

## CARDIOVASCULAR CHANGES IN INDIVIDUALS WITH MOOD DISORDERS: A COMPREHENSIVE REVIEW

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**Abstract: INTRODUCTION** Mood disorders, including major depressive disorder, bipolar disorder, and anxiety disorders, are prevalent mental health conditions that significantly impact global health. These disorders are characterized by complex pathophysiologies involving genetic, neurochemical, and environmental factors. Cardiovascular diseases, such as coronary artery disease and hypertension, are the leading causes of mortality worldwide. The connection between mood disorders and cardiovascular diseases has been increasingly recognized, highlighting the importance of understanding the biological mechanisms and risk factors that link these conditions. **OBJECTIVE** A The main objective of this work was to comprehensively analyze the cardiovascular changes observed in individuals with mood disorders, elucidating the complex interactions between these prevalent health issues. **METHODS** This is a narrative review which included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases, using as descriptors: “Mood Disorders” AND “Cardiovascular Diseases” AND “Pathophysiology” AND “Mental Health” AND “Inflammation” in the last years. **RESULTS AND DISCUSSION** The impact of depression on cardiovascular health is well-documented, with strong associations between depressive symptoms and increased risks of myocardial infarction, heart failure, and stroke. Bipolar disorder presents unique cardiovascular risks, with metabolic syndrome and hypertension being prevalent among these patients. Anxiety disorders also significantly impact cardiovascular health through heightened sympathetic nervous system activity and chronic stress. Pharmacological treatments for mood disorders, including antidepressants and mood stabilizers, can have varying cardiovascular effects, necessitating

careful management. Lifestyle modifications, such as regular physical activity, a balanced diet, smoking cessation, and moderate alcohol consumption, are crucial for mitigating cardiovascular risk in patients with mood disorders. The roles of inflammation, autonomic dysfunction, and genetic predispositions further complicate the relationship between mood disorders and cardiovascular diseases. **CONCLUSION** The intricate interactions between mood disorders and cardiovascular diseases underscore the necessity for integrated and comprehensive care approaches. Understanding the biological mechanisms, shared risk factors, and effective management strategies is essential for improving health outcomes in individuals with comorbid mood disorders and cardiovascular diseases. Future research should focus on developing targeted interventions that address both mental and cardiovascular health in a holistic manner, emphasizing the importance of integrated care to achieve optimal health outcomes.

**Keywords:** Mood Disorders; Cardiovascular Risk; HPA Axis Dysregulation; Inflammatory Pathways; Autonomic Nervous System.

## INTRODUCTION

Mood disorders, a broad category encompassing various mental health conditions characterized by significant disturbances in mood and affect, represent a substantial portion of the global mental health burden<sup>1</sup>. These disorders are primarily categorized into major depressive disorder (MDD), bipolar disorder (BD), and anxiety disorders, each with distinct diagnostic criteria and clinical presentations<sup>1</sup>. The prevalence of these conditions is alarmingly high, with major depressive disorder affecting hundreds of millions of individuals worldwide, making it one of the leading causes of disability globally<sup>1</sup>. The epidemiology of mood disorders reveals a profound impact on both individual

and societal levels, contributing significantly to morbidity, mortality, and healthcare costs<sup>2</sup>.

Pathophysiologically, mood disorders are complex and multifactorial, involving an intricate interplay of genetic, neurochemical, and environmental factors<sup>3</sup>. The dysregulation of key neurotransmitters such as serotonin, norepinephrine, and dopamine is central to the pathogenesis of these disorders<sup>4</sup>. Additionally, structural and functional abnormalities in critical brain regions, including the prefrontal cortex, hippocampus, and amygdala, have been consistently observed in individuals with mood disorders<sup>5</sup>. These neurobiological alterations contribute to the characteristic symptoms, which include persistent sadness, anhedonia, irritability, and cognitive impairments<sup>6</sup>. The impact of mood disorders extends beyond the psychological realm, significantly influencing overall health and increasing the risk of various physical health conditions, particularly cardiovascular diseases (CVD)<sup>7</sup>.

Cardiovascular diseases, encompassing conditions such as coronary artery disease, hypertension, heart failure, and stroke, remain the leading cause of mortality and morbidity worldwide<sup>8</sup>. The pathogenesis of CVD involves a complex interplay of factors, including endothelial dysfunction, inflammation, metabolic disturbances, and lifestyle factors<sup>9</sup>. The intricate relationship between mental health and physical health, particularly the association between mood disorders and cardiovascular diseases, has garnered significant attention in recent years<sup>10</sup>. Historical perspectives on this relationship reveal that the connection between depression and heart disease was first noted in the early 20th century, with subsequent research consistently demonstrating that individuals with mood disorders are at a significantly higher risk of developing CVD<sup>11</sup>.

Biological mechanisms linking mood disorders and cardiovascular diseases are multifactorial, involving dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, chronic inflammation, autonomic nervous system dysfunction, and behavioral factors<sup>12</sup>. The HPA axis, a critical component of the body's stress response system, is often dysregulated in individuals with mood disorders, leading to sustained elevations in cortisol levels<sup>13</sup>. Chronic hypercortisolemia is associated with several adverse cardiovascular outcomes, including hypertension, insulin resistance, and central obesity<sup>14</sup>. Inflammatory pathways also play a significant role, with elevated levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- $\alpha$ ), commonly observed in patients with depression<sup>15</sup>. These inflammatory markers are implicated in the pathogenesis of atherosclerosis and other cardiovascular conditions<sup>16</sup>.

Autonomic nervous system dysfunction, characterized by reduced heart rate variability and increased sympathetic activity, is another critical factor linking mood disorders with cardiovascular diseases<sup>17</sup>. This autonomic imbalance contributes to the development and progression of hypertension and other cardiovascular conditions<sup>18</sup>. Furthermore, genetic predisposition and shared risk factors, such as obesity, diabetes, and smoking, also contribute to the comorbidity of mood disorders and CVD<sup>19</sup>. Lifestyle factors, including diet, physical activity, and substance use, significantly impact both mental and cardiovascular health, highlighting the need for comprehensive and integrated care approaches<sup>20</sup>.

Pharmacological treatments for mood disorders, including antidepressants, mood stabilizers, and antipsychotics, can also influence cardiovascular risk<sup>21</sup>. While these medications are essential for managing mood disorders, they can have significant

cardiovascular side effects, necessitating careful monitoring and management<sup>22</sup>. Antidepressants, particularly tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs), have varying effects on cardiovascular health<sup>23</sup>. Tricyclic antidepressants are known to have cardiotoxic effects, including arrhythmias and orthostatic hypotension, while SSRIs, although generally considered safer, can still affect platelet function and increase bleeding risk<sup>24</sup>. Mood stabilizers such as lithium and valproate can cause weight gain, dyslipidemia, and insulin resistance, further complicating cardiovascular risk management<sup>25</sup>.

The intersection of mood disorders and cardiovascular risk factors, such as hypertension, diabetes, and dyslipidemia, underscores the need for integrated care approaches<sup>26</sup>. Effective management of these comorbid conditions requires a comprehensive understanding of the complex interactions between mental and physical health<sup>27</sup>. Gender differences in the prevalence and manifestation of mood disorders and cardiovascular diseases further complicate the clinical picture, necessitating tailored interventions that consider these differences<sup>28</sup>.

## **OBJETIVES**

The main objective of this work was to comprehensively analyze the cardiovascular changes observed in individuals with mood disorders, elucidating the complex interactions between these prevalent health issues.

### **SECUNDARY OBJETIVES**

1. To examine the biological mechanisms linking mood disorders and cardiovascular diseases.
2. To assess the impact of pharmacological treatments for mood disorders on cardiovascular health.

3. To evaluate the influence of lifestyle factors on cardiovascular risk in patients with mood disorders.

4. To investigate the role of inflammation and autonomic dysfunction in the comorbidity of mood disorders and cardiovascular diseases.

5. To explore gender differences in the intersection of mood disorders and cardiovascular diseases.

## **METHODS**

This is a narrative review, in which the main aspects of analyze the cardiovascular changes observed in individuals with mood disorders, elucidating the complex interactions between these prevalent health issues in recent years were analyzed. The beginning of the study was carried out with theoretical training using the following databases: PubMed, sciELO and Medline, using as descriptors: “Mood Disorders” AND “Cardiovascular Diseases” AND “Pathophysiology” AND “Mental Health” AND “Inflammation” in the last years. As it is a narrative review, this study does not have any risks.

Databases: This review included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases.

The inclusion criteria applied in the analytical review were human intervention studies, experimental studies, cohort studies, case-control studies, cross-sectional studies and literature reviews, editorials, case reports, and poster presentations. Also, only studies writing in English and Portuguese were included.

## RESULTS AND DISCUSSION

The impact of depression on cardiovascular health is profound and multifaceted<sup>29</sup>. Numerous studies have demonstrated a strong association between depressive symptoms and increased risk of myocardial infarction, heart failure, and stroke<sup>30</sup>. Depression contributes to poor cardiovascular outcomes through various mechanisms, including increased inflammation, autonomic dysfunction, and behavioral factors such as poor medication adherence and unhealthy lifestyle choices<sup>31</sup>. The chronic stress associated with depression leads to persistent activation of the HPA axis, resulting in elevated cortisol levels and subsequent cardiovascular damage<sup>32</sup>. Elevated cortisol levels have been linked to hypertension, insulin resistance, and central obesity, all of which are significant risk factors for cardiovascular diseases<sup>33</sup>.

Bipolar disorder presents unique cardiovascular risks, with studies indicating that individuals with bipolar disorder are more likely to develop conditions such as hypertension, metabolic syndrome, and atherosclerosis<sup>34</sup>. The manic and depressive phases of bipolar disorder are associated with varying degrees of autonomic nervous system imbalance, which can exacerbate cardiovascular risk<sup>35</sup>. During manic episodes, increased sympathetic activity can lead to elevated heart rates and blood pressure, while depressive episodes may result in reduced heart rate variability and increased parasympathetic activity<sup>36</sup>. Furthermore, the use of mood stabilizers and antipsychotic medications in bipolar disorder can lead to metabolic side effects that increase cardiovascular risk<sup>37</sup>. These medications can cause weight gain, dyslipidemia, and insulin resistance, further complicating the management of cardiovascular risk in individuals with bipolar disorder<sup>38</sup>.

Anxiety disorders, including generalized anxiety disorder (GAD) and panic disorder, also have significant cardiovascular implications<sup>39</sup>. These conditions are associated with heightened sympathetic nervous system activity, which can increase heart rate and blood pressure, contributing to the development of hypertension and coronary artery disease<sup>40</sup>. Chronic anxiety and stress can lead to persistent activation of the HPA axis, resulting in elevated cortisol levels and subsequent cardiovascular damage<sup>41</sup>. In addition to the direct physiological effects, anxiety disorders can also impact cardiovascular health through behavioral factors<sup>42</sup>. Individuals with anxiety disorders are more likely to engage in unhealthy behaviors such as smoking, poor diet, and physical inactivity, all of which contribute to increased cardiovascular risk<sup>43</sup>.

The pharmacological treatment of mood disorders plays a critical role in cardiovascular outcomes<sup>44</sup>. Antidepressants, particularly tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs), have varying effects on cardiovascular health<sup>45</sup>. Tricyclic antidepressants are known to have cardiotoxic effects, including arrhythmias and orthostatic hypotension, while SSRIs are generally considered safer but can still affect platelet function and increase bleeding risk<sup>46</sup>. Mood stabilizers such as lithium and valproate can cause weight gain, dyslipidemia, and insulin resistance, further complicating cardiovascular risk management<sup>47</sup>. Antipsychotic medications, commonly used in the treatment of bipolar disorder and other mood disorders, are associated with significant metabolic side effects, including weight gain, dyslipidemia, and increased risk of diabetes<sup>48</sup>.

Lifestyle modifications are essential in managing cardiovascular risk in patients with mood disorders<sup>49</sup>. Regular physical activity,



a balanced diet, smoking cessation, and moderate alcohol consumption are all critical components of cardiovascular health<sup>50</sup>. Exercise has been shown to improve mood and reduce cardiovascular risk through its effects on weight, blood pressure, and insulin sensitivity<sup>51</sup>. Diet plays a crucial role in managing cardiovascular risk, with evidence supporting the benefits of a Mediterranean diet rich in fruits, vegetables, whole grains, and healthy fats<sup>52</sup>. Smoking cessation is particularly important, as smoking is a significant risk factor for both mood disorders and cardiovascular diseases<sup>53</sup>. Reducing alcohol consumption can also help mitigate cardiovascular risk, as excessive alcohol intake is associated with hypertension, dyslipidemia, and cardiomyopathy<sup>54</sup>.

Obesity is a significant risk factor for both mood disorders and cardiovascular diseases<sup>55</sup>. The interplay between obesity, mood disorders, and cardiovascular health involves complex mechanisms, including inflammation, insulin resistance, and hormonal imbalances<sup>56</sup>. Obesity is associated with increased levels of pro-inflammatory cytokines, which contribute to the development of atherosclerosis and other cardiovascular conditions<sup>57</sup>. Insulin resistance, a common feature of obesity, is also implicated in the pathogenesis of mood disorders and cardiovascular diseases<sup>58</sup>. Hormonal imbalances, particularly involving cortisol and other stress hormones, further exacerbate the relationship between obesity, mood disorders, and cardiovascular health<sup>59</sup>.

Sleep disorders, commonly comorbid with mood disorders, further exacerbate cardiovascular risk by disrupting metabolic and autonomic regulation<sup>60</sup>. Chronic sleep deprivation is associated with increased sympathetic activity, elevated blood pressure, and impaired glucose metabolism<sup>61</sup>. Sleep disorders such as insomnia and sleep apnea are particularly prevalent in individuals with

mood disorders and contribute to increased cardiovascular morbidity and mortality<sup>62</sup>. Addressing sleep disorders through behavioral and pharmacological interventions can help mitigate cardiovascular risk in this population<sup>63</sup>.

Diabetes and hypertension are prevalent comorbidities in patients with mood disorders, contributing to the overall cardiovascular risk profile<sup>64</sup>. Dyslipidemia, characterized by elevated levels of low-density lipoprotein (LDL) cholesterol and triglycerides, is also commonly observed in this population<sup>65</sup>. Chronic kidney disease, another common comorbidity, adds to the cardiovascular burden through mechanisms such as fluid overload, electrolyte imbalances, and increased vascular stiffness<sup>66</sup>. Managing these comorbid conditions requires a comprehensive and integrated approach that addresses both mental and physical health<sup>67</sup>.

Inflammation plays a central role in the pathophysiology of both mood disorders and cardiovascular diseases<sup>68</sup>. Elevated levels of pro-inflammatory cytokines, such as IL-6 and TNF- $\alpha$ , are found in patients with depression and have been linked to increased cardiovascular risk<sup>69</sup>. These inflammatory markers contribute to endothelial dysfunction, a key factor in the development of atherosclerosis and other cardiovascular conditions<sup>70</sup>. Oxidative stress, characterized by an imbalance between reactive oxygen species and antioxidant defenses, further contributes to endothelial dysfunction and atherogenesis<sup>71</sup>. Autonomic dysfunction, including reduced heart rate variability and increased sympathetic nervous system activity, is a common feature in patients with mood disorders and is associated with adverse cardiovascular outcomes<sup>72</sup>.

Heart rate variability, a marker of autonomic balance, is often reduced in patients with depression and anxiety,

indicating impaired parasympathetic activity and increased cardiovascular risk<sup>73</sup>. Elevated cortisol levels, resulting from chronic HPA axis activation, contribute to hypertension, insulin resistance, and dyslipidemia, further increasing cardiovascular risk<sup>74</sup>. Catecholamines, including norepinephrine and epinephrine, play a critical role in the stress response and have been implicated in the pathophysiology of both mood disorders and cardiovascular diseases<sup>75</sup>. Elevated levels of these stress hormones can lead to increased heart rate, vasoconstriction, and hypertension, contributing to cardiovascular morbidity and mortality<sup>76</sup>.

Serotonin, a key neurotransmitter involved in mood regulation, also affects cardiovascular health through its effects on platelet aggregation and vascular tone<sup>77</sup>. Genetic factors and epigenetic changes play a significant role in the comorbidity of mood disorders and cardiovascular diseases<sup>78</sup>. Polymorphisms in genes related to the HPA axis, inflammatory pathways, and neurotransmitter systems have been associated with increased risk of both conditions<sup>79</sup>. Epigenetic modifications, such as DNA methylation and histone acetylation, can alter gene expression in response to environmental stressors, contributing to the pathogenesis of mood disorders and cardiovascular diseases<sup>80</sup>.

Social determinants of health, including socioeconomic status, access to healthcare, and social support, significantly impact the cardiovascular health of individuals with mood disorders<sup>81</sup>. Low socioeconomic status is associated with increased stress, poor health behaviors, and limited access to healthcare, all of which contribute to cardiovascular risk<sup>82</sup>. Social support systems play a crucial role in managing both mood disorders

and cardiovascular health, with evidence suggesting that strong social networks can mitigate the effects of stress and improve health outcomes<sup>83</sup>. Psychological interventions, such as cognitive-behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR), have been shown to improve mood and reduce cardiovascular risk in patients with mood disorders<sup>84</sup>. CBT, which focuses on identifying and changing negative thought patterns and behaviors, has been shown to be effective in treating depression and anxiety and improving cardiovascular health<sup>85</sup>. MBSR, which involves mindfulness meditation and stress reduction techniques, can help reduce stress and improve cardiovascular outcomes in individuals with mood disorders<sup>86</sup>.

## CONCLUSION

The complex interactions between mood disorders and cardiovascular diseases underscore the need for integrated and comprehensive care approaches. By understanding the underlying biological mechanisms, shared risk factors, and effective management strategies, healthcare providers can better address the needs of individuals with comorbid mood disorders and cardiovascular diseases. Future research should continue to explore the intricate relationships between these conditions, with the goal of developing targeted interventions that improve both mental and cardiovascular health outcomes. This review highlights the critical importance of addressing both mental and physical health in a holistic and integrated manner to achieve optimal health outcomes for individuals with mood disorders and cardiovascular diseases.

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