Effectiveness of psychological therapies versus antidepressants in adults with major depression: a systematic review.

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Abstract

Background: Major depression is a leading cause of disability among people worldwide. Although there is no disagreement as to the effectiveness of any psychotherapy or pharmacotherapy methods in the treatment of depression, their efficacy in comparison with each other remains debated.

Objective: This systematic review aims to critically evaluate and compare the efficacy of psychological therapies and pharmacological approaches towards major depression, with a focus on symptom reduction and treatment response.

Methods: A systematic review of PubMed and Scopus databases was performed, identifying randomized controlled trials and meta-analyses published in the last decade. Inclusion criteria required studies to evaluate depression severity using validated scales such as HAM-D, with adult participants aged 18–64 years. A total of 18,622 articles were initially identified, filtered to 6 eligible studies through a rigorous review process.

Results: It was determined that both psychotherapy and pharmacotherapy demonstrated significant decline in depressive symptoms. While psychotherapy was particularly beneficial for individuals preferring non-pharmacological approaches, pharmacotherapy provided more rapid symptom relief, especially in moderate to severe cases. The combination of the treatments lead to the most favorable effects.

Conclusion: Psychotherapy and pharmacotherapy are equally effective for treating major depression, with variations likely influenced by differences in intervention types. Combined therapy offers additional benefits.

Key Words: Depression; Psychotherapy; Antidepressant; Systematic review

1. Introduction

Major depression is one of the leading causes of disability worldwide, according to the World Health Organization (WHO) [1]. Is a severe mood disorder characterized by debilitating low mood, impaired cognition and loss of interest [2]. It has an impact in multiple areas including psychosocial, family and academic functioning [3]. Symptoms often include deep sadness, hopelessness, sorrow, emptiness and despair. [2] Represents a significant contributor to disability, morbidity, and mortality, and constitutes a significant risk for suicide [3].

It is well established that psychotherapies and pharmacological therapies are effective in the treatment of adult depression. Numerous clinical trials have shown superior effects of psychotherapies over control conditions. [4] They have advantages and disadvantages relative to medication. For instance, time-limited psychotherapies have few side effects relative to pharmacotherapy. While antidepressant medications often tend to improve neurovegetative symptoms before mood, psychotherapies usually alleviate mood symptoms before. Moreover, psychotherapies help patients to resolve interpersonal conflicts at home or in the workplace and to make executive decisions about their lives. Disadvantages include a slower response time: medications frequently show benefit in 2 to 6 weeks, whereas psychotherapies can take twice that time. Medication is also indicated for patients with delusional depression or symptoms so severe as to require hospitalization. [15]

Several psychotherapeutic modalities, such as cognitive behavioral therapy (CBT), interpersonal psychotherapy (IPT), and behavioral therapy, have now demonstrated benefits in treating DSM-IV major depressive disorder in randomized clinical trials: in particular. CBT and IPT have been shown not only to induce acute remission, [12] but to provide prophylaxis against relapse and recurrence. [17]

Psychotherapy appears to be a valid therapeutic tool, with efficacy superior to placebo [14] and comparable to pharmacological therapy in reducing mild and moderate depressive symptoms in the acute phase. [15] However, the differences among various types of psychotherapy treatments have not been significant enough to help clinicians make a definitive therapeutic choice. There are many variables that influence the outcome of psychotherapy, including social functioning, symptom severity, the patient's cognitive profile, the presence of atypical symptoms, age, sex, and the type of attachment formed in the therapeutic relationship. [16] While first-line treatments include both antidepressants and psychological therapies, debate persists about their relative effectiveness. [3].

In recognition of these elements, this systematic review aims to critically analyze all available data on patients treated with pharmacological treatment and psychotherapy as well as identify which is more effective.

2. Materials and Methods

2.1. Protocol and Registration

This study employed a detailed search strategy across two electronic databases to examine the existing literature on the effectiveness of psychological therapies against pharmacological treatments. Databases including PubMed and Scopus were systematically searched for literature published up until November 2024, to include the most current studies available on this critical topic.
Key search terms included: "Depression", "Psychotherapy", "Antidepressant" Boolean operators (AND, OR, NOT) were strategically employed to refine and link the search terms effectively. The search string was constructed as follows: ("Depression" AND "Psychotherapy" AND "Antidepressant")

2.2. Inclusion and Exclusion Criteria

The review considered the following inclusion criteria: [1] Study population involves adult patients over 18 years [2] Intervention: That compared pharmacological and psychological treatments. [3]

Type of studies: Only randomized controlled trials and meta-analyses addressing these therapeutic approaches were considered [4] Language: All included studies had to be published in English. [5] Outcomes: Studies that measured depression severity, as assessed by validated depression scales such as the Hamilton Depression Rating Scale (HDRS) [6] Publication Type: Published in the last 10 years. [7] Human studies: all the research must include human participants.

Studies were excluded on the following criteria: [1] Type of study: Cohort studies and clinical cases were excluded [2] Patients: Studies in which the participants did not have a confirmed diagnosis of major depression or presented mental disorder or underlying medical disease that could cofound the results [3] Studies that did not address drug-resistant depression, severe or chronic depression were excluded to maintain consistency. [4] Treatment Types: Studies focused only on one treatment modality, either psychotherapy or pharmacological treatment, without comparing it were excluded [5] non-human studies were also excluded, as this review focuses exclusively on outcomes in human patients. [6] Studies that do not report validated measures of depression severity were excluded, [7] Studies published in languages other than English or outside the last 10 years were excluded.

2.3. Data Collection Process

Our initial search according to our key words yielded a total of 18,622 articles from which we applied filters in PubMed and Scopus databases, leaving us with a total of 2,319 articles. We removed 58 duplicate records. In addition, records were excluded based on titles, leaving 2,155 full-text articles for further consideration. A total of 51 articles were reviewed by three independent reviewers to assess the relevance of each study based on predefined inclusion and exclusion criteria. Inconsistencies between reviewers were resolved by discussion. The initial database search panned out in 18,622 articles, of which 6 studies were identified as eligible for the final study. The PRISMA flowchart describing the inclusion process is presented in Figure 1.

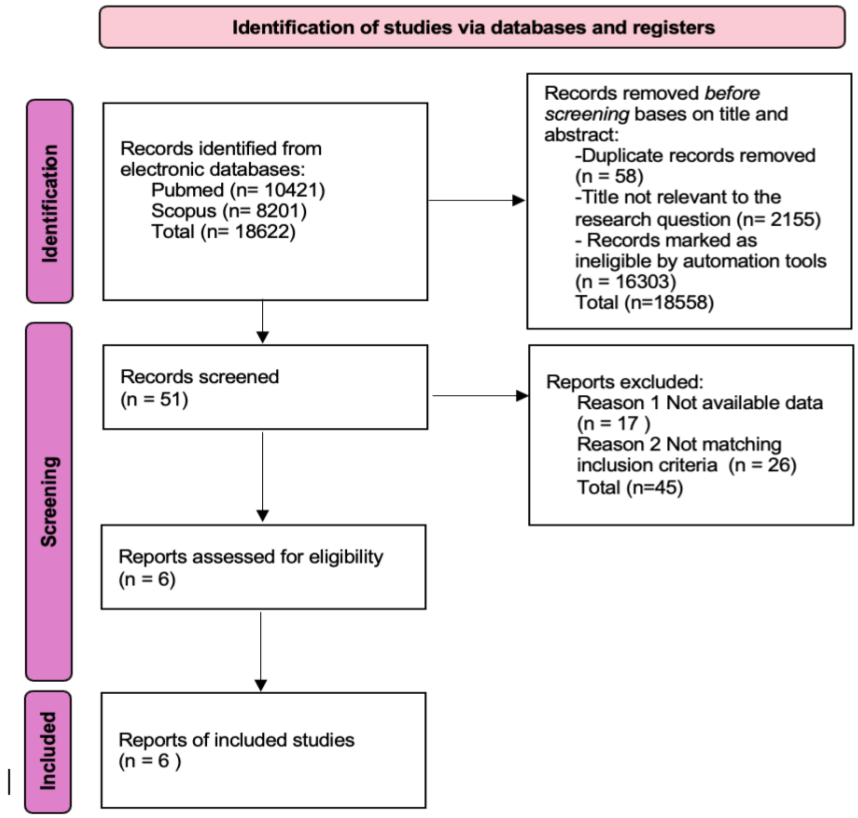

Figure 1. PRISMA flow diagram

2.4. Risk of Bias and Quality Assessment

Independent investigators reviewed the studies included in the systematic review to assess the risk of bias and quality. Each study was carefully reviewed for the possibility of bias in areas like study design, methodology, generation of randomized sequences, and blinding of participants and assessors. Discrepancies between reviews were resolved by discussion and agreement. This process lets us determine the quality of the papers and the validity regarding the inclusion and exclusion criteria established in the review.

3. Results

3.1. Study Characteristics

This systematic review analyzed a total of 6 studies published between 2014 and 2024. These studies are focused on the effectiveness of various psychological therapies against pharmacological treatments. Most of the studies were rated as medium to high quality, highlighting their methodological reliability.

Table 1. Study Characteristics

Study Number	Title	Author	Journal	YOP	Type of Study	Quality of Study
1	A network meta-analysis of the effects of	Cuijpers, P. Noma, H. Karyotaki, E.	World Psychiatry	2020	Meta-Analysis	High

	psychotherapies, pharmacotherapies and their combination in the treatment of adult depression (5)	Vinkers, C.H. Cipriani, A. Furukawa, T.A.				
2	Psychotherapy effectiveness for major depression: a randomized trial in a Finnish community (6)	Saloheimo HP, Markowitz J, Saloheimo TH, Laitinen JJ, Sundell J, Huttunen MO, A Aro T, Mikkonen TN, O Katila H.	BMC psychiatry	2019	Randomized Controlled Trial	Medium
3	Cognitive change in cognitive-behavioural therapy v. pharmacotherapy for adult depression: a longitudinal mediation analysis (7)	Quigley L, Dozois DJA, Bagby RM, Lobo DSS, Ravindran L, Quilty LC.	Psychological Medicine	2019	Randomized Controlled Trial	Medium-High
4	Role of pill-taking, expectation and therapeutic alliance in the placebo response in clinical trials for major depression (8)	Leuchter AF, Hunter AM, Tartter M, Cook IA.	The British Journal of Psychiatry: The Journal of Mental Science	2014	Clinical Trial	Medium-High
5	Efficacy of trial-based cognitive therapy, behavioral activation and treatment as usual in the treatment of major depressive disorder: preliminary findings from a randomized clinical trial (9)	Hemanny C, Carvalho C, Maia N, Reis D, Botelho AC, Bonavides D, Seixas C, de Oliveira IR.	CNS spectrums	2020	Clinical Trial	Medium-High
6	Psychological interventions to prevent the onset of major depression in adults: a systematic review and individual participant data meta-analysis (10)	Buntrock, Claudia A. Harrer, Mathias b Sprenger, Antonia A. Illing, Susan B. Sakata, Masatsugu c,d	The Lancet Psychiatry	2024	Systematic Review and individual participant data meta-analysis	High

YOP – Year of publication

3.2. Patients Characteristics

The studies included has a diverse population of adult patients, with a wide sample size ranging from 76 to 11910 participants; the age ranged is between 18 – 64 years among the participants, ensuring a focus on working-age adults commonly affected by major depression. The gender distribution within these studies revealed a female predominance, across the studies, with approximately 60% being women

<u>Table 2. Patient's Characteristics</u>

Study Number	Sample Size	Age (Years)	Gender	Psychotherapy	Pharmacotherapy
1	11 910			CBT CT IPT DYN REBT	TCA SSRI
2	134	18 - 64	37 Male (28%) 97 Female (72)	IPT PeGT	TAU
3	104	18 - 65	Female (53%) Male (47%)	CBT	ADM
4	88	18 - 65	55 Female (63%) 33 Male (37%)	Supportive Care	Duloxetine, Venlafaxine XR, Escitalopram Placebo
5	76		86% women (n = 66) 14% man (n =10)	TBCT	Fluoxetine, Escitalopram, Amitriptyline, Desvenlafaxine, Sertraline, Venlafaxine
6	7 201	Mean age: 49.9	2227 Male (30.9%) 4957 Female (68.9%) 17 preferred not to report their sex (0.2%)	CBT	TCA SSRI

CBT – cognitive behavior therapy, DYN – psychodynamic therapy, CT – cognitive therapy, REBT – rational-emotive behavior therapy, TCA – tricyclic antidepressant, SSRI – selective serotonin reuptake inhibitor, IPT – interpersonal psychotherapy, MBCT - Mindfulness-Based Cognitive Therapy, TAU - Treatment-as-usual, TBCT, trial-based cognitive therapy.

3.3. Depression Scale Initial and changes at Psychotherapy treatment

All studies employed the Hamilton Depression Rating Scale (HAM-D) to rate the severity of depression at baseline and after treatment. Initial HAM-D scores connote a moderate to severe depression across study participants.

The HDRS (also known as the Ham-D) is the most widely used clinician-administered depression assessment scale. The original version contains 17 items (HDRS17) related to symptoms of depression experienced over the past week. In most clinical trials, the HDRS is used as a standard to determine severity and response. [13] Originally developed for hospital inpatients, thus the emphasis on melancholic and physical symptoms of depression. (Rating Clinician-Rated, n.d.) Multiple versions of the HDRS exist, with the number of items usually varying between 17 and 24, however, up to 36 items have been described. [13] The HAM-D score is defined from 8 to 15 indicating mild depression, 16 to 26 moderate depression and above 27 severe depressions. [12]

Table 3. Analysis of follow-up duration, Depression scale changes and conclusion of the efficacy of psychological treatment versus pharmacological

Study Number	**Follow-up**	**Depression Scale Initial and final evaluation at Psychotherapy treatment (HAM-D)**	**Conclusions: Efficacy of psychological treatment vs pharmacological**
1	6 – 12 months	Initial: In most of the included studies, patients had moderate to severe depression based on baseline HAM-D scores. Final evaluation: -Psychotherapy vs. pharmacotherapy: No significant differences -Combination vs. Psychotherapy: More effective -Combination vs. pharmacotherapy: More effective	The difference between psychotherapy alone and pharmacotherapy alone was not significant. Combined treatment was superior to either psychotherapy alone or pharmacotherapy alone in terms of response.
2	12 months	Initial: >14 Final evaluation: There was significant improvement in all three treatment modalities: -IPT: Average HAM-D reduction of 9.1 points. -PeGT: Average reduction of 8.3 points. -TAU: Average reduction of 11.1 points	All treatment groups showed significant and sustained improvements over time. However, pharmacological treatment (TAU) showed slightly better results.
3	16 weeks	ADM Week 0 (pretreatment) 16.42 Week 4 10.84 Week 9.74 Week 16 (postreatment) 8.50 CBT Week 0 (pretreatment) 16.79 Week 4 14.71 Week 12.29 Week 16 (postreatment) 7.43 -Cronbach's α values for the HAM-D in the present sample were 0.69 at week 0, 0.77 at week 4, 0.83 at week 8 and 0.86 at week 16.	Participate in both conditions showed significant decreases in depression symptoms over the treatment period.
4	8 weeks	-Initial (Baseline): Mean score = 21.51 (SD ± 4.49). -Final (Week 8): Medication group: Mean = 12.41 (SD ± 7.36). Placebo group: Mean = 13.48 (SD ± 8.68). Supportive care only: Mean = 19.45 (SD ± 5.76).	These results highlight that both medication and placebo combined with supportive care significantly improved symptoms compared to supportive care alone The efficacy analysis revealed that the reduction in HRSD symptoms from baseline to week 8 was greater for participants

			taking medication compared with those receiving supportive care alone
5	12 weeks	<u>TBCT</u> Initial Evaluation 20.62 ± 5.3 Intermediate Evaluation 13.00 ± 6.0 Final Evaluation 9.84 ± 5.9 <u>BA</u> Initial Evaluation 22.38 ± 5.8 Intermediate Evaluation 12.80 ± 6.9 Final Evaluation 9.10 ± 7.3 <u>TAU</u> Initial Evaluation 20.42 ± 4.3 Intermediate Evaluation 19.27 ± 6.0 Final Evaluation 17.98 ± 6.3	The study shows that combining TBCT or BA with antidepressants works better than using TAU alone. Both therapies reduced depression severity by more than 50%. BA also helped decrease disability, making it slightly more effective in improving functionality. These results suggest that adding psychotherapy to medication can provide better results, especially for patients with recurring symptoms or additional health issues
6	24 months	<u>Baseline (Pretreatment):</u> Mean HAM-D score across all patients entering Phase 2: 12.6 ± 5.3. CBT plus medication group: 14.1 ± 5.0. Medication plus CBT group: 11.7 ± 5.3 (<u>Post-treatment at Week 24):</u> Mean improvement in HAM-D for the CBT plus medication group: 8.2 ± 2.0 points from baseline. Mean improvement in HAM-D for the Medication plus CBT group: 5.3 ± 1.2 points from baseline.	Both CBT and antidepressant medications are equally effective for initial treatment, showing significant reductions in depression severity.

HAM-D: Hamilton Depression Rating Scale

4. Discussion

4.1. Summary of evidence

Both psychotherapy and pharmacotherapy significantly reduce depressive symptoms. While the studies demonstrate equivalency in overall outcomes, specific contexts and patient profiles may benefit from one approach over the other. Psychotherapy such as cognitive-behavioral therapy (CBT), interpersonal therapy (IPT) may be particularly advantageous for patients preferring non-pharmacological interventions or those at risk of medication side effects. Pharmacotherapy, especially selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressant (TCAs), provided more rapid relief of symptoms Notably, Combined markedly decrease depressive symptoms. Although the studies show equality in overall results, certain clinical settings and patient composites may find one option more beneficial than the other. These results highlight the importance of tailoring treatment strategies to individual patient needs, considering factors such as symptom severity, treatment preferences, and clinical context.

4.2. Limitations

This study has several limitations. A challenge was the attrition of patients during the studies led to the exclusion of certain studies due to the insufficient data potentially impacting the comprehensiveness of the review. Moreover, the short-term focus of many interventions limits the evaluation of the long-term efficacy or late adverse effects.

Another limitation is the representativeness of the study group. Participants were primarily form clinical or research settings which may not accurately reflect the general population or in rural areas. Furthermore, the studies are compounded by the overrepresentation of patients with mild to moderate depression, excluding those with severe or refractory depression. This restricts the reducing generalizability of findings.

Lastly, A significant limitation was the sample variability, with 60% being women. Additionally, the adherence to the treatment protocols varied significantly, likely influencing the reported outcomes.

Future studies should address these gaps by a diversity in study populations, extend follow-up periods to evaluate long-term effects, and integrate adherence monitoring to enhance the robustness and applicability of findings.

5. Conclusions

In all trials, we found that both therapies were beneficial, some more than others. Both pharmacological and psychological treatment proved to be effective in treating depression, even though the participants in each study were of the same average age. We believe that the variations in the results are due to each study observed having different types of psychological and pharmacological treatment. This could have affected the targeting of the results.

Although psychotherapy is most appropriate for patients who are medication-free or tolerant to those effects, pharmacotherapy offers quicker symptom reduction especially in moderate-to-severe depression. Combined therapy is associated with the best outcomes to be high first line treatment of choice in treatment resistant or refractory depression, or a recurrent episode.

Futures research must investigate longer-term efficacy of these interventions, promote adherence to improve the external validity of findings and seek to recruit greater ethnic diversity to provide generalizable results. By prioritizing personalized care pathways that consider the patient's needs and requirements to match clinical requirements, we can improve care and outcomes for patients with major depression.

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