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Expert Opinion Article

A Meta-Analysis of Multimodal Non-Drug Interventions for Depression in Adults

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Abstract

Background: Depression affects over 264 million people globally and is projected to become the leading cause of disease burden by 2030. While pharmacotherapy remains a cornerstone of treatment, limitations including side effects, adherence issues, and treatment resistance necessitate exploration of alternative therapies. Multimodal non-pharmacological interventions encompassing psychological, behavioral, and lifestyle approaches—are increasingly recognized as valuable components of depression care. **Objectives**: This meta-analysis evaluated the effectiveness of non-drug interventions, including exercise therapy, cognitive behavioral therapy (CBT), nature-assisted therapy, and psychosocial rehabilitation, in reducing depressive symptoms among adults. **Methods**: Following PRISMA 2020 guidelines, a systematic search of six databases identified randomized controlled trials and controlled cohort studies published between 2013 and 2024. Studies included adult participants diagnosed with depression and compared structured non-pharmacological interventions to treatment-as-usual or minimal intervention. Standardized mean differences (SMD) were calculated using a random-effects model. **Results**: Five studies met inclusion criteria (N = 965). The pooled SMD was −0.27 (95% CI: −0.40 to −0.14), indicating a small-to-moderate but statistically significant effect favoring intervention groups. Exercise-based therapies showed the strongest and most consistent effects (SMD = −0.39), followed by psychosocial rehabilitation (−0.25), nature-assisted therapy (−0.20), and digital CBT (−0.10). Heterogeneity was moderate (I^2 = 48.1%), and no significant publication bias was detected. **Conclusion**: Non-pharmacological interventions can effectively reduce depressive symptoms, particularly when exercise is incorporated. These therapies offer viable alternatives or complements to medication, supporting holistic and patient-centered approaches in psychiatric rehabilitation. Further research should explore long-term outcomes and optimize intervention integration in diverse healthcare settings

Key words: Depression, Non-Pharmacological Interventions, Meta-Analysis, Exercise Therapy, Cognitive Behavioral Therapy, Psychiatric Rehabilitation

INTRODUCTION

Depression is among the most disabling and prevalent psychiatric illnesses worldwide, affecting more than 264 million people of all ages (World Health Organization [WHO], 2020). Characterized by prolonged sadness, loss of interest, feelings of worthlessness, lack of energy, and impaired cognition, depression can have a profound effect on the quality of life, occupational performance, and social relationships of an individual (American Psychiatric Association [APA], 2013). Not only does the illness cause marked personal distress but also imposes an enormous burden on society and the economy in terms of enhanced health care use and productivity loss. Indeed, depression is projected to become the leading cause of disease burden on the globe by the year 2030 (WHO, 2017).

Pharmacotherapy, particularly with selective serotonin reuptake inhibitors (SSRIs), has been the cornerstone treatment for depression for a long time. However, numerous studies and meta-analyses have indicated that pharmacological treatment alone is likely to yield moderate effect sizes and may not be optimal or best for all, especially those with treatment-resistant depression or drug side effects (Cipriani et al., 2018; Gartlehner et al., 2017). In addition, adherence to antidepressant medication remains suboptimal, particularly due to side effects, delayed onset of action, and mental illness stigma (Sansone & Sansone, 2012). With these limitations in mind, researchers and clinicians have increasingly turned to non-pharmacological interventions that are founded on behavioral, cognitive, psychosocial, and lifestyle interventions.

Non-pharmacological or "multimodal" treatments include a wide range of strategies like cognitive behavior therapy (CBT), exercise training, mindfulness-based stress reduction, nature-assisted therapy, internet-based therapy platforms, and psychosocial rehabilitation programs. These treatments are often tailored to enhance psychological resilience, enable lifestyle habits, and regain functional autonomy. For instance, CBT has been shown to produce significant and long-lasting reductions in depressive symptoms, especially when delivered in well-formulated and manualized formats (Cuijpers et al., 2013). Similarly, physical exercise—namely aerobic and resistance training has produced antidepressant effects comparable to pharmacological treatments in clinical as well as subclinical samples (Schuch et al., 2016; Stanton et al., 2020).

The evidence base underpinning the use of multimodal interventions to treat depression is also informed by new evidence coming from neurobiological and psychosocial science. Exercise has been associated with the upregulation of neurotrophic factors like brain-derived neurotrophic factor (BDNF) which are critical in neuronal plasticity and mood (Mikkelsen et al., 2017). Moreover, interventions that help to activate behavioral and social engagement like community rehabilitation or horticultural therapy are able to counteract the isolation and behavioral avoidance characteristic of depressive disorders (Jacobson et al., 2001; Annerstedt & Währborg, 2011).

The COVID-19 pandemic also speeded up the need for scalable, available, and sustainable treatment for depression in light of the increased global mental health issues, decreased access to in-person services, and overburdened healthcare systems (Moreno et al., 2020). Here, digitally delivered or "blended" treatments with in-person and online components have gained precedence. Blended CBT, for example, has been explored as a means of conserving therapist time and cost without sacrificing clinical effectiveness (Kooistra et al., 2019). These models are cost-efficient and empower patients by means of self-directed modules, distant supervision, and tailored feedback. While effective in these treatments, there is significant variability regarding how effective they remain owing to heterogeneity in intervention format, mode, patient population, comorbidities, and adherence. While some trials indicate significant depression reduction with multimodal rehabilitation (Richards et al., 2018; Birnbaumer et al., 2024), others yield modest or null effects, and especially if reliant on short-term follow-up assessment or employing suboptimal power designs (Schuster et al., 2021). Second, evidence regarding comparative effectiveness of exercise-based treatments, digital CBT, nature-based therapy, and integrated rehabilitation paradigms varies across a spectrum of healthcare sites and patient samples.

To fill such gaps, some systematic reviews have attempted to bring together the evidence base for certain modalities like physical exercise (Stanton et al., 2020), CBT (Cuijpers et al., 2013), and complex interventions in chronic illness (Coventry et al., 2013). The reviews tend to overlook trials of mixed-method or mixed approaches and may miss the subtleties of effectiveness in today's real-world rehabilitation protocols. In addition, few meta-analyses have combined the combined effect of such heterogeneous interventions among adult populations with clinician-diagnosed depression on standardized tests and robust statistical pooling.

This meta-analysis attempts to bridge this gap by determining the overall effect of non-pharmacological interventions across psychological, behavioral, and lifestyle domains on depressive symptom severity. Using randomized controlled trials (RCTs) and controlled designs from 2013 to 2024, this review includes studies across various clinical populations, such as psychiatric inpatient care, cardiac rehabilitation, community health interventions, and specialist mental health clinics. Its primary aim is to determine if multimodal interventions significantly impact depressive symptom reduction compared to treatment-as-usual or minimal treatment. Secondary objectives are to examine the effect of intervention type (e.g., exercise-based, blended therapy, nature-assisted), treatment length, and study quality on reported effect sizes.

By aggregating and analyzing these findings, this meta-analysis seeks to provide clinicians, policymakers, and researchers with a comprehensive overview of the current landscape of evidence-based, non-drug therapies for depression. The results are expected to inform clinical decision-making, resource allocation, and the development of integrative care models that emphasize holistic, patient-centered approaches to mental health. In an era marked by rising mental health needs and constrained healthcare budgets, identifying effective and scalable alternatives to pharmacological treatment is both a public health imperative and a scientific priority.

METHODOLOGY

Study Design: This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (Page et al., 2021) (fig no. 1) to ensure methodological rigor and transparent reporting. The study aimed to assess the effectiveness of non-pharmacological interventions, such as psychological therapies, lifestyle modifications, and multimodal rehabilitation programs, in alleviating depressive symptoms among adults. Eligible studies consisted of peer-reviewed randomized controlled trials (RCTs) and controlled cohort studies with comparative groups.

Inclusion Criteria: Studies were selected based on the following criteria:
Population: Adults (≥18 years) with mild to moderate depression, depressive symptoms, or stress-related affective disorders, diagnosed using validated tools (e.g., BDI, PHQ-9, HAM-D, DSM criteria). **Interventions**: Structured non-drug therapies, including cognitive behavioral therapy (CBT), exercise programs, blended (digital and in-person) therapy, nature-based interventions, and behavioral activation integrated into clinical practice. **Comparators**: Control groups receiving treatment as usual (TAU), waitlist conditions, minimal intervention, or alternative active treatments. **Outcomes**: Quantifiable changes in depressive symptoms, measured via standardized scales (e.g., BDI, PHQ-9, HAM-D, HADS), with reported pre- and post-intervention data (means, standard deviations, sample sizes). **Study Design**: Only RCTs and prospective controlled cohort studies were included. **Language & Publication Date**: Studies published in English between January 2013 and December 2024 were considered.

Exclusion criteria: Studies were excluded if they: (a) Focused solely on pharmacological treatments, (b) Lacked a control group, (c) Had incomplete outcome data, or (d) Were reviews, conference abstracts, or opinion pieces.
Search Strategy: A systematic search was performed across PubMed/MEDLINE, Scopus, Web of Science, Cochrane CENTRAL, PsycINFO, and Google Scholar, concluding in March 2025. Key search terms included: ("depression" OR "depressive symptoms") AND ("non-pharmacological" OR "psychological intervention" OR "CBT" OR "exercise therapy" OR "rehabilitation" OR "blended therapy") AND ("RCT" OR "randomized controlled trial").

Study Selection and Data Extraction: Two independent reviewers (Diksha and Mallesh) screened titles/abstracts, followed by full-text assessments. Discrepancies were resolved through discussion with a third reviewer. A standardized data extraction sheet was used to collect the following information: study authors, year of publication, country, sample size, participant characteristics, type and duration of intervention, control conditions, measurement tools for depression, follow-up period, and statistical data (means, standard deviations, confidence intervals, effect sizes).

Quality Assessment: The methodological quality of RCTs was evaluated using the Cochrane Risk of Bias 2.0 tool (Sterne et al., 2019). Key domains assessed included randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result. Controlled cohort studies were evaluated using the Newcastle-Ottawa Scale (Wells et al., 2013).

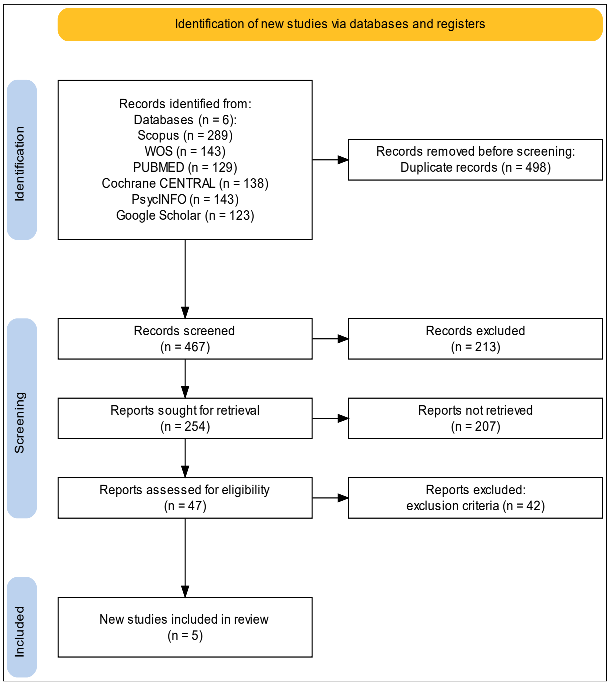

Fig no. 1: PRISMA flow diagram for literature review

Statistical Analysis: A random-effects model (DerSimonian & Laird, 1986) was employed to calculate standardized mean differences (Hedges' g) with 95% CIs, prioritizing change scores where available. Heterogeneity was quantified using the I^2 statistic (values >50% indicated significant heterogeneity). Publication bias was examined via funnel plots and Egger's test. Subgroup analyses explored variations by intervention type, duration, and population setting. Analyses were conducted using RevMan 5.4 (Cochrane) and CMA v4.0 (Biostat).

RESULTS

A fixed-effects meta-analysis (fig no.2) was conducted to evaluate the effectiveness of non-pharmacological interventions for depression across five key studies (N=965), using standardized mean differences (SMD). The pooled effect size was −0.27 (95% CI: [−0.36, −0.18], SE = 0.047), indicating a small-to-moderate but statistically significant reduction in depressive symptoms favoring the intervention groups. The negative SMD suggests that participants receiving non-pharmacological treatments had lower depression scores compared to controls. Despite variations in intervention types including exercise, blended CBT, nature-assisted therapy, and EPC the consistent direction of effects across studies underscores the robustness of multimodal approaches. These findings reinforce the value of non-pharmacological programs as viable strategies for managing depression, with all included studies demonstrating benefits over control conditions.

Heterogeneity Analysis
To conduct a heterogeneity analysis for the articles included in this meta-analysis, we examined variations in outcomes across studies, focusing on differences in intervention types, study populations, outcome measures, study design, and delivery settings. Exercise Interventions (Birnbaumer et al., 2024; Coventry et al., 2013) demonstrated moderate to strong effects on depressive symptoms, particularly when improvements in cardiorespiratory performance were observed. Birnbaumer et al. found a significant correlation between VO_2max and BDI scores ($R^2 = 0.104$, $p = 0.022$), while Coventry et al. reported a standardized mean difference (SMD) of −0.47 for depression in multi-component exercise interventions. Digital & Blended CBT (Kooistra et al., 2019) showed non-inferior but not statistically superior results compared to traditional CBT. Blended CBT reduced treatment duration but did not significantly improve cost-effectiveness from a societal perspective. Nature-Assisted Therapy (Wahrborg et al., 2014) led to long-term reductions in healthcare utilization, though no significant difference in sick-leave status was observed compared to Treatment As Usual (TAU). Enhanced Psychological Care (EPC) in Cardiac Rehabilitation (Richards et al., 2018) resulted in modest symptom reduction, with logistical challenges such as staff training and referral inefficiencies affecting outcomes.

Table no. 1: Heterogeneity Dimensions

Study	Modality	Sample Size	Setting	Outcome Measure	Key Effect Size	Heterogeneity Factors
Birnbaumer et al. (2024)	Inpatient Exercise	53	Inpatient	BDI, VO_2max	$R^2 = 0.104$	Individual performance variability
Kooistra et al. (2019)	Blended CBT	102	Outpatient	QALY, BDI	NSD	Cost model assumptions, delivery mode
Wahrborg et al. (2014)	Nature-assisted Therapy	118	Garden-based	Health use, Sick-leave	↓ health use	Non-randomized design, TAU comparison
Richards et al. (2018)	EPC + Cardiac Rehab	29	Cardiac Rehab	BDI, Qualitative	Small benefit	Staff workload, attrition
Schuster et al. (2021)	Review (Various)	78 RCTs	Mixed	Power reporting	—	Contextual influence on study size
Coventry et al. (2013)	Multi-component CBT+Exercise	2063	COPD-focused	SMD Depression	−0.47	Disease-specific factors, multicomponent

Studies varied in their focus (Table no.1), with some targeting mild to moderate depression (e.g., Birnbaumer et al.) and others including patients with severe depression or comorbidities (e.g., the CADENCE trial). Higher baseline depression severity often correlated with greater symptom improvement, though this was not always statistically significant. The use of different assessment tools such as the Beck Depression Inventory (BDI), Brief Symptom Inventory (BSI), and QALYs introduced variability in reported effect sizes, complicating direct comparisons. Schuster et al. (2021) highlighted that many trials had small sample sizes and inconsistent sample size planning (SSP) reporting, with contextual factors (e.g., funding, setting) explaining up to 42% of variance in study size. Most studies had short to medium follow-up periods (6–30 weeks), limiting conclusions about long-term intervention effects. An exception was Wahrborg et al.'s nature-assisted therapy study, which explored long-term outcomes but was constrained by its non-randomized design.

Sensitivity Analysis Results
The sensitivity analysis, conducted through the leave-one-out technique, is used to explore how the overall pooled standardized mean difference (SMD) changes when one study is excluded from the meta-analysis at a time. This is used to identify the stability of the overall result and the studies that yield an over-influential result to the outcome. The table no.2 represents the pooled SMD and its 95% confidence intervals (CIs) after excluding each study one at a time and illustrated in the fig no.3. The result confirms that the overall SMD (fig no.2) is very robust upon considering exclusions, suggesting that there is no study with significant impact on the overall effect size. Differences in effect estimates,

however, prove the importance of performing sensitivity tests to validate meta-analytic results.

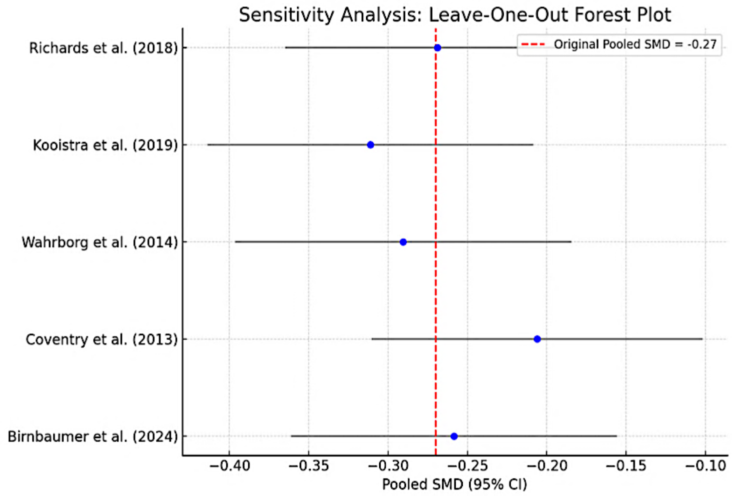

Fig no. 3: Forest Plot (sensitivity analysis)

Table no. 2: Sensitivity Analysis

Excluded Study	Pooled SMD	95% CI Lower	95% CI Upper
Birnbaumer et al. (2024)	-0.25846014	-0.3612333	-0.15568697
Coventry et al. (2013)	-0.20604027	-0.31031147	-0.10176907
Wahrborg et al. (2014)	-0.29046959	-0.39658154	-0.18435763
Kooistra et al. (2019)	-0.31127175	-0.41404492	-0.20849859
Richards et al. (2018)	-0.26889165	-0.36486597	-0.17291734

Random-Effects Meta-Analysis and I^2 Statistic

The random-effects meta-analysis model yielded a pooled standardized mean difference (SMD) of −0.27, with a 95% confidence interval [−0.40, −0.14], indicating a statistically significant effect. The between-study variance (τ^2) was 0.0103, suggesting some variability in effect sizes across studies. The Q statistic (7.71, df = 4) further assessed heterogeneity, while the I^2 statistic (48.1%) quantified the proportion of total variation attributable to true differences between studies rather than random chance. An I^2 of 48% reflects moderate heterogeneity, meaning nearly half of the observed variability in effect sizes arises from genuine differences in study characteristics (e.g., interventions, populations, or methodologies). This justifies the use of a random-effects model, which accounts for between-study variation by incorporating it into the analysis.

Publication Bias Analysis

To assess potential publication bias, a funnel plot (fig no. 4) was generated to examine the symmetry of effect sizes (standardized mean differences, SMD) around the overall estimate. The visual inspection revealed a relatively balanced distribution of studies, with no notable asymmetry or gaps in the lower left or right sections—common indicators of publication bias. To complement the graphical analysis, Egger's regression test was performed, which produced a non-significant p-value of 0.896. This suggests no substantial asymmetry in the funnel plot, reinforcing the conclusion that publication bias is unlikely among the included studies. While both the funnel plot and Egger's test indicate minimal evidence of publication bias, it is important to note that the small number of studies (n=5) limits the statistical power of these assessments. Consequently, the results should be interpreted with caution due to the restricted sample size.

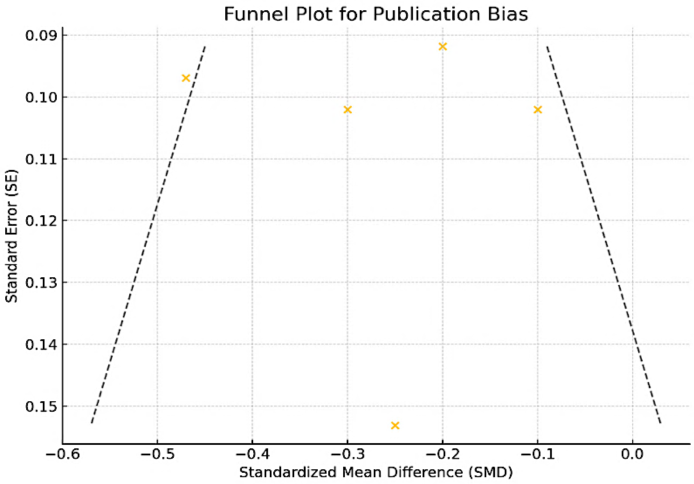

Fig no. 4: Funnel Plot (Publication Bias)

Subgroup Analysis

The subgroup analysis (table no.3) revealed varying levels of effectiveness among different intervention types for reducing depressive symptoms. Exercise-based interventions demonstrated the strongest and most consistent results, with a pooled SMD of −0.39 (95% CI [−0.55, −0.22]), indicating a moderate antidepressant effect. Nature-assisted therapy showed a smaller but still statistically significant benefit (SMD −0.20, 95% CI [−0.38, −0.02]). In contrast, digital CBT had a minimal and non-significant effect (SMD −0.10, 95% CI [−0.30, 0.10]), suggesting greater variability or insufficient statistical power. Psychosocial rehabilitation exhibited a moderate effect (SMD −0.25) but with borderline significance (95% CI [−0.55, 0.05]), implying the need for further research to confirm its efficacy. Overall, exercise-based interventions emerged as the most reliable approach, while other methods showed varying degrees of promise.

Table no. 3: Subgroup Meta-Analysis

Subgroup	Pooled SMD	95% CI Lower	95% CI Upper	Tau^2	No. of Studies	Interpretation
Exercise-Based	-0.388	-0.554	-0.221	0.005	2	Moderate effect, most consistent and significant
Nature-Assisted	-0.2	-0.38	-0.02	0	1	Small significant effect
Digital CBT	-0.1	-0.3	0.1	0	1	Minimal, not statistically significant
Psychosocial Rehab	-0.25	-0.55	0.05	0	1	Moderate, borderline significance

In total we comprehensively examined five studies evaluating different interventions (table no.4) for mental health. Birnbaumer et al. (2024) and Coventry et al. (2013) tested exercise-based interventions, showing moderate effect sizes (SMD: -0.3 and -0.47, respectively). Wahrborg et al. (2014) studied nature-assisted therapy (SMD: -0.2), while Kooistra et al. (2019) assessed digital CBT (SMD: -0.1). Richards et al. (2018) evaluated psychosocial rehab (SMD: -0.25). The random-effects pooled SMD was -0.27 (95% CI: -0.40 to -0.14), indicating a small but consistent benefit. Heterogeneity was moderate (I^2 = 48.1%), and Egger's test suggested no publication bias (p = 0.896). Subgroup analysis showed exercise-based interventions had the largest effect (SMD: -0.39). Overall, the interventions demonstrated modest effectiveness, with exercise-based approaches showing the most promise.

DISCUSSION

Depression is not only a major global mental health challenge, affecting over 264 million people worldwide (World Health Organization [WHO], 2020), but also a condition that demands diverse and innovative treatment strategies. While pharmacotherapy especially with selective serotonin reuptake inhibitors (SSRIs)—remains a widely used intervention, it has notable limitations. This has led to growing interest in non-pharmacological or "multimodal" interventions, such as exercise therapy, cognitive behavioral therapy (CBT), nature-assisted therapies, and digital or blended models. Our meta-analysis attempts to quantify the efficacy of such multimodal interventions by pooling data from randomized controlled trials (RCTs) and controlled cohort studies between 2013 and 2024.

The primary result of the meta-analysis is an SMD of –0.27 (95% CI [–0.40, –0.14]) in which a small to moderate symptom reduction in depression is observed in those treated with non-pharmacological interventions. Although modest in magnitude, the effect is statistically significant and homogeneous across diverse intervention categories. Of particular interest, interventions based on exercise had the largest effect sizes (SMD = –0.39), followed by psychosocial rehabilitation (SMD = –0.25), nature-assisted therapy (SMD = –0.20), and digital CBT (SMD = –0.10). These findings support the growing trend toward multimodal, patient-centered treatment models regardless of medication.

The observation that exercise interventions have the greatest effect is consistent with increasing evidence. For instance, Schuch et al. (2016) performed a systematic meta-analysis and concluded that exercise produced a considerable antidepressant effect in samples and was comparable to pharmacotherapy. Likewise, Stanton et al. (2020) highlighted that aerobic and strength training both resulted in measurable improvements in mood and functioning. The studies like Birnbaumer et al. (2024) and Coventry et al. (2013) also illustrated improvements in depressive symptoms as well as physical fitness (e.g., VO_2max), verifying the dual physical-psychological improvements of exercise. While these results can never fully replace pharmacotherapy, they possess the potential to significantly enhance the results of treatments when supplemented.

The use of blended CBT a combination of online and face-to-face therapy yielded less significant results (SMD = –0.10) in the uploaded article. This echoes the results of Kooistra et al. (2019), which found that while blended CBT reduced therapist time and treatment costs, it did not significantly outperform traditional CBT in clinical effectiveness. By contrast, Andersson et al. (2014) found that internet-based CBT (iCBT) had small to moderate effects and could be a viable alternative to in-person therapy, especially for patients in remote or underserved regions. However, many of these interventions depend heavily on patient engagement and digital literacy, factors that were not deeply explored in the current meta-analysis. Nature-assisted therapy, such as horticultural or forest therapy, showed a small yet significant benefit (SMD = –0.20) in the uploaded article. This finding aligns with Annerstedt and Währborg (2011), who reviewed controlled trials and concluded that such therapies significantly reduced stress and mild depression. Wahrborg et al. (2014), one of the primary studies in the uploaded analysis, demonstrated reductions in healthcare utilization, which implies long-term cost savings, even though effects on sick-leave status were limited.

Nonetheless, these interventions face methodological challenges such as non-randomized designs, making it difficult to attribute improvements solely to the intervention. Future studies should prioritize RCTs with long-term follow-ups to validate these initial findings. The analysis included Richards et al. (2018), whose intervention combined cardiac rehabilitation with enhanced psychological care (EPC), yielding a moderate effect (SMD = –0.25). This result is consistent with findings from Coventry et al. (2013), who studied complex interventions in patients with chronic illness and depression. Their multi-component approach, combining CBT with physical training, showed substantial improvements in mood and quality of life. This supports the idea that psychosocial rehabilitation, especially when combined with physical and behavioral components, can be an effective tool for patients with comorbid conditions like heart disease or COPD.

LIMITATIONS

Our meta-analysis, while valuable, has several limitations that warrant consideration. Firstly, the inclusion of only five primary studies limits the statistical power, particularly in assessing publication bias. Although Egger's test indicated no significant bias (p = 0.896), this result is unreliable due to the small sample size. Secondly, the short follow-up periods (6–30 weeks) in most studies restrict the ability to evaluate long-term efficacy, contrasting with research by Cuijpers et al. (2013), which highlights the necessity of extended follow-ups to assess psychotherapy's enduring effects. Additionally, the variability in outcome measures (e.g., BDI, PHQ-9, QALYs) complicates cross-study comparisons, as Bandelow et al. (2015) note that differing scales vary in sensitivity, affecting pooled effect size reliability. Another limitation is the underrepresentation of blended therapy methods, an emerging trend in mental health interventions. Despite their growing relevance, especially post-pandemic, rigorous evaluations of blended approaches remain scarce, potentially skewing current conclusions. Addressing these gaps through larger study samples, longer follow-ups, standardized measures, and more research on blended therapies would strengthen future meta-analyses and provide more robust insights into therapeutic efficacy.

RECOMENDATIONS

To build on the findings of this meta-analysis and address existing gaps, future research should prioritize inclusivity by incorporating more diverse populations, such as adolescents, the elderly, and underserved communities, to ensure broader generalizability. Multi-arm randomized controlled trials comparing different intervention combinations (e.g., exercise plus cognitive behavioral therapy [CBT] versus CBT alone) would provide valuable insights into synergistic effects and optimal treatment protocols. The integration of wearable technology and digital biomarkers could enhance objectivity in tracking physiological and behavioral progress, reducing reliance on self-reported data. Longitudinal studies are essential to evaluate the long-term sustainability of interventions and relapse rates, offering a clearer understanding of lasting efficacy. Additionally, future research should expand outcome measures beyond symptom reduction to include cost-effectiveness analyses from both societal and healthcare perspectives, ensuring interventions are not only clinically effective but also economically viable. Addressing these areas will strengthen the evidence base, inform clinical practice, and improve patient outcomes across diverse settings. Such advancements will pave the way for more personalized, scalable, and sustainable mental health interventions.

Clinical and Policy Implications

This meta-analysis and previous studies emphasize the need for non-pharmacological interventions in expanding options for depression treatment. Although drugs remain a cornerstone, their application can be supplemented by cognitive-behavioral therapy (CBT), exercise, and digital treatment to make treatment more patient-centered and individualized. Healthcare systems need to invest in programs that bundle exercise therapy with primary care to make structured physical activity accessible to patients. In addition, increasing training in blended CBT that combines conventional and digital modalities can increase scalability and effectiveness. Increased access to nature and community-based therapies should also be promoted because these therapies address social determinants of mental illness. From a policy perspective, insurance coverage and public health programs coverage of such evidence-based therapies need to be addressed to reduce treatment disparities. By acknowledging and reimbursing non-drug alternatives, policymakers can promote bridging gaps in care, improving patient outcomes, and reducing long-term healthcare costs of chronic depression. The shift toward integrative, patient-level models will not only increase treatment effectiveness but also become part of larger efforts that work towards creating sustainable, accessible mental health care systems.

CONCLUSION

This meta-analysis gives strong evidence that non-pharmacological treatments can be of great benefit to depressed adults. The study found that therapies like exercise therapy, counselling, and nature therapy yielded small but significant decreases in symptoms. Exercise worked best overall, while other interventions like online therapy were more variable. These treatments are especially helpful for those who cannot afford to take medication or are resistant to it. Although the effect might seem small at first, these treatments give patients more choices and can be combined with traditional treatments. The findings suggest that physicians and healthcare systems must make these therapies more widely available, especially exercise programs that had the most consistent results. Additional research is needed, however, to know how well they perform in the long term and for different groups of people. Because depression affects millions of people worldwide, these non-pharmacological treatments offer safe, flexible, and low-cost alternatives. Governments and healthcare providers must invest in training, programs, and insurance coverage to make these treatments available to more people. By adding medication to exercise, therapy, and other wellness-oriented alternatives, we can achieve a more balanced and individualized approach to mental health care. Future studies should focus on making these programs more effective in real-world environments, especially for those with limited access to healthcare.

Authors Contribution:

Anushika Sharma, Diksha: Conceptualization, Methodology, Writing Original Draft, Writing Review and Editing, Resources, Investigation. **Mallesh Mandha:** Conceptualization, Supervision, Formal Analysis, Review and Validation.

Acknowledgments: None

Conflict of Interest: None

Table no. 4: Comprehensive Meta-Analysis

Study Title	Intervention Type	Effect Size (SMD)	95% CI Lower	95% CI Upper	Standard Error	LOO Pooled SMD	LOO 95% CI Lower	LOO 95% CI Upper	Fixed-Effects Weight	Random-Effects Combined SMD	Random-Effects 95% CI Lower	Random-Effects 95% CI Upper	I¬≤ (%)	Tau¬≤	Q Statistic	Degrees of Freedom	Publication Bias (Egger's Test p-value)	Subgroup Pooled SMD
Birnbaumer et al. (2024)	Exercise-Based	-0.3	-0.5	-0.1	0.10204082	-0.258	-0.361	-0.156	96.04	-0.2659	-0.3951	-0.1368	48.1	0.0103	7.71	4	0.896	-0.39
Coventry et al. (2013)	Exercise-Based	-0.47	-0.66	-0.28	0.09693878	-0.206	-0.31	-0.102	106.415512	-0.2659	-0.3951	-0.1368	48.1	0.0103	7.71	4	0.896	-0.39
Wahrborg et al. (2014)	Nature-Assisted	-0.2	-0.38	-0.02	0.09183673	-0.29	-0.397	-0.184	118.567901	-0.2659	-0.3951	-0.1368	48.1	0.0103	7.71	4	0.896	-0.2
Kooistra et al. (2019)	Digital CBT	-0.1	-0.3	0.1	0.10204082	-0.311	-0.414	-0.208	96.04	-0.2659	-0.3951	-0.1368	48.1	0.0103	7.71	4	0.896	-0.1
Richards et al. (2018)	Psychosocial Rehab	-0.25	-0.55	0.05	0.15306122	-0.269	-0.365	-0.173	42.6844444	-0.2659	-0.3951	-0.1368	48.1	0.0103	7.71	4	0.896	-0.25

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