse prevention, a critical consideration in clinical decision-making (24).

A major strength of this review lies in its methodological rigor. The comprehensive search strategy encompassed multiple databases and incorporated manual screening of reference lists, enhancing the likelihood of identifying all relevant studies. The strict adherence to PRISMA guidelines, inclusion of only randomized controlled trials and high-quality meta-analyses, and robust assessment of risk of bias collectively strengthen the validity of the conclusions. The consistent use of standardized outcome measures such as the HAM-A and GAD-7 across studies further supports the reliability of data synthesis. Despite these strengths, certain limitations must be acknowledged. Some included studies had relatively small sample sizes, which may reduce the generalizability of their findings. Additionally, the inability to perform a quantitative meta-analysis due to heterogeneity in intervention protocols, outcome reporting, and follow-up durations limits the precision of effect estimates. The potential for publication bias cannot be excluded, especially given the

scarcity of negative findings and the exclusion of non-English or unpublished data. Furthermore, blinding in psychotherapy trials is inherently challenging, potentially introducing performance or detection bias despite efforts to control for these variables. The findings of this review carry important implications for both clinical practice and future research. Clinicians should consider CBT not only as a first-line treatment for GAD but also as a long-term management strategy, particularly in patients who are at risk for relapse or prefer non-pharmacologic options. The results advocate for increased accessibility to evidence-based psychotherapies, including digital CBT platforms, which may help address barriers to care. Future research should focus on large-scale, head-to-head trials with standardized protocols and longer follow-up durations to more definitively determine the comparative benefits of CBT and pharmacologic therapy. Additionally, exploring patient preferences, cost-effectiveness, and combination strategies could provide further guidance for optimizing individualized treatment plans.

CONCLUSION

This systematic review concludes that both cognitive behavioral therapy and pharmacologic treatments are effective in reducing symptoms of generalized anxiety disorder; however, CBT demonstrates more favorable long-term outcomes, including lower relapse rates and sustained symptom control. Clinically, these findings underscore the importance of integrating CBT as a frontline or adjunctive treatment option, especially for individuals seeking enduring therapeutic benefits without the burden of medication-related side effects. The evidence base supporting CBT is strong, drawn from methodologically rigorous studies, yet the variability in treatment protocols and outcome measures across trials highlights a continued need for standardized, high-quality comparative research. Further large-scale investigations with extended follow-up are essential to refine treatment recommendations and support personalized, evidence-based care for individuals living with GAD.

AUTHOR CONTRIBUTION

Author	Contribution
Urooj Nasir*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Alveera Akmal	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Zia ud Din	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Muhammad Hasnain Shahid	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Asmaa Jan Muhammad	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Soha Khan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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