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Commentary

Physical activity and exercise as a synergistic mediator of cardiovascular and mental resilience

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Introduction

Cardiovascular diseases (CVD) and mental disorders represent two of the most prevalent causes of global disability, contributing significantly to the escalating economic burden and high mortality rates worldwide [1–6]. Physical activity (PA) has emerged as a critical non-pharmacological intervention with a profound positive impact on both domains [7,8]. This commentary provides a comprehensive description of the bidirectional relationship between mental health and physical activity, and its subsequent influence on cardiovascular outcomes. These complex associations are driven by intricate biological and behavioral mechanisms that necessitate a closer examination of their clinical implications [7,8].

Extensive evidence demonstrates that regular PA and structured exercise training not only enhance cardiovascular function but also markedly alleviate psychiatric symptoms [9–12]. Conversely, mental disorders are independently associated with an elevated risk of developing CVD, a link often exacerbated by symptom-related sedentary behavior and reduced exercise adherence [13–15]. While PA is proven to improve both mental well-being and cardiorespiratory fitness, research indicates that structured exercise programs – particularly those incorporating professional motivational support – are significantly more effective than unsupervised or self-directed interventions [7,16].

Given the well-established epidemiological link between mental health, PA, and CVD, the systematic identification and treatment of psychological conditions in cardiac patients is essential [7,17]. Integrating targeted physical activity promotion into clinical practice must become a priority to harness its synergistic benefits for both mental and cardiovascular health [7,13,17,18].

Cardiovascular Disease and Mental Health Disorders

Clinical data indicate a high prevalence of comorbid mental disorders among patients with CVD, with reported rates ranging from 30% to 45% [8]. The prevalence of depression and anxiety among heart patients is four times higher (15%–20%) than in the general population (5%) [9–12]. The bidirectional relationship between CVD and mental health is mediated by several integrated pathways that bridge physiological and psychological domains. Central to this connection is vascular health, as systemic damage to blood vessels often results in cerebral hypoperfusion; this reduction in oxygenated blood flow to the brain serves as a primary driver for cognitive decline and the development of vascular dementia [19]. Furthermore, cardiac events act as potent biological triggers for physiological stress responses. These events can induce chronic systemic inflammation and significant hormonal imbalances – specifically the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and subsequent elevation of cortisol – which have been shown to adversely affect neuroplasticity and brain function [20]. Investigations into acute mental stress and its subsequent

inflammatory responses also demonstrate that a physically active state leads to a markedly reduced stress-induced leukocyte infiltration into atherosclerotic plaques compared to a sedentary state. This protective mechanism is associated with a blunted stress-induced release of norepinephrine and a concomitant reduction in endothelial activation, as evidenced by a lower expression of adhesion molecules and chemokines [21]. When a patient ceases PA due to fatigue or kinesiophobia (fear of movement), they also lose the natural antidepressant effects associated with exercise – such as the release of endorphins and brain-derived neurotrophic factor (BDNF) – thereby further accelerating the onset or exacerbation of mental illness [17,22]. Crucial to this dynamic is also the role of the anti-aging gene Sirtuin 1, which is vital for the success of exercise interventions aimed at enhancing mental health and mitigating long-term cardiovascular risk [23,24]. Exercise-induced increases in plasma Sirtuin 1 levels significantly optimize the heart-brain axis by promoting neuronal proliferation and improving cardiovascular function [25]. Consequently, incorporating Sirtuin 1-activating diets into exercise programs also represents an essential component for maximizing neuro- and cardiovascular benefits [26–29].

Beyond biological mechanisms, the psychosocial stress associated with a CVD diagnosis often precipitates profound emotional trauma, characterized by feelings of loss, grief, and a heightened fear of mortality or long-term disability. This burden is compounded by the lifestyle changes necessitated by the disease. The rigorous demands of managing complex medication regimens, adhering to strict dietary restrictions, and participating in physical rehabilitation create a persistent strain that can frequently overwhelm a patient's coping capacities, further exacerbating the cycle of psychological distress [30,31].

The relationship between these conditions is inherently bidirectional. While cardiac events frequently precipitate psychological distress, individuals diagnosed with mental disorders conversely exhibit a significantly elevated risk of developing CVD, as evidenced by recent longitudinal data [14,32]. This suggests that mental health conditions are not merely consequences of heart disease but serve as independent risk factors for its onset. According to the 2025 ESC Clinical Consensus Statement, mental disorders are now considered major independent risk factors for CVD, similar to smoking or high blood pressure [17].

The impact of mental health on cardiovascular risk is profound and documented across various psychiatric conditions. Major depression serves as a potent independent risk factor, increasing the likelihood of developing coronary artery disease by approximately 72% [17]. Even more severe implications are observed in patients with severe mental illness (SMI), such as schizophrenia or bipolar disorder. These individuals face a two-to-threefold higher risk of CVD-related mortality, which represents a primary driver behind the significantly reduced life expectancy in this population – typically 10 to 20 years shorter than the general average [33]. Furthermore, conditions characterized by persistent psychological tension, such as PTSD and chronic stress, are linked to a 60% higher risk of myocardial infarction and stroke [34]. This elevated risk is largely attributed to the physiological toll of a sustained "fight or flight" state, which triggers maladaptive autonomic and endocrine responses that accelerate cardiovascular deterioration.

Overall, this increased cardiovascular risk is driven by four primary pathways. First, biological factors play a critical role, as mental disorders often trigger a chronic activation of the hypothalamic-pituitary-adrenal (HPA) axis. This sustained stress response leads to elevated cortisol levels, systemic inflammation, and hypertension, which collectively induce endothelial dysfunction and damage the arterial lining [17]. Second, behavioral factors significantly contribute to cardiac deterioration. Conditions such as depression and anxiety frequently lead to maladaptive "coping behaviors," including increased tobacco use, physical inactivity, and poor dietary choices, all of which are established drivers of CVD [13,17]. Third, the impact of treatment side effects must be considered; certain antipsychotic and mood-stabilizing medications are associated with substantial weight gain and metabolic alterations, such as dyslipidemia and insulin resistance, further elevating the patient's cardiac risk profile [13,35]. Finally, the phenomenon of diagnostic overshadowing creates a systemic barrier to care. Physical symptoms in psychiatric patients are occasionally dismissed by clinicians as manifestations of the underlying mental illness, leading to critical delays in the diagnosis and treatment of life-threatening cardiovascular conditions [17,36].

Given the established bidirectional relationship and the significantly elevated risk profile, modern clinical guidelines have shifted toward a proactive prevention strategy. It is now strongly recommended that individuals diagnosed with significant mental disorders undergo regular cardiovascular screening – including blood pressure monitoring, lipid profiling, and glucose testing – starting at an earlier age than the general population [17,36]. To effectively bridge the mortality gap between individuals with severe mental illness (SMI) and the general population, a comprehensive six-pillar framework is proposed in a recent publication, comprising: (1) enhancement of physical health literacy through targeted psychoeducation, (2) systematic smoking cessation interventions, (3) proactive management of obesity and early-onset weight gain, (4) routine hypertension screening and evidence-based treatment, (5) metabolic optimization of dyslipidemia and diabetes, and (6) the implementation of integrated care models [37]. This integrated approach aims to bridge the gap in life expectancy by identifying metabolic and vascular changes before they escalate into acute cardiac events. By addressing both psychiatric and somatic health simultaneously, clinicians can mitigate the effects of diagnostic overshadowing and improve long-term survival rates for this vulnerable population [17,36].

Reduced Physical Activity as a Mediating Mechanism

A critical mechanism linking mental disorders and CVD is the significant reduction in PA. Recent longitudinal and cross-sectional data indicate that individuals diagnosed with mental health conditions exhibit a markedly higher risk of developing CVD, with sedentary behavior serving as a key mediating factor [32,38–41]. More specifically, the core symptoms of many mental disorders – such as anhedonia, fatigue, and social withdrawal – often lead to a decrease in exercise frequency and intensity [14,15,42]. Consequently, low levels of PA and prolonged sedentary behavior are recognized as independent risk factors for both cardiovascular onset and premature mortality in this population [14].

This relationship, however, is not unidirectional. Reduced PA in existing CVD patients creates a vicious cycle that further compromises psychological well-being. For those already diagnosed with heart disease, the physical limitations and fear of exertion can lead to a sedentary lifestyle, which significantly increases the risk of developing comorbid depression and anxiety. This self-reinforcing

cycle demonstrates that physical inactivity is not only a consequence of mental illness but also a biological and behavioral driver that exacerbates the overall disease burden, highlighting the urgent need for integrated exercise interventions in both psychiatric and cardiological care [6,14,15,32,38–41].

Physical Activity and Exercise for Cardio-Mental Health

There is evidence of a link between physical PA and mental health [43,44]. PA is an effective intervention for decreasing symptoms of anxiety and depression across multiple age groups, and has positive effects on several different sleep outcomes, which may also play an important role in mental disorders [43]. Current Research indicates that PA enhances anxiety regulation by engaging local inhibitory mechanisms within the ventral hippocampus, thereby mitigating the interference of anxiety with homeostatic brain functions. This regulatory capacity is part of a broader systemic impact, as physical exercise is currently understood to bolster immunity through several synergistic pathways. These include the optimization of neuroendocrine and physiological responses to both physical and psychosocial stressors, the promotion of a systemic anti-inflammatory milieu, and the up-regulation of neuroplasticity and growth factor expression [45]. Positive effects of PA on mental parameters of health-related quality of life (HR-QoL) – which is a multi-dimensional concept that examines the impact of an individual's health status on their perceived well-being and ability to function in different aspects of life – are also described in data from clinical studies conducted in individuals who often experience significant losses in QoL [38,43].

However, the specific modality of exercise is of critical importance. Longitudinal cohort analyses indicate that a higher skeletal muscle mass (SMM) is positively associated with elevated blood pressure (BP) and an increased left ventricular mass index (LVMI), independent of adiposity. Furthermore, longitudinal data demonstrate that increases in muscle mass are independently correlated with higher systolic (SBP) and diastolic blood pressure (DBP). These associations remain significant after adjusting for age, sex, and fat mass index (FMI), with a quantifiable increase in SBP per 1 kg/m² increment of muscle mass [46]. Apart from that, the literature provides consistent evidence that PA and exercise significantly reduce symptoms of mental illness [40,47–50]. Even modest changes can be beneficial – individuals do not need to engage in intense or prolonged exercise to achieve health benefits, and any amount of PA is better than none [50]. However, in clinical management, it is imperative to tailor the modality, duration, and intensity of PA and exercise to ensure a favorable dose-response profile, thereby balancing therapeutic efficacy with cardiovascular safety [51].

In this context, there is also evidence that PA and exercise provide significant benefits for patients with CVD [43,52–54], and it is therefore recommended in the clinical guidelines of the American Heart Association and the European Society of Cardiology [55,56]. A meta-analysis [6] examined the effects of different types of exercise and settings on brain structure/function, cognition, HR-QoL and mental health in patients with CVD. Regardless of the type of exercise, whether high-intensity interval training combined with resistance training or moderate training, all forms of exercise were associated with improvements in depressive and anxiety symptoms, and HR-QoL, compared to no exercise (i.e., usual care) [6]. Other studies also showed improvements in mental health symptoms and QoL in patients with heart disease [57–61]. CVD and mental health share a strong, bidirectional connection; in this regard, each condition acts as both a potential cause and a consequence of the other.

By improving both mental and physical well-being, PA and exercise acts as a protective "buffer" against the negative health impacts of stress and mental disorders. PA and exercise are therefore a dual-action intervention: This intervention is effective both as a treatment for mental health conditions and as a direct way to improve cardiovascular health. Significant positive effects of PA and exercise interventions (aerobic and/or resistance exercise) have been demonstrated [50]. WHO recommendations for PA are at least 150–300 minutes of moderate aerobic PA per week or 75–150 minutes of vigorous-intensity aerobic PA per week or an equivalent combination of moderate and vigorous PA and muscle-strengthening exercises for the major muscle groups on at least two days per week [62].

Motivation for Physical Activity and Exercise

Quantitative studies providing data on the motivating factors and/or barriers towards exercise participation among patients with severe mental disorders were eligible [63]. A meta-analysis showed significant positive effects of motivational interviewing (MI), a conversation technique used to explore and resolve ambivalence, on increasing participation in PA [16]. Importantly, as potential motivators, meta-analyses showed that 91% of individuals with severe mental illness endorsed "improving health" as a reason for exercise [63]. The other most common reasons for PA included losing weight (83%), "improving mood" (81%) and "reducing stress" (78%). Low mood and stress were identified as the most prevalent barriers towards exercise (61% of patients), followed by "lack of support" (50%).

Providing patients with professional support to identify and achieve their exercise goals may enable them to overcome psychological barriers [49,64,65]. Moreover, individually tailored exercise programs, matched to participants' preferred intensity, along with motivational support, were shown to be more effective in reducing symptoms of mental disorders than regular exercise programs without motivational components [16,66–68]. Studies also show that exercise improves physical health, body image, coping strategies for stress, and QoL in individuals with mental disorders, but also increases their overall levels of PA [15,41,43,69]. Interestingly, these studies showed that exercise itself has a positive effect on increasing overall levels of PA [42,70].

Synthesis

The relationship between CVD and mental health is inherently bidirectional, characterized by a complex interplay where mental disorders serve as both independent risk factors for the onset of CVD and frequent biopsychological consequences of cardiac events. A critical mediator in this relationship is the reduction in PA often observed among individuals with mental disorders, which substantially contributes to an elevated cardiovascular risk profile [71–73]. Consequently, the promotion of PA and structured exercise is of paramount clinical importance for this population [18]. Evidence consistently demonstrates that adherence to PA recommendations not only enhances mental well-being and QoL but also significantly reduces long-term CVD-related morbidity

and premature mortality. To optimize outcomes, exercise programs should be designed to include individualized and motivational support, as these components are particularly effective in alleviating symptoms of mental disorders and fostering sustained behavioral change. Integrating such interventions into standard care is essential for mitigating the health disparities faced by patients at the intersection of cardiovascular and mental health [73,74].

Key Recommendations for Clinical Practice

Integrated diagnosis and management

Clinicians should consistently screen for, diagnose, and treat mental disorders in individuals with CVD to address the psychological dimensions of cardiac care.

Comprehensive patient assessment

It is essential to systematically assess the mental health status of patients alongside their PA levels and exercise habits.

Early cardiovascular screening

Individuals diagnosed with significant mental disorders should undergo regular cardiovascular screening – including blood pressure monitoring, lipid profiling, and glucose testing – starting at an earlier age than the general population.

Exercise as a therapeutic intervention

PA and structured exercise should be prescribed as primary interventions to improve mental health outcomes, reduce long-term CVD-related morbidity, and mitigate the risk of premature mortality.

Supervised and motivational support

Exercise programs should adopt a multidisciplinary approach that incorporates clinical supervision and motivational support. Such programs should be integrated as part of basic cardiac care in the treatment of CVD and is also becoming increasingly established as part of standard treatment.

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