



Literature Review: Major Depression with Somatic Comorbidities

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Abstract

Major depressive disorder (MDD) is a mood disorder often accompanied by somatic symptoms and chronic physical illness. Complaints such as pain, fatigue, insomnia, headaches, and palpitations are often the primary reasons patients seek medical help, often resulting in a delayed diagnosis. This study aims to determine the relationship between major depression and somatic comorbidities based on published research. The method used was a literature review with a narrative review design. Articles were searched in the PubMed and Google Scholar databases using the keywords "major depressive disorder," "major depression," and "somatic comorbidities." A selection process based on inclusion and exclusion criteria yielded 12 articles published between 2016 and 2026. The review results indicate that major depression is significantly associated with somatic symptoms and chronic physical illnesses such as cardiovascular disease, diabetes mellitus, heart failure, migraines, and metabolic disorders. This relationship is bidirectional, with physical illnesses increasing the risk of depression and depression worsening physical conditions. Management of major depression requires a holistic approach through pharmacotherapy, psychotherapy, and optimal management of physical illnesses.

Introduction

Depression is a mood disorder characterized by depressed mood, loss of interest and enjoyment, and loss of energy, including fatigue and decreased activity. According to the PPDGJ-III, depression is a mood disorder characterized by depressed mood, loss of interest and enjoyment, and loss of energy, characterized by fatigue and decreased activity (Muhariyono & Fitriana, 2024; Daulay & Husada, 2023). Additionally, other symptoms include decreased concentration, low self-confidence, feelings of guilt and worthlessness, pessimism, self-harm, disturbed sleep, and decreased appetite (Kusuma, 2020; Munirah, 2024; Park et al., 2025).

Depression is more common in women than in men, with prevalence increasing with age, particularly in women aged 40–50 years (Suman et al., 2023; Hurtado et al., 2024; Blanchflower et al., 2024). Epidemiological studies indicate that approximately 10–15% of women in this age group may experience depression, with factors such as the loss of a family member or parent, life stress, and hormonal changes being significant triggers (Aqila &

Prasetya, 2025; Hulubă et al., 2025; Abed & Hussein, 2025; Bertollo et al., 2024; Dag & Deger, 2025).

Somatic Symptom Disorder (SSD) is a psychological condition characterized by excessive health concerns about one or more physical symptoms, unexplained by a medical condition or disproportionate to the underlying cause (Löwe et al., 2022; Tonge et al., 2022; Hu et al., 2025; Alqahtani 2025).

Several studies have shown a significant association between depression and various somatic diseases. In patients with diabetes mellitus, the risk of depression is reported to be twice as high as in individuals without diabetes, which impacts poor glycemic control and increases complications (Susanti, 2025; Horsbøl et al., 2024; Fanelli et al., 2025; Tomic et al., 2022; Cai et al., 2024).

Furthermore, in patients with coronary heart disease, depression has been shown to be associated with a decreased quality of life and is influenced by psychological factors such as anxiety. A similar condition has also been found in patients with chronic kidney disease undergoing hemodialysis, where depression is a common psychological problem and is associated with sleep disturbances and a decreased quality of life (Nuraeni & Mirwanti; Dewi & Hendrati, 2022).

Methods

This study employed a literature review using a narrative review approach to summarize and synthesize current evidence regarding the relationship between major depressive disorder (MDD) and somatic comorbidities. A literature search was conducted using the PubMed and Google Scholar databases with the keywords "major depressive disorder," "major depression," and "somatic comorbidities."

The inclusion criteria were: (1) full-text articles published in English between 2019 and 2026; (2) studies investigating the association between major depressive disorder and somatic symptoms or somatic/physical comorbidities; and (3) articles available through PubMed or Google Scholar. Articles were excluded if they were duplicates, unrelated to the review topic, unavailable in full text, or did not meet the inclusion criteria.

The article selection process involved screening titles and abstracts, followed by full-text eligibility assessment. A total of 165 articles were initially identified. After screening and applying the eligibility criteria, 153 articles were excluded, leaving 12 studies for qualitative review.

Data extracted from each study included the author, publication year, journal, study design, study characteristics, and main findings. The selected studies were then analyzed using a narrative synthesis approach by comparing similarities and differences in study findings to identify the relationship between major depressive disorder and somatic comorbidities.

Result and Discussion

Article Selection Process

Based on the search results, 165 articles were obtained from the keywords "major depression" and "somatic comorbidities." All journals were included in the search and screening. The researchers then screened the titles and abstracts of the articles. During this screening stage, 153 articles were excluded due to research that did not meet the inclusion criteria or was published more than 10 years ago. Ultimately, 12 articles remained, meeting the inclusion criteria, and will be used for this literature review.

Article Description

Table 1. Article Description

Steffen et al.	2020	Google Scholar
Lallukka et al.	2019	Google Scholar
Shahini et al.	2023	Google Scholar
Subinuer Yiming et al.	2025	PubMed
Milan Latas et al.	2024	PubMed
Michael Berk et al.	2023	PubMed
Thomas Muller et al.	2024	PubMed
Federico Triolo et al.	2024	Google Scholar
Gernot Fugger et al.	2020	PubMed
Nilüfer Subaşı Tekintaş et al.	2022	PubMed
Tummala Sri et al.	2026	PubMed
Phi Nguyen Yen Ho et al.	2023	PubMed

A total of 12 articles were reviewed and analyzed from various national and international journal search sites. The research articles ranged from 2016 to the most recent, 2026.

Based on the summary results after conducting the search, 12 journals were found that were related to major depression with somatic comorbidities:

Table 1. Characteristics and Main Findings of the Included Studies

Author	Year	Title	Journal	Study Design	Main Findings
Steffen et al.	2020	Mental and Somatic Comorbidity of Depression	BMC Psychiatry	Cross-sectional	Depression was significantly associated with various somatic diseases, particularly cardiovascular and metabolic disorders.
Lallukka et al.	2019	Co-occurrence of Depressive and Somatic Symptoms	BMC Psychiatry	Cross-sectional	Depressive and somatic symptoms frequently co-occur in the general population.
Shahini et al.	2023	The Comorbidity of Somatic Symptom and Major Depressive Disorders in the Times of COVID-19 Lockdown in Adolescence: A Case-Report Study	SAGE Open Medical Case Reports	Case Report	An adolescent presenting with physical pain without an organic cause was diagnosed with severe depression and somatic symptom disorder. Cognitive behavioral therapy (CBT) and pharmacological treatment improved the patient's condition.

Subinuer Yiming et al.	2025	Longitudinal Association Between Somatic Symptoms and Suicidal Ideation in Adults with Major Depressive Disorder	Frontiers in Psychiatry	Cohort	Somatic symptoms, including pain, fatigue, and autonomic symptoms, were significantly associated with increased suicidal ideation throughout the 72-week follow-up, demonstrating a nonlinear relationship.
Latas et al.	2024	Diagnostic Psychiatric and Somatic Comorbidity in Patients with Depression in the Western Balkan Countries	PLOS ONE	Cross-sectional	Psychiatric comorbidities (72.5%), particularly anxiety and sleep disorders, and somatic comorbidities (80.3%), especially cardiovascular disease, metabolic disorders, and chronic pain, were highly prevalent among patients with depression.
Berk et al.	2023	Comorbidity Between Major Depressive Disorder and Physical Diseases	World Psychiatry	Narrative Review	Major depressive disorder and physical illnesses exhibit a bidirectional relationship, leading to poorer clinical outcomes, higher mortality, and greater treatment complexity due to biological, social, and therapeutic interactions.
Muller et al.	2024	Somatic Symptom Profile in Patients with Chronic Heart Failure with and Without	Frontiers in Psychiatry	Cross-sectional	Patients with chronic heart failure and comorbid depression experienced significantly more severe somatic symptoms than those without depression.

		Depressive Comorbidity			
Triolo et al.	2024	Somatic Disease Burden and Depression Risk in Late Life: A Community-Based Study	Epidemiology and Psychiatric Sciences	Cohort	Multimorbidity significantly increased the risk of depression in a dose-response pattern, particularly among patients with cardiometabolic, thyroid/musculoskeletal, and sensory/anemia disease clusters.
Fugger et al.	2020	Clinical Correlates and Outcome of Major Depressive Disorder and Comorbid Migraine	International Journal of Neuropsychopharmacology	Cross-sectional	Migraine affected 11.1% of patients with major depression and was associated with female sex, younger age, greater disability, asthma, and differences in treatment patterns.
Tekintas et al.	2022	Functional Somatic Symptoms and Their Predictors in Patients with Major Depressive Disorder and Fibromyalgia Syndrome	Noropsikiyatri Arsivi	Cross-sectional	In major depressive disorder, somatization was associated with age, anxiety, and alexithymia, whereas in fibromyalgia syndrome it was primarily associated with anxiety.
Sri et al.	2026	The Impact of Major Depressive Disorder on Somatic and Psychiatric Outcomes Following Elective Single-Level Lumbar Fusion: A Propensity Score-Matched Analysis	SAGE Publications	Cohort	Patients with major depressive disorder had higher risks of psychiatric disorders, somatic symptoms, and hospital readmission after lumbar fusion surgery, although mortality and reoperation rates were not significantly different.

Ho et al.	2023	Somatic Symptoms in Major Depressive Disorder: A Cross-sectional Study in a Mental Health Setting, Vietnam	Journal of University of Medicine and Pharmacy at Ho Chi Minh City	Cross-sectional	Nearly all patients with major depressive disorder (99.7%) experienced somatic symptoms. Fatigue, insomnia, palpitations, headache, and dizziness were the most common symptoms, and the number of somatic symptoms increased with depression severity.
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Based on an analysis of 12 articles, major depressive disorder (MDD) is closely linked to somatic symptoms and various physical illnesses. Patients with depression experience not only mood disturbances but also physical complaints such as pain, fatigue, insomnia, headaches, gastrointestinal disorders, and musculoskeletal disorders, which often lead to delayed diagnosis.

Steffen's (2020) study, *Mental and Somatic Comorbidity of Depression*, shows that depression is significantly associated with cardiovascular disease, hypertension, diabetes mellitus, and metabolic disorders. This relationship is influenced by hormonal changes, systemic inflammation, and neuroendocrine dysregulation, which worsen both physical and mental health conditions. In the study *Co-occurrence of Depressive and Somatic Symptoms*, Lallukka (2019) found that depressive and somatic symptoms frequently coexist in the general population. This condition causes patients to seek treatment more frequently at general healthcare facilities, often delaying the diagnosis of depression (Steffen et al., 2020; Lallukka et al., 2019).

Shahini (2023), in the study *The Comorbidity of Somatic Symptom and Major Depressive Disorders in the Times of COVID-19 Lockdown in Adolescence*, reported a case of a patient with physical pain without an organic disorder who turned out to have major depression and a somatic symptom disorder. Pharmacological therapy and cognitive behavioral therapy (CBT) resulted in significant improvement. The study *Longitudinal Association between Somatic Symptoms and Suicidal Ideation in Adults with Major Depressive Disorder* by Yiming et al. (2025) showed that somatic symptoms such as pain, fatigue, and sleep disturbances were associated with increased suicidal ideation in patients with MDD. Latas et al. (2024), in the study *Diagnostic Psychiatric and Somatic Comorbidity in Patients with Depression in the Western Balkan Countries*, found a high prevalence of psychiatric and non-psychiatric comorbidities in depressed patients, particularly anxiety disorders, cardiovascular disease, and chronic pain (Shahini et al., 2023; Yiming et al., 2025; Latas et al., 2024).

In the study *Comorbidity between Major Depressive Disorder and Physical Diseases*, Berk et al. (2023) explained that the relationship between depression and physical illness is bidirectional. Chronic illness can increase the risk of depression, while depression can worsen physical conditions through sleep disturbances, chronic inflammation, and poor adherence to therapy. In the study *Somatic Symptom Profile in Patients with Chronic Heart Failure with and without Depressive Comorbidity*, Muller et al. (2024) found that heart failure patients with comorbid depression experienced more severe somatic symptoms and a lower quality of life than patients without depression. The study *Somatic Disease Burden and Depression Risk in Late Life: A Community-Based Study* by Triolo et al. (2024) showed that the more physical

illnesses a person has, the higher the risk of developing depression, especially in older age (Berk et al., 2023; Muller et al., 2024; Triolo et al., 2024).

Fugger et al. (2020), in the study *Clinical Correlates and Outcome of Major Depressive Disorder and Comorbid Migraine*, found that migraines are more common in patients with major depression and are associated with higher levels of disability. Tekintaş et al. (2022), in the study *Functional Somatic Symptoms and Their Predictors in Patients with Major Depressive Disorder and Fibromyalgia Syndrome*, stated that somatization is influenced by anxiety, age, and alexithymia, so psychological approaches such as CBT are important for reducing somatic symptoms. The study *Somatic Symptoms in Major Depressive Disorder: A Cross-sectional Study in a Mental Health Setting, Vietnam* by Ho et al. (2023) showed that almost all MDD patients experience somatic symptoms, particularly fatigue, insomnia, and headaches. The number of somatic symptoms is also related to the severity of depression (Fugger et al., 2020; Tekintaş et al., 2022; Ho et al., 2023).

Overall, somatic symptoms are an important part of MDD manifestations and significantly impact patients' quality of life. Treatment of depression requires a holistic approach through a combination of pharmacotherapy, psychotherapy, and integrated management of physical illnesses for more effective diagnosis and therapy (Berk et al., 2023; Steffen et al., 2020).

Major depressive disorder (MDD) is a mood disorder characterized by feelings of profound sadness, loss of interest in daily activities, sleep disturbances, changes in appetite, fatigue, decreased concentration, and even suicidal ideation. Depression not only impacts the patient's psychological well-being but also impacts social and cognitive functioning and overall quality of life. According to the WHO, depression is one of the leading causes of disability worldwide and is a growing global health problem. In Indonesia, the prevalence of depression in those aged 15 years and older reaches approximately 6.1%, with higher rates among women, the elderly, and urban populations. This high incidence indicates that depression is a public health problem that requires serious attention in terms of diagnosis and management (Munirah, 2024).

The relationship between depression and physical illness is bidirectional. Chronic physical illnesses such as diabetes mellitus, coronary heart disease, chronic kidney failure, hypertension, arthritis, cancer, and chronic respiratory disorders can be triggers for depression due to activity limitations, prolonged pain, psychological stress, and hormonal changes experienced by patients. Conversely, depression can exacerbate the course of physical illness through decreased adherence to therapy, sleep disturbances, decreased physical activity, changes in dietary patterns, and increased systemic inflammation. This condition significantly decreases the patient's quality of life, increases hospitalization rates, increases medical costs, and increases mortality compared to patients without depression (Berk et al., 2023).

In patients with somatic symptom disorder (SSD), the dominant physical complaints are often not accompanied by a clear organic disorder, yet they cause significant distress to the patient. This condition can lead to doctor shopping, repeated examinations, and prolonged treatment without optimal results. Shahini et al. (2023) reported the case of a patient with physical pain without an organic basis who was found to have severe depression and a somatic symptom disorder. After receiving pharmacological therapy and cognitive behavioral therapy (CBT), the patient's condition showed significant improvement. These findings emphasize the importance of psychiatric evaluation in patients with persistent somatic complaints to ensure a more timely diagnosis and more effective therapy (Shahini et al., 2023).

The pathophysiology of depression also supports a close relationship with somatic comorbidities. Dysregulation of neurotransmitters such as serotonin, norepinephrine, dopamine, GABA, and glutamate plays a role in the development of depressive symptoms and accompanying physical complaints. Furthermore, hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis leads to increased cortisol levels due to chronic stress, which impacts

emotional regulation, the immune system, and organ function. Activation of the inflammatory system through increased proinflammatory cytokines such as IL-6, TNF- α , and CRP also contributes to neurotransmitter depletion and worsening depression. Decreased neuroplasticity, hippocampal atrophy, and low levels of brain-derived neurotrophic factor (BDNF) further exacerbate brain dysfunction in depressed patients (Berk et al., 2023).

Conclusion

Based on the results of a literature review of 12 analyzed journals, it can be concluded that major depressive disorder (MDD), or severe depression, is closely related to somatic comorbidities, both in the form of somatic symptoms and chronic physical illnesses. Symptoms such as pain, fatigue, insomnia, palpitations, headaches, dizziness, and gastrointestinal disorders are common manifestations in patients with depression and are often the primary complaints, leading to delayed diagnosis. Furthermore, depression is often found alongside chronic diseases such as cardiovascular disease, diabetes mellitus, hypertension, heart failure, migraines, and metabolic disorders, which mutually exacerbate the patient's condition. This relationship is bidirectional, where physical illness can trigger depression and depression can exacerbate physical illness through biological, psychological, and social changes. Therefore, the management of major depression requires a holistic and multidisciplinary approach through a combination of pharmacological therapy, psychotherapy, and optimal management of physical illnesses to improve the patient's quality of life and improve long-term prognosis.

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