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Physical activity as a component of depression therapy: Narrative Review

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Abstract

Introduction and purpose: Depression is a common and disabling mental disorder associated with impaired quality of life, reduced social and occupational functioning, and increased mortality. Growing evidence indicates that lifestyle-related factors, including physical activity, may influence both the risk and course of depressive disorders. The aim of this narrative review is to evaluate the current evidence regarding the role of physical activity as a supportive component in the prevention and treatment of depression.

Brief description of the state of knowledge: The available literature suggests that exercise may reduce depressive symptoms through several interacting biological and psychosocial mechanisms. These include modulation of neurotransmitter systems, improvement of neuroplasticity and brain-derived neurotrophic factor activity, regulation of the hypothalamic-pituitary-adrenal axis, and reduction of chronic low-grade inflammation. Aerobic exercise remains the most widely studied modality, but resistance training, combined exercise programs, yoga, and mind-body interventions have also shown beneficial effects in various populations. Evidence from cohort

studies additionally supports a preventive association between regular physical activity and lower risk of incident depression.

Summary: Physical activity should not be considered a universal replacement for pharmacotherapy or psychotherapy, particularly in severe depression. However, it may represent a valuable adjunctive strategy within comprehensive and individualized mental health care. Further research is needed to define optimal exercise parameters, improve adherence, and clarify the mechanism of action of physical activity on patients with depression in different clinical populations.

Key words: depression; physical activity; exercise therapy; mental health; lifestyle medicine

1. Introduction

Depression is currently recognized as one of the most significant public health challenges worldwide. It affects individuals of all age groups and contributes substantially to disability, impaired quality of life, social dysfunction and increased mortality. In recent years, the global burden associated with depressive disorder has continued to rise, making depression one of the leading causes of years lived with disability [1]. Beyond emotional suffering, depression negatively influences cognitive functioning, interpersonal relationships, occupational performance, and overall daily functioning. In severe cases, it may lead to self-harm and suicide, which remains one of the most common causes of death among adolescents and young adults. Despite the availability of pharmacological and psychotherapeutic interventions, a considerable proportion of patients either do not receive adequate treatment or fail to achieve full remission of symptoms.

The etiology of depression is complex and multifactorial. Contemporary evidence no longer supports the simplified concept of depression as solely the result of serotonin deficiency. Instead, current research suggests that depressive disorders arise from the interaction of numerous biological, psychological, and environmental factors. Dysregulation of neurotransmitter systems, including serotonin, dopamine, and norepinephrine, is considered important, but growing attention is also being paid to abnormalities involving glutamatergic signaling, gamma-aminobutyric acid (GABA), the hypothalamic-pituitary-adrenal (HPA) axis, neuroplasticity, inflammatory pathways, and brain-derived neurotrophic factor (BDNF) [2,3,4,5]. Additionally, chronic stress, social adversity, loneliness, and early-life trauma may contribute to the development of depression through long-term neurobiological and epigenetic changes [6,7].

Recent studies in psychoneuroimmunology and social neuroscience have further expanded understanding of the relationship between mental health and physiological functioning. Depression is increasingly associated with chronic low-grade inflammation, immune dysregulation, and disturbances in endocrine and metabolic processes. Elevated concentrations of inflammatory cytokines and markers such as C-reactive protein have been observed in many patients with depressive disorders. At the same time, prolonged psychosocial stress may activate inflammatory pathways and contribute to maladaptive neurobiological responses [2,3,8]. This bidirectional relationship between psychological experiences and biological processes supports the concept that depression should be understood as a systemic condition affecting both the brain and the body.

Lifestyle-related factors have become an important area of interest in depression research and treatment. Among these factors, physical activity appears to play a particularly significant role. Sedentary behavior and insufficient physical activity are increasingly recognized as modifiable risk factors associated with poorer mental health outcomes, including an increased risk of depressive symptoms [9,10]. Contrawise, regular physical activity has been associated with reduced incidence of depression as well as improvement in depressive symptoms among affected individuals. Importantly, beneficial effects have been observed across different age groups and clinical populations [11,12,13,14].

The antidepressant effects of physical activity are believed to result from the interaction of multiple biological and psychological mechanisms. Exercise has been shown to influence neurotransmitter availability, stimulate neuroplasticity, regulate the HPA axis, and reduce inflammatory activity [15]. Physical activity may also increase BDNF expression, which is involved in neuronal survival, synaptic plasticity, learning, and emotional regulation [5,16]. In addition to these neurobiological mechanisms, exercise contributes to improved self-esteem, enhanced self-efficacy, better stress management, and reduced social isolation. Group physical activity may additionally strengthen social connectedness and emotional support, both of which are important in individuals experiencing depressive symptoms.

Numerous clinical trials, systematic reviews, and meta-analyses indicate that physical activity may significantly reduce depressive symptoms, particularly in patients with mild to moderate depression [14,17,18,19,20]. Some studies suggest that the therapeutic effects of exercise may be comparable to those observed with standard treatments under specific conditions, especially when interventions are supervised and performed regularly. Aerobic exercise remains the most extensively studied form of activity; however, resistance training, combined exercise programs, yoga, and mind-body interventions have also demonstrated beneficial effects on mood and mental wellbeing [17,21,22,23,24,25]. Evidence additionally suggests that even relatively low levels of physical activity may provide protective effects against the development of depression, highlighting the importance of promoting movement as part of preventive health strategies [11].

Although the growing body of evidence supporting exercise in depression therapy is promising, several limitations remain. Considerable heterogeneity exists between studies regarding exercise protocols, intervention duration, intensity, patient characteristics, and methodological quality [14,17,21,26]. Furthermore, adherence to exercise programs may be particularly challenging in individuals with severe depressive symptoms, fatigue, or coexisting somatic conditions. Therefore, physical activity should not be viewed as a universal replacement for conventional treatment but rather as a potentially valuable component of comprehensive and individualized depression management.

Given the increasing prevalence of depression and the growing interest in lifestyle medicine, further evaluation of the therapeutic role of physical activity appears justified. Understanding the biological and psychological mechanisms underlying the antidepressant effects of exercise may contribute to the development of more effective, accessible, and holistic treatment strategies for patients with depressive disorders.

The aim of this narrative review is to evaluate the current evidence regarding the role of physical activity as a supportive component in the prevention and treatment of depression. The study aims to analyze the effects of different forms of exercise on depressive symptoms, discuss the neurobiological and psychological mechanisms underlying the antidepressant effects of physical activity, and assess the potential clinical significance of exercise

interventions in individuals with depressive disorders. Particular attention is given to the relationships between physical activity, neuroplasticity, inflammation, stress regulation, and psychosocial functioning, as well as to the effectiveness of aerobic exercise, resistance training, and mind-body interventions in various populations. Additionally, this review seeks to summarize current recommendations concerning exercise prescription in depression therapy and to identify the main limitations and future directions of research in this field.

2. Description of the state of knowledge

2.1. Methodology of literature selection

This study was conducted as a narrative review aimed at evaluating the current evidence regarding the role of physical activity in the prevention and supportive treatment of depression. A structured literature search was performed using electronic scientific databases, primarily PubMed, as well as additional sources including Scopus, Web of Science, and Google Scholar, to identify relevant publications related to physical activity, exercise interventions, depression, neurobiological mechanisms, and lifestyle medicine. The search included articles published in English between 2015 and 2026, with emphasis placed on systematic reviews, meta-analyses, randomized controlled trials, prospective cohort studies, and clinically relevant narrative reviews. Earlier publications were additionally included when considered foundational or highly influential for understanding the biological and psychological mechanisms associated with depression and exercise. The search strategy was based on combinations of keywords and Medical Subject Headings (MeSH) terms such as “depression,” “major depressive disorder,” “physical activity,” “exercise,” “exercise therapy,” “aerobic exercise,” “resistance training,” “mental health,” “BDNF,” “inflammation,” “neuroplasticity,” “psychoneuroimmunology,” and “lifestyle medicine,” combined using Boolean operators. Publications were selected according to their relevance to the topic, methodological quality, and contribution to the understanding of the relationship between physical activity and depressive symptoms. Particular attention was given to studies investigating the antidepressant effects of exercise, dose-response relationships, neurobiological pathways, psychophysiological mechanisms, and the effectiveness of different exercise modalities in various populations. Articles focused exclusively on pharmacological treatment without reference to physical activity or lifestyle-related interventions, conference abstracts without full-text availability, duplicate studies, and publications unrelated to depressive disorders were excluded from the review. The collected literature was analyzed descriptively and narratively to provide a comprehensive overview of current evidence concerning the therapeutic and preventive role of physical activity in depression.

2.2. Neurobiological and psychoneuroimmunological mechanisms

Depression involves complex neurobiological, endocrine, immune, and psychosocial mechanisms. In this context, psychoneuroimmunology helps explain how chronic stress and adverse environmental experiences may contribute to the development and persistence of depressive symptoms [2,3,27].

One of the central biological systems involved in depression is the hypothalamic-pituitary-adrenal (HPA) axis, which regulates the physiological stress response. Lasting psychological stress may lead to persistent activation of the HPA axis and excessive secretion of cortisol [3,4]. In many individuals with depressive disorders, hyperactivity of this system has been associated with impaired emotional regulation, cognitive dysfunction, sleep disturbances, and structural changes within brain regions involved in mood regulation, particularly the hippocampus and

prefrontal cortex. Chronic exposure to elevated glucocorticoid levels may additionally impair neurogenesis and reduce neuronal resilience, thereby contributing to the progression of depressive symptoms over time.

Growing evidence also suggests that inflammation plays a significant role in the pathogenesis of depression. Increased concentrations of pro-inflammatory cytokines, including interleukin-6, tumor necrosis factor alpha and C-reactive protein, have been observed in many patients with depressive disorders. Importantly, inflammatory mediators may influence central nervous system functioning through several mechanisms, including alterations in neurotransmitter metabolism, reduced synaptic plasticity, disturbances in glutamatergic signaling, and activation of microglial cells [3,8]. This has led to the development of inflammatory models of depression, according to which chronic low-grade inflammation may contribute not only to emotional symptoms but also to fatigue, anhedonia, psychomotor slowing, and cognitive impairment commonly observed in depressive states.

Brain-derived neurotrophic factor (BDNF) is another important component in the neurobiology of depression. BDNF is involved in neuronal survival, synaptic plasticity, learning, and memory processes. Reduced BDNF expression has been associated with impaired neuroplasticity and structural brain changes observed in depressive disorders, particularly within the hippocampus. Experimental and clinical studies suggest that stress-related reductions in BDNF signaling may contribute to vulnerability to depression, whereas restoration of neuroplasticity appears to be associated with symptom improvement [5]. These findings support the hypothesis that impaired neuronal adaptability represents one of the key mechanisms underlying depressive pathology.

Psychosocial stressors and adverse life experiences additionally appear to influence depression through epigenetic mechanisms. Chronic stress, loneliness, social isolation, and early-life adversity may induce long-term biological changes affecting gene expression, inflammatory regulation, and stress responsiveness. Research in social genomics and psychoneuroimmunology indicates that environmental experiences may become biologically embedded, contributing to persistent dysregulation of immune and neuroendocrine systems [6,7,27]. This perspective highlights the dynamic relationship between psychological experiences and physiological functioning and supports the concept that depression should be viewed as a systemic disorder rather than an isolated disturbance of brain chemistry alone.

Physical activity appears to influence many of the biological pathways associated with depression. Regular exercise has been shown to modulate neurotransmitter systems, increase BDNF availability, improve neuroplasticity, regulate HPA axis activity, and reduce inflammatory processes [15,16]. Exercise may additionally improve mitochondrial functioning, cerebral blood flow, and metabolic regulation, all of which may contribute to improved mental functioning and emotional stability. Importantly, the effects of physical activity are not limited to neurobiological changes alone. Exercise is also associated with psychological benefits, including improved self-efficacy, reduced rumination, enhanced stress coping, and increased social interaction, particularly in group activities [13,14,17]. Therefore, the antidepressant effects of physical activity are likely to result from the interaction of multiple biological and psychosocial mechanisms rather than from a single isolated process.

Current evidence suggests that these mechanisms may partially explain why physically active individuals demonstrate lower risk of developing depression. Nevertheless, the exact interactions between neurobiological, inflammatory, psychological, and behavioral factors remain incompletely understood. Further research is needed to clarify the mechanisms through which physical activity exerts its therapeutic effects and to determine which forms and intensities of exercise may be most beneficial for specific patient populations.

2.3. Physical activity as prevention of depression

In addition to its therapeutic role in individuals with diagnosed depressive disorders, physical activity appears to play an important role in the prevention of depression. Over the past decade, growing evidence from large prospective cohort studies and metanalyses has demonstrated that physically active individuals present a lower risk of developing depressive symptoms compared with individuals characterized by sedentary lifestyle and insufficient levels of movement [11,12]. This relationship has been observed across different age groups, including adolescents, adults, and older populations, suggesting that the protective effects of physical activity may be relatively universal and not limited to specific demographic groups. Importantly, preventive benefits have been reported in both healthy individuals and populations exposed to increased psychological stress or chronic somatic diseases.

Several mechanisms may explain the protective influence of physical activity against the onset of depression. Regular exercise contributes to the regulation of stress-response systems, particularly the HPA axis, reducing the physiological consequences of chronic stress exposure. At the same time, physical activity appears to improve neuroplasticity, support neurotransmitter balance, and decrease systemic inflammation, all of which are considered important factors in the pathophysiology of depressive disorders. Exercise may additionally influence sleep quality, metabolic health, and cardiovascular functioning, indirectly supporting mental wellbeing and emotional resilience. From a psychological perspective, physically active individuals often report higher levels of self-esteem, greater self-efficacy, improved stress management, and better social functioning, which may further reduce vulnerability to depressive symptoms.

An important observation emerging from epidemiological studies is the existence of a dose-response relationship between physical activity and depression risk. Higher levels of regular activity are generally associated with lower incidence of depressive disorders; however, current evidence also suggests that even relatively small amounts of exercise may provide measurable mental health benefits. In some studies, levels of physical activity below standard public health recommendations were still associated with reduced risk of depression compared with complete inactivity [11]. These findings are particularly important from a public health perspective, as they indicate that promoting moderate and achievable forms of movement may still contribute to the meaningful improvements in mental health outcomes.

The preventive effects of physical activity have also gained attention in the context of modern lifestyle related challenges. Sedentary behavior, prolonged screen exposure, reduced social interaction, chronic stress, and sleep disturbances have become increasingly common in contemporary societies and are considered important contributors to worsening mental health. This issue became especially visible during the COVID-19 pandemic, when social isolation and reduced opportunities for movement were associated with increased prevalence of depressive symptoms in many populations, particularly among adolescents and university students [28]. In this context, regular physical activity may represent not only a therapeutic strategy but also an accessible and relatively low-cost preventive intervention supporting psychological resilience during periods of increased stress and social disruption.

2.4. Exercise as treatment for depression

A growing body of evidence indicates that physical activity may represent an effective supportive intervention in the treatment of depression. Over the last two decades, numerous randomized controlled trials, systematic reviews, and meta-analyses have evaluated the impact of exercise on depressive symptoms, with most studies demonstrating beneficial effects of regular physical activity on mood, emotional functioning, and overall mental wellbeing. Although the magnitude of these effects varies between studies, current evidence generally supports the view that exercise may contribute to clinically meaningful reductions in depressive symptoms, particularly in individuals with mild to moderate depression [14,17,18,19]. Importantly, positive outcomes have been observed in both general population and patients with clinically diagnosed depressive disorders.

Aerobic exercise remains the most extensively investigated form of physical activity in depression treatment. Activities such as walking, jogging, cycling, and swimming have consistently been associated with reductions in depressive symptoms and improvements in quality of life. Several studies suggest that supervised aerobic exercise performed regularly over a period of several weeks may produce effects comparable to some standard therapeutic approaches in selected patient groups [17]. At the same time, evidence indicates that exercise intensity and adherence may significantly influence treatment outcomes. Moderate intensity exercise appears to be particularly beneficial for many individuals, as it combines physiological effectiveness with relatively good tolerability and long-term sustainability [19,20,26].

In recent years, increasing attention has also been directed toward resistance training as a potentially effective intervention in depression therapy. Earlier research focused primarily on aerobic exercise; however, newer studies suggest that resistance programs may also lead to significant improvements in mood and psychological functioning [23,29]. Strength training may be especially relevant for older adults and individuals with chronic somatic conditions, where improvements in physical functioning, independence, and self-efficacy may additionally support mental health outcomes. Some evidence indicates that combined exercise programs involving both aerobic and resistance components may provide broader benefits by simultaneously improving cardiovascular fitness, muscular strength, and psychosocial functioning [21,24].

Mind-body interventions, including yoga and other movement mindfulness practices, have likewise demonstrated promising results in reducing depressive symptoms and related to stress complaints [25]. These forms of activity may exert therapeutic effects not only through physiological mechanisms but also through breathing regulation, relaxation, attention control, and reduction of psychological tension. For some individuals, particularly those experiencing anxiety, emotional dysregulation, or high stress sensitivity, mind-body approaches may represent a more accessible and acceptable form of physical activity than conventional exercise programs. Nevertheless, the heterogeneity of interventions and methodological differences between studies make it difficult to directly compare the effectiveness of specific exercise modalities.

One of the most clinically relevant findings emerging from recent research is that the antidepressant effects of exercise appear to depend not only on the type of activity but also on factors such as regularity, duration, supervision, and individual patient characteristics [14,17,20]. Programs lasting at least several weeks and performed consistently seem to produce more stable psychological benefits. Supervised interventions often

demonstrate greater effectiveness than unsupervised exercise, possibly due to improved adherence, increased motivation, and additional social support. At the same time, patient preferences and baseline physical condition should be considered when designing treatment, since excessive intensity or unrealistic expectations may reduce persistent participation.

Despite the encouraging evidence supporting exercise in depression treatment, several limitations should be acknowledged. Many studies differ substantially in methodology, participant selection, exercise protocols, and outcome measures, contributing to considerable heterogeneity across the literature. In addition, blinding is difficult to achieve in exercise interventions, which may increase the risk of expectancy effects and performance bias. Some metanalyses have reported weaker antidepressant effects after including only studies with higher methodological quality, suggesting that the true magnitude of benefit may be more moderate than initially estimated [14,17,18,26]. Furthermore, individuals with severe depression often experience fatigue, psychomotor slowing, and lack of motivation, all of which may interfere with adherence to physical activity programs.

2.5. Exercise prescription

The growing recognition of physical activity as a supportive component of depression therapy has increased interest in determining the most effective exercise prescription for individuals with depressive symptoms. Current evidence suggests that exercise interventions should be individualized and adapted to the patient's physical condition, symptom severity, preferences, and overall health status [14,17,20]. Although no single exercise protocol appears universally optimal, several studies indicate that regular, moderate intensity physical activity performed consistently over time may provide the greatest therapeutic benefit while remaining achievable for most patients. Importantly, exercise prescription in depression should not focus solely on physiological outcomes but should also consider motivation, adherence, emotional wellbeing, and psychosocial functioning.

Public health recommendations generally advise adults to engage in at least 150 minutes of moderate intensity physical activity per week, or 75 minutes of vigorous intensity activity combined with muscle strengthening exercises [30]. In the context of depression treatment, many clinical studies have used exercise programs involving three to five sessions per week, with individual sessions lasting approximately 30 to 60 minutes [17,20,28]. Moderate intensity aerobic exercise, such as brisk walking, cycling, swimming, or jogging, appears to be particularly effective and well tolerated. Nevertheless, emerging evidence suggests that resistance training and combined exercise programs may also produce meaningful reductions in depressive symptoms, especially when interventions are performed regularly and under professional supervision [21,23,24].

The intensity of exercise appears to be an important factor influencing both effectiveness and adherence. Moderate intensity exercise is often considered the most practical and sustainable option for individuals with depression, particularly during the early stages of treatment. Excessively demanding exercise programs may reduce motivation and increase dropout rates, especially in patients experiencing fatigue, low energy, psychomotor slowing, or anxiety. On the other hand, some studies suggest that higher intensity exercise may produce stronger neurobiological responses, including greater increases in BDNF and improved stress regulation [10,15]. Therefore, the optimal intensity likely depends on individual patient characteristics, physical fitness, and psychological readiness rather than on a single standardized recommendation.

Adherence remains one of the most significant challenges in interventions involving physical activity for depression management. Depressive symptoms themselves, including lack of motivation, anhedonia, impaired concentration, and reduced energy, may substantially limit participation in regular physical activity. For this reason, interventions emphasizing gradual progression, realistic goals, and enjoyable forms of movement may be more successful in long-term implementation. Supervised exercise programs often demonstrate better adherence and greater therapeutic effects compared with unsupervised interventions, potentially due to structured support, external motivation, and increased social interaction [14,17]. Group activities may additionally reduce feelings of loneliness and social withdrawal, which are common in individuals with depressive disorders.

An individualized and flexible approach appears particularly important in specific clinical populations. Older adults, individuals with chronic diseases, and patients with reduced physical functioning may require modified exercise programs adjusted to their physical capabilities and medical limitations [31,32,33]. In such cases, lower intensity aerobic activity, resistance training with gradual progression, balance exercises, or mind-body interventions such as yoga may represent safer and more accessible options [25]. Similarly, physically inactive individuals may benefit from initially focusing on increasing daily movement and reducing sedentary behavior rather than immediately attempting structured high-volume exercise programs.

Consequently, exercise prescription for depression should be viewed as a dynamic and individualized process integrated within broader psychiatric and lifestyle care. Rather than applying rigid training protocols, clinicians should aim to encourage sustainable and realistic forms of physical activity that support both mental and physical wellbeing over the course of treatment.

2.6. Exercise in specific populations

The effectiveness of physical activity in reducing depressive symptoms has been observed across a wide range of populations. However, the characteristics of exercise interventions and their clinical outcomes may differ depending on age, physical condition, comorbidities, and psychosocial factors. Increasing attention has been directed toward understanding how interventions based on exercise can be adapted to the needs of specific groups, including older adults, university students, individuals with chronic diseases, and patients with neurological disorders or cognitive impairment [25,28,31,32,33]. Current evidence suggests that although the general antidepressant effects of physical activity remain relatively consistent, individualized approaches are necessary to optimize both safety and therapeutic effectiveness.

Older adults represent one of the most frequently studied populations in research about exercise treatment in depression. Aging is often associated with increased social isolation, reduced mobility, chronic disease burden, cognitive decline and loss of independence, all of which may contribute to a higher prevalence of depressive symptoms. In this population, regular physical activity appears to improve not only mood but also functional capacity, mobility, balance, and quality of life [31,34,35]. Aerobic exercise, resistance training, and combined interventions have all demonstrated beneficial effects in older individuals, particularly when programs are supervised and adapted to physical limitations. Recent studies additionally suggest that online programs and exercising at home may provide psychological and social benefits for older adults with limited access to traditional rehabilitation or fitness programs [35]. Importantly, improvements in depressive symptoms in this group are often accompanied by better social engagement and greater independence in daily functioning.

Exercise interventions have also shown promising effects among individuals with cognitive impairment and neurodegenerative conditions. In such populations, physical activity may contribute not only to mood improvement but also to enhanced cognitive functioning, reduced stress, and better performance of daily activities. Resistance training and dual task exercise programs combining cognitive and physical components appear particularly relevant in older adults with mild cognitive impairment [32]. Although the mechanisms underlying these effects remain incompletely understood, improvements in cerebral blood flow, neuroplasticity, and functional connectivity may partially explain the observed benefits. Nevertheless, exercise prescription in cognitively impaired populations requires careful supervision and individualized adjustment to ensure both safety and adherence.

University students and young adults constitute another population in which physical activity appears to have important mental health benefits. Academic pressure, social stress, sleep disturbances, financial concerns, and increased screen exposure contribute to high levels of psychological distress in this group. Several studies have demonstrated that regular exercise may significantly reduce depressive symptoms, anxiety, and perceived stress among students [28,36]. Programs involving moderate aerobic activity performed multiple times per week seem to produce particularly favorable outcomes. At the same time, exercise may support concentration, sleep quality, and academic functioning, indirectly contributing to improved emotional wellbeing. These findings became especially relevant during and after the COVID-19 pandemic, when social isolation and reduced opportunities for movement were associated with worsening mental health among adolescents and university populations.

Clinical populations with chronic somatic diseases also appear to benefit from working out. Patients with cardiovascular disease, obesity, diabetes, chronic pain, and cancer frequently experience depressive symptoms associated with both biological and psychosocial factors. In these groups, physical activity may simultaneously improve physical health and mental functioning, potentially reducing inflammation, fatigue, and functional limitations that contribute to depressed mood. Emerging evidence additionally suggests that exercise may improve quality of life and emotional resilience in patients undergoing oncological treatment or living with chronic neurological conditions such as Parkinson’s disease [25,33]. Mind-body interventions and low-impact exercise programs may be particularly valuable in patients with reduced physical capacity or increased vulnerability to stress.

In many vulnerable populations, depressive symptoms themselves may reduce motivation to participate in physical activity, creating additional challenges for prolonged intervention success. Therefore, exercise programs should be individualized and integrated within broader multidisciplinary care strategies rather than applied using uniform recommendations for all patient groups.

3. Limitations of current evidence

Although evidence supports the beneficial effects of physical activity on depressive symptoms, several methodological limitations remain. Existing studies differ in participant characteristics, diagnostic criteria, depression severity, exercise modalities, intervention duration, intensity, frequency, and outcome measures, which limits direct comparisons and universal recommendations.

Methodological limitations also affect the interpretation of many published findings. A substantial proportion of exercise-based studies involve relatively small sample sizes, short intervention periods, and limited long-term

follow up. Consequently, although short-term improvements in depressive symptoms are frequently reported, less is known about the sustainability of these effects over extended periods. In addition, participant dropout rates are often high, particularly among individuals with more severe depressive symptoms, low motivation, fatigue, or coexisting physical illnesses. This issue may introduce attrition bias and reduce the generalizability of study outcomes to broader clinical populations.

Another important limitation involves the difficulty of maintaining methodological rigor in exercise intervention studies. Unlike pharmacological trials, blinding participants and researchers is often impossible in physical activity research, increasing the risk of expectancy effects and performance bias. In some cases, positive outcomes may be partially influenced by increased social interaction, structured support, or therapeutic attention rather than by exercise itself. Furthermore, many studies rely on self-reported measures of physical activity and psychological wellbeing, which may introduce recall bias and subjective inaccuracies.

The variability in exercise prescription additionally complicates interpretation of the available evidence. Although aerobic exercise is the most extensively studied modality, research protocols frequently differ in exercise intensity, supervision, progression, and adherence monitoring. Similar inconsistencies are observed in studies investigating resistance training, yoga, high-intensity interval training, and combined exercise programs. Consequently, it remains unclear which specific exercise parameters are most effective for different subgroups of patients. Individual factors such as age, baseline physical fitness, comorbidities, medication use, and psychosocial environment may also substantially influence treatment response, further limiting the possibility of creating standardized recommendations.

Another issue concerns the bidirectional relationship between depression and physical activity. While low levels of physical activity may contribute to the development of depressive symptoms, depression itself often reduces motivation, energy, concentration, and willingness to engage in exercise. This relationship makes it difficult to determine causality in some observational studies. In addition, individuals who participate regularly in physical activity may differ from inactive populations in several lifestyle and socioeconomic factors, including diet, sleep quality, social support, education, and access to healthcare, all of which may independently affect mental health outcomes.

Current evidence also remains limited in several specific clinical populations. Although increasing research has focused on older adults, individuals with chronic diseases, and university students, fewer studies have examined exercise interventions in patients with severe depression, treatment resistant depression, bipolar depression, or complex psychiatric comorbidities. Similarly, the neurobiological mechanisms underlying the antidepressant effects of exercise, including the roles of inflammation, neuroplasticity, and epigenetic regulation, are not yet fully understood and require further investigation using more advanced and standardized methodologies.

Despite these limitations, the evidence generally supports physical activity as a useful strategy in depression prevention and adjunctive treatment, while future studies should improve methodological quality, standardize protocols, and evaluate sustained outcomes across diverse patient populations.

4. Future directions

Although the relationship between physical activity and depression has been extensively investigated in recent years, several important areas still require further exploration. One of the main priorities for future research should

be the development of more standardized and methodologically rigorous exercise intervention studies. Considerable heterogeneity currently exists regarding exercise type, intensity, duration, supervision, and outcome assessment, making comparisons between studies difficult. Future trials should therefore aim to establish more clearly defined exercise protocols and evaluate lasting outcomes in larger and more diverse patient populations. Better standardization may contribute to the development of more precise clinical recommendations for integrating physical activity into depression management.

Another important direction involves the growing concept of personalized exercise medicine. Current evidence suggests that the antidepressant effects of exercise may vary depending on age, sex, genetic background, baseline fitness level, severity of depressive symptoms, inflammatory status, and coexisting medical conditions. As a result, future research should focus on identifying individual factors that influence treatment response and determining which forms of physical activity may be most effective for specific patient groups. Such an approach could improve adherence, increase therapeutic effectiveness, and support more individualized mental health care strategies.

Further investigation of neurobiological and psychoneuroimmunological mechanisms also appears necessary. Although exercise has been associated with changes in inflammatory markers, stress response systems, neurotransmitter regulation, and neuroplasticity, the exact pathways responsible for these effects remain incompletely understood. Future studies using neuroimaging, molecular biology, epigenetic analysis, and biomarker assessment may provide a more detailed understanding of how physical activity influences brain function and emotional regulation. Increasing attention is being directed toward the role of inflammation, gut-brain interactions, mitochondrial functioning, and epigenetic modifications in depression and exercise adaptation.

Another promising area concerns the use of digital and assisted by technology exercise interventions. Online exercise programs, mobile applications, wearable devices, and telehealth supervision may improve accessibility to physical activity interventions, particularly for individuals living in remote areas, older adults, or patients with mobility limitations. The COVID-19 pandemic highlighted both the mental health consequences of social isolation and the potential value of remotely delivered physical activity programs. However, more research is needed to evaluate the long-term effectiveness, adherence, and psychological outcomes associated with digital exercise interventions in patients with depressive disorders.

Future studies should additionally focus on populations that remain underrepresented in the current literature. Although substantial evidence exists for mild to moderate depression, fewer studies have examined exercise interventions in individuals with severe depression, treatment-resistant depression, bipolar disorder, or complex psychiatric comorbidities. Similarly, there is limited evidence regarding exercise prescription in patients with significant cognitive impairment or severe chronic illness. Understanding how physical activity may be safely and effectively adapted for these populations represents an important clinical challenge.

Finally, future research should increasingly consider physical activity within the broader framework of lifestyle medicine and multidimensional mental health care. Depression is influenced by numerous interconnected biological, psychological, and environmental factors, including sleep quality, nutrition, stress exposure, social relationships, and sedentary behavior. Consequently, exercise interventions may be most effective when combined with other lifestyle and psychosocial approaches rather than applied in isolation. A more integrative understanding

of mental health may therefore contribute to the development of holistic prevention and treatment strategies that address both the psychological and physiological dimensions of depressive disorders.

5. Summary

Current evidence suggests that physical activity may represent an important supportive component in both the prevention and treatment of depression. The beneficial effects of exercise appear to involve multiple interacting mechanisms, including improvements in neuroplasticity, regulation of stress response systems, reduction of inflammatory activity, and positive influences on psychological and social functioning. Regular physical activity has been associated with reduced risk of developing depressive symptoms as well as clinically meaningful improvements in mood and quality of life among individuals with depressive disorders. Aerobic exercise remains the most extensively studied intervention; however, resistance training, combined exercise programs, and mind-body activities have also demonstrated beneficial effects in various populations.

At the same time, current evidence indicates that the therapeutic effectiveness of exercise may depend on several factors, including exercise intensity, duration, supervision, patient adherence, and individual clinical characteristics. Although physical activity should not be considered a universal replacement for pharmacological or psychotherapeutic treatment, particularly in severe depression, it may serve as a valuable adjunctive intervention within comprehensive and individualized mental health care. Importantly, exercise interventions additionally contribute to improvements in physical health, functional capacity, and overall wellbeing, which may be especially relevant in patients with chronic diseases and sedentary lifestyles.

Despite the encouraging findings, several methodological limitations remain within the available literature, including heterogeneity of exercise protocols, variability in study quality, and limited long-term follow up data. Further research is therefore needed to better understand the neurobiological mechanisms underlying the antidepressant effects of physical activity and to determine the most effective exercise strategies for different patient populations. Nevertheless, considering the relatively low cost, accessibility, and broad health benefits of physical activity, promoting regular exercise may represent an important element of future public health and lifestyle-oriented approaches to depression prevention and treatment.

Disclosure

Author's contribution

Conceptualization, N.N.; methodology, N.N. and A.W.; formal analysis, Z.T., O.F., and Ju.K.; investigation, N.N., A.W., Z.T., O.F., Ju.K., Ja.K., N.D., E.F., M.K., S.K., and F.N.; resources, N.N., A.W., Z.T., O.F., Ju.K., Ja.K., N.D., E.F., M.K., S.K., and F.N.; data curation, N.N., A.W., and Z.T.; writing - original draft preparation, N.N., A.W., Z.T., O.F., and Ju.K.; writing - review and editing, N.N., A.W., Z.T., O.F., Ju.K., N.D., E.F., Ja.K., M.K., S.K., and F.N.; visualization, N.N.; supervision, N.N.; project administration, N.N. All authors have read and agreed to the published version of the manuscript.

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