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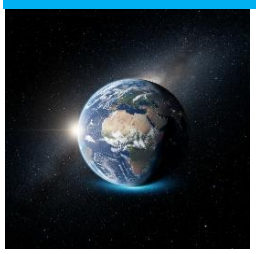

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Physical Activity in the Prevention and Treatment of Depression and Anxiety Disorders: A Narrative Literature Review

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Abstract

Background. Depression and anxiety represent a massive global health burden. Because standard pharmacotherapy and psychotherapy often exhibit clinical limitations, there is a need

for a multidisciplinary approach. In this context, physical activity serves as an effective complementary strategy.

Aim. The aim of this study was to synthesize current literature regarding the impact of physical activity on the prevention and treatment of depression and anxiety disorders.

Material and methods. A narrative literature review search of PubMed and Google Scholar was conducted to retrieve high-quality evidence, including meta-analyses, systematic reviews, and randomized controlled trials published between 2015 and 2026.

Results. Evidence suggests that exercise interventions may produce symptom reductions comparable to those reported in some pharmacotherapy trials. The benefits follow a "some is better than none" principle, where even low volumes of exercise significantly reduce psychiatric symptoms. These protective and therapeutic effects are driven by a dual mechanism. Neurobiological adaptations, such as Brain-Derived Neurotrophic Factor (BDNF) upregulation and reduced inflammation, work alongside psychosocial improvements.

Conclusions. Physical activity is a robust, evidence-based intervention. Therefore, clinicians should integrate the "Exercise as Medicine" framework into psychiatric care. Furthermore, future research should prioritize longitudinal designs and protocols to effectively overcome motivational barriers.

Key words: physical activity; depression; anxiety; exercise as medicine; neurobiology.

1. Introduction

Mental disorders are highly prevalent and represent a significant global health challenge. According to recent estimates, approximately 12% of the global population lives with a mental disorder, accounting for roughly 5% of disability-adjusted life years (DALYs) and 16% of years lived with disability worldwide [1,2]. Depression, in particular, is recognized as a leading cause of disability globally [3]. The burden of these conditions has been further exacerbated by the COVID-19 pandemic, with World Health Organization (WHO) estimates indicating a 25% increase in the prevalence of anxiety and depression during the first year of the pandemic [4].

Despite the widespread nature of these conditions, standard treatments such as pharmacotherapy and psychotherapy face significant limitations. While antidepressants and antipsychotics remain frontline strategies, they often fail to result in clinically meaningful improvement for a substantial proportion of patients, and long-term remission rates remain suboptimal [2, 5]. Furthermore, pharmacological interventions are frequently associated with adverse side effects, including weight gain and metabolic disturbances, which can lead to treatment discontinuation [6]. Accessibility is another critical barrier. Estimates suggest that only 10% to 25% of individuals with depression seek therapy, often due to financial costs, a scarcity of trained professionals, and social stigma [3]. In the context of addressing these

challenges, it is essential to distinguish between general activity and specific interventions. Physical Activity (PA) is defined as any bodily movement produced by skeletal muscles that requires energy expenditure, encompassing daily tasks, work, and leisure activities [1, 4]. In contrast, "Exercise" is defined specifically as a subset of physical activity that is planned, structured, and repetitive, with the specific objective of improving or maintaining physical fitness [2]. This distinction is important for evaluating clinical interventions, as structured exercise allows for dosage and intensity control similar to medical treatments.

Consequently, there is growing support for the concept of "Exercise as Medicine" within psychiatry. Physical activity is increasingly recognized as a cost-effective, accessible, and "transdiagnostic" intervention capable of preventing onset and managing symptoms across a spectrum of disorders, from depression to schizophrenia [1, 2]. Clinical guidelines are beginning to position lifestyle factors, including exercise, smoking cessation, and diet, as "step zero" targets to be addressed prior to or alongside pharmacotherapy [5].

The aim of this study is to synthesize current literature regarding the impact of physical activity on the prevention and treatment of depression and anxiety disorders, with a particular focus on underlying neurobiological mechanisms, dose-response relationships, and clinical implementation.

2. Materials and methods

A literature review search was conducted to identify relevant studies investigating the therapeutic and preventive role of physical activity in mental health disorders. Electronic databases, including PubMed/MEDLINE and Google Scholar, were queried to ensure comprehensive coverage of the available evidence. Based on. The search strategy specifically covered the period from 2015 to 2026, with particular emphasis placed on recent literature published between 2020 and 2026 to capture the most up-to-date clinical data, epidemiological statistics and neurobiological models. The following English keywords and their combinations were employed during the search process: "physical activity", "exercise therapy", "mental health", "depression", "anxiety", "neuroplasticity", "BDNF", and "inflammation". Initially, approximately 56 relevant articles were identified and screened based on thei titles and abstracts. Studies were subsequently evaluated for full-text eligibility. Exclusion criteria included publication dates prior to 2020, lack of direct relevance to the research questions, absence of quantitative data on clinical efficacy or mechanistic pathways, and publication in languages other than English. Priority was given to high-quality evidence, specifically umbrella reviews, systematic reviews and meta-analyses. Following this rigorous selection process, a total of 37 peer-reviewed articles met all inclusion criteria and were incorporated into the final narrative review.

3. Current state of knowledge

3.1. Prevention

Large-scale longitudinal research has indicated an inverse relationship between habitual physical activity and the risk of developing mental disorders. A comprehensive systematic review and meta-analysis by Pearce et al., which included over 190,000 participants, reported that individuals with higher levels of physical activity have significantly lower odds of developing depression compared to those with lower levels [7]. The authors estimated that 11.5% of incident depression cases could potentially be prevented if less active adults achieved current physical activity recommendations [7]. Furthermore, the research indicates that individuals with the highest levels of physical activity have approximately 17% lower odds of developing depression compared with those who are least active, supporting the hypothesis that sedentary behavior may be an independent risk factor for the onset of psychiatric conditions [8].

Regarding the dose-response relationship, recent findings appears to challenge the assumption that high volumes of vigorous exercise are required for protective effects. Pearce et al. identified an inverse curvilinear association between physical activity volume and depression risk, with the steepest gradients of risk reduction observed at the lower end of the activity spectrum [7]. Specifically, accumulating just half the recommended weekly volume of physical activity was associated with an 18% reduction in the risk of depression compared to no activity [7]. While engaging in the full recommended dose (equivalent to 2.5 hours of brisk walking per week) was linked to a 25% lower risk, the additional benefits appeared to diminish at volumes exceeding these levels. This suggests that a highly critical preventative intervention may be the initial transition from inactivity to some activity rather than necessarily the pursuit of high-intensity athletic training [7, 8].

In the general adult population (aged 18–64), physical activity is thought to act as a valuable buffer against daily life stress and occupational burnout. Recent reviews indicate that physical activity interventions in workplace are associated with significant reductions in stress levels and emotional exhaustion, thereby potentially enhancing overall employee resilience [8, 9]. Specifically, Leisure-Time Physical Activity (LTPA) has been highlighted as a robust protective factor. Prospective data synthesized by White et al. suggest that engagement in LTPA may facilitate “psychological detachment” from work, helping individuals to disconnect from professional stressors and reduce the cognitive burden of rumination [10]. While these benefits are pronounced in working-age adults, this protective effect seems to persist into later life, where regular activity is considered important for supporting cognitive functioning and mitigating the risk of age-related psychiatric conditions [8].

Consequently, health education emphasizing lifestyle modification, including regular physical activity, is recommended as a routine component of mental health prevention efforts [11].

3.2. Depression treatment

Some studies suggest physical activity as a potential treatment strategy for major depressive disorder (MDD), comparing it with standard first-line interventions. A recent comprehensive meta-analysis indicated that when compared to non-active controls, exercise interventions yield large effect sizes (SMD=−0.95) in reducing depressive symptoms, with a number needed to treat (NNT) of 2, suggesting it could be a potent therapeutic option [12]. Furthermore, studies have directly compared the efficacy of structured exercise against antidepressant pharmacotherapy. A 16-week trial by Verhoeven et al. comparing running therapy to antidepressant medication (escitalopram or sertraline) found no significant difference in remission rates (43.3% vs. 44.8%, respectively). These findings suggest that structured exercise may serve as a viable alternative to pharmacotherapy in managing symptoms for specific patients with depression and anxiety disorders [13]. It appears that exercise interventions may achieve symptom reduction comparable to pharmacotherapy in selected populations, although the evidence base continues to evolve.

The clinical application of physical activity varies depending on the severity of the condition, potentially functioning either as a monotherapy or an adjunctive treatment. For mild-to-moderate depression, exercise is increasingly being considered as a viable monotherapy or alternative to medication, particularly for patients who may refuse or not tolerate pharmacotherapy [8, 13]. In contrast, for moderate-to-severe or treatment-resistant depression, physical activity is frequently recommended as an adjunctive therapy. Research by Imboden et al. involving inpatients with moderate-to-severe depression demonstrated that adding structured aerobic exercise to standard inpatient care (medication and psychotherapy) was associated with significant symptom alleviation. Additionally, it has been observed to improve cognitive domains such as working memory, which standard treatments often fail to address [14]. Thus, exercise appears to serve a versatile role across the spectrum of depressive severity, potentially enhancing outcomes when integrated into multimodal treatment plans [15, 16].

Regarding the modality of exercise, both aerobic and resistance training have demonstrated significant efficacy in treating depression. While aerobic exercise is the most extensively researched modality, a major systematic review by Heissel et al. supported its beneficial effects[12]. However, resistance training (RET) also appears to be highly effective. A recent trial by O'Sullivan et al. reported large-magnitude reductions in depressive symptoms, even among young adults with subclinical or mild depression [17] Moreover, a 2025 systematic review and meta-analysis by Banyard et al. comparing these modalities found no statistically significant difference in their efficacy [18]. Consequently, current evidence supports the recommendation of either aerobic or resistance exercise (or a combination), emphasizing that

patient adherence to the chosen activity is likely more critical for clinical benefit than the specific mode itself [15, 18].

3.3. Anxiety disorders and stress

The anxiolytic effects of physical activity are well-documented, with current literature suggesting they occur through both acute and chronic mechanisms that help regulate the body's physiological response to stress. A single bout of exercise has been observed to provide an immediate reduction in state anxiety and tension, often described as a "time-out" effect that may distract from rumination and help reset emotional regulation. Biologically, acute bouts of physical activity are thought to moderate stress systems by significantly influencing the hypothalamic-pituitary-adrenal (HPA) axis. Specifically, exercise has been associated with substantial increases in circulating levels of atrial natriuretic peptide, which inhibits HPA axis activity, thereby potentially blunting the physiological manifestation of stress [19, 20]. Furthermore, mind-body interventions such as yoga have been linked to increased parasympathetic activity (vagal tone) and elevated thalamic gamma-aminobutyric acid (GABA) levels, which are proposed to contribute to immediate improvements in mood and reductions in state anxiety [21].

In the context of specific clinical diagnoses, physical activity has demonstrated potential efficacy in the management of Generalized Anxiety Disorder (GAD) and other anxiety-related conditions. Evidence from randomized controlled trials indicates that resistance exercise training (RET) appears to be effective for young adults with GAD, with significant reductions in worry symptoms observed after eight weeks of intervention [22]. Furthermore, a comprehensive umbrella review by Singh et al. established that physical activity yields medium effect sizes in reducing anxiety symptoms across a wide range of adult populations, including those with diagnosed anxiety disorders [23]. Expanding on this, recent meta-analytic data by Banyard et al. suggests even stronger effects specifically for resistance and mixed-mode exercise in diagnosed anxiety populations [18]. While all modalities of physical activity, including aerobic, resistance, and mind-body exercises, are considered beneficial, recent data suggest that higher-intensity interventions might be more effective than low-intensity regimens [22, 23]. This is likely because high-intensity exercise induces physiological sensations similar to the anxiety (e.g., rapid heart rate, breathlessness), functioning as a form of 'interoceptive exposure'. This process is believed to help patients habituate to physiological arousal, potentially reducing their fear of somatic symptoms [24].

Beyond therapeutic interventions, physical activity serves as a potential protective buffer for individuals exposed to significant life stressors and trauma. A systematic review by Wang et al. focusing on individuals exposed to major traumatic events revealed that physical activity is positively correlated with mental resilience and subjective well-being, while being

negatively correlated with post-traumatic stress symptoms [25]. Regular engagement in physical activity appears to foster self-efficacy and a more optimistic mood, thereby potentially enhancing the individual's capacity to cope with future stressors. Consequently, physical activity is increasingly regarded as a valuable adjunctive measure and a important component of psychological intervention strategies for maintaining mental health under conditions of high stress [25].

3.4. Mechanisms

The Neurotrophic Hypothesis of depression posits that the disorder is associated with neuronal atrophy and reduced synaptic plasticity, particularly in the hippocampus and prefrontal cortex. This deficit may be partially reversed by regular physical activity through the upregulation of Brain-Derived Neurotrophic Factor (BDNF). Current models suggest that exercise triggers a peripheral-central signaling cascade. Skeletal muscle contraction releases myokines, such as irisin (cleaved from FNDC5) and cathepsin B, which are hypothesized to cross the blood-brain barrier to stimulate central BDNF expression [26, 27]. Upon binding to its receptor, Tropomyosin receptor kinase B (TrkB), BDNF activates intracellular signaling pathways, specifically the PI3K/Akt and MAPK/ERK pathways, which are crucial for cell proliferation, survival, and long-term potentiation [27, 28]. Structurally, it is widely theorized that this molecular cascade manifests as increased hippocampal volume. Longitudinal studies suggest that aerobic training can offset age-related hippocampal atrophy by 1-2% annually, preserving gray matter density in regions essential for mood regulation and memory [29, 30]. Furthermore, recent transcriptomic analyses in animal models indicate that exercise also modulates the Wnt5a/CamkII pathway, activating autophagy in hippocampal neurons to remodel synaptic structures and enhance plasticity [31].

Complementing neuroplastic changes, the Inflammatory Hypothesis suggests that physical activity functions as a systemic anti-inflammatory intervention, counteracting the systemic low-grade chronic inflammation (SLGCI) observed in approximately one-third of patients with depression. Chronic stress and sedentary behavior elevate pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1 β (IL-1β), which can permeabilize the blood-brain barrier and induce neuroinflammation [32, 33]. Evidence indicates that regular physical activity can reduce these basal inflammatory markers and promote the release of anti-inflammatory mediators like IL-10 [32, 34]. A critical mechanism within this hypothesis involves the kynurenine pathway. Inflammation typically diverts tryptophan toward the production of neurotoxic kynurenine metabolites (e.g., quinolinic acid). Translational studies suggest that exercise enhances the expression of kynurenine aminotransferase (KAT) in skeletal muscle, which converts kynurenine into kynurenic acid.

Given its limited ability to cross the blood-brain barrier, the process is believed to effectively protect the brain from stress-induced neurotoxicity [26, 33].

Finally, physical activity exerts a significant modulatory effect on monoamines, addressing the classic targets of pharmacological antidepressants: serotonin (5-HT), dopamine, and norepinephrine. Exercise is thought to increase the bioavailability and synthesis of these neurotransmitters, enhancing communication between brain regions implicated in emotional processing [35]. Novel circuit-level analyses in preclinical models have identified a specific "tri-synaptic pathway" linking motor activity to mood regulation. In this models, exercise activates neurons in the gracile nucleus (GR), which project directly to the dorsal raphe nucleus (DRN), stimulating serotonergic neurons that subsequently innervate the medial prefrontal cortex (mPFC) [36]. Preclinical models in mice suggest a link between motor activity and forebrain serotonergic release, alleviating depressive-like behaviors [36]. Additionally, exercise appears to modulate the dopaminergic reward system (Ventral Tegmental Area to Nucleus Accumbens), potentially improving reward sensitivity and alleviating anhedonia, a core symptom of depression often resistant to standard medication [27, 29]. However, it is important to note that while these mechanistic pathways are strongly supported by preclinical data, their exact translation to human clinical populations remains an active area of ongoing research.

4. Discussion

The synthesis of the reviewed literature positions physical activity as a broad-spectrum intervention potentially affecting multiple pathways. Recent reviews indicate that exercise can effectively reduce disease-specific symptoms across a wide spectrum of disorders, including depression and anxiety. By simultaneously targeting neurobiological mechanisms, such as Brain-Derived Neurotrophic Factor (BDNF) expression and systemic inflammation, exercise appears to bridge the gap between traditional medical treatments and psychosocial therapies [1, 30]. Current evidence suggest that effect sizes for exercise in Major Depressive Disorder (MDD) are comparable to those of standard pharmacotherapy and psychotherapy. This positions physical activity as far more than a simple lifestyle recommendation. Rather, it may serve as a viable monotherapy for mild-to-moderate cases and a important adjunctive strategy for severe or treatment-resistant presentations [12, 13].

Regarding clinical prescription, adherence to World Health Organization guidelines, recommending 150–300 minutes of moderate-intensity activity per week, is generally considered ideal for maximal health benefits. However, current evidence strongly supports a "some is better than none" principle for mental health. Dose-response meta-analyses indicate that accumulating just half of the recommended volume can yield significant protective effects against depression. Moreover, curvilinear associations suggest diminishing returns at very high volumes [7]. Therefore, it is suggested that the clinical priority could shift from enforcing high-

intensity athletic training to ensuring consistency. A primary goal might be facilitating the transition from complete sedentary behavior to any form of regular movement, as both aerobic and resistance modalities demonstrate robust efficacy [15, 18].

Despite this potential, the implementation of exercise interventions faces significant barriers inherent to the symptomatology of mental disorders. Patients with MDD or chronic anxiety frequently experience anhedonia, fatigue, and profound volitional deficits. These symptoms can render self-directed exercise regimens ineffective or unsustainable [2]. To overcome these motivational hurdles, the literature emphasizes the importamce of supervised, structured interventions delivered by qualified professionals, such as physiotherapists or exercise physiologists, rather than simple advice to "exercise more" [12, 20]. Group-based settings can further enhance adherence by providing social scaffolding. Additionally, initiating treatment with low-intensity activities helps build self-efficacy before progressing to higher intensities. [17].

Finally, the interpretation of current evidence should account for methodological limitations of this review and the challenges intrinsic to exercise research. As a narrative synthesis restricted to English-language publications from 2020 to 2026, the potential for selection bias exists. Unlike pharmacological trials, double blinding is impossible in exercise interventions. This limitation can potentially inflate effect sizes due to participant expectancy and the lack of inert placebos [14, 37]. Furthermore, substantial heterogeneity exists across study protocols regarding the type, duration, and frequency of exercise, which complicates the formulation of precise prescriptions [18]. Additionally, many neurobiological mechanisms rely on preclinical models requiring human validation. This highlights an urgent need for future research to determine how physical activity habits can be sustained independently to prevent relapse [1, 20].

5. Conclusions

The comprehensive synthesis of current evidence indicates that physical activity can be an effective intervention for both the prevention and treatment of depression and anxiety. Its therapeutic efficacy appears to be mediated through dual neurobiological mechanisms, such as the upregulation of Brain-Derived Neurotrophic Factor, alongside psychosocial improvements. Furthermore, current data support a "some is better than none" paradigm, indicating that even low volumes of activity yield significant mental health benefits. Consequently, the "Exercise as Medicine" framework should be considered as a part of integrated psychiatric care. To optimize this integration, future research should prioritize longitudinal designs to assess long-term maintenance and relapse prevention. Additionally, developing personalized protocols to effectively overcome motivational barriers in clinical populations represents a key area for future investigation.

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Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used large language models (e.g. Gemini / NotebookLM) in order to improve English language, readability, and text formatting. After using this tool/service, the authors thoroughly reviewed and edited the content as needed and take full and sole responsibility for the final content of the publication.

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