International Journal of Health Science & Biomedicine (IJHSB)

REVIEW ARTICLE OPEN ACCESS

Depression in Nutrition-Related Pathologies: Mechanisms, Clinical Interactions and Emerging Therapeutic Strategies

Ana-Maria Dumitrescu[1*], Anca Sava[1], Nicoleta Loredana Hilițanu[2], Lucia Corina Dima Cozma[3], Laurian Frâncu[1], Cătălin Alexandru Pohaci-Antonesei[4], Luiza-Simona Pohaci-Antonesei[4], Mihaela Mitrea[1], Laura Marieta Alexa[5], Roxana Florentina Gavril[1], Liviu Ciprian Gavril[1]

[1]Department of Morpho-Functional Sciences I, *Grigore T. Popa* University of Medicine and Pharmacy, Iasi, Romania

[2]Department of Preventive Medicine and Interdisciplinarity, *Grigore T. Popa* University of Medicine and Pharmacy, Iași, Romania

[3]Department of Medicals I, *Grigore T. Popa* University of Medicine and Pharmacy, Iasi, Romania

[4]Department of Morpho-Functional Sciences II, *Grigore T. Popa* University of Medicine and Pharmacy, Iasi, Romania

[5]*Grigore T. Popa* University of Medicine and Pharmacy Iasi, Romania

Correspondence: Ana-Maria Dumitrescu, Department of Morpho-Functional Sciences I, *Grigore T. Popa* University of Medicine and Pharmacy, Iasi, Romania

Citation: Dumitrescu AM, Sava A, Hilițanu NL, Cozma LCD, Frâncu L, et al (2026). Depression in Nutrition-Related Pathologies: Mechanisms, Clinical Interactions and Emerging Therapeutic Strategies. Int J Health Sci Biomed. 3(2): 1-4. DOI: 10.5281/zenodo.19712842

Received Date: 2026-03-2, **Accepted Date:** 2026-03-23, **Published Date:** 2026-03-30

Keywords: Depression; Nutrition; Inflammation; Gut–brain axis; Obesity; Intermittent fasting

Abstract

Depression is a leading cause of global disability and is increasingly recognized as a multifactorial disorder influenced by biological, psychological, and lifestyle-related factors, including nutrition. This narrative review examines the relationship between depression and nutrition-related pathologies, such as obesity, type 2 diabetes mellitus, cardiovascular disease, and gout, with a focus on shared pathophysiological mechanisms and therapeutic strategies.A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science to identify studies investigating the association between depression, dietary factors, metabolic and inflammatory disorders, and emerging nutritional interventions. The initial search yielded approximately 300 records. Following title and abstract screening, 110 articles were selected for full-text assessment, of which 16 studies were included in the final analysis based on relevance and methodological quality.Key mechanisms linking depression and nutrition-related disorders include chronic low-grade inflammation, oxidative stress, metabolic dysfunction, and alterations in the gut–brain axis. These processes contribute to impaired neurotransmission, reduced neuroplasticity, and increased vulnerability to depressive symptoms. Evidence suggests that dietary patterns play a significant role in mental health outcomes, with Western diets associated with increased risk of depression, while Mediterranean and anti-inflammatory dietary patterns appear protective.Emerging therapeutic strategies, including microbiota-targeted interventions and metabolic approaches such as intermittent fasting, show potential benefits in modulating mood and cognitive function. Integrating nutritional strategies with conventional treatments may enhance clinical outcomes. Future research should focus on personalized, evidence-based dietary interventions in the management of depression and associated metabolic disorders.

Introduction

Depression represents one of the leading causes of disability worldwide and constitutes a major public health concern, affecting more than 280 million individuals globally [1]. It is a multifactorial disorder characterized by persistent low mood, anhedonia, cognitive impairment, and functional decline, with profound social and economic consequences. Traditionally, depression has been conceptualized primarily through neurochemical models, particularly involving monoaminergic dysfunction. However, contemporary research has broadened this perspective to include complex interactions between biological, psychological, environmental, and lifestyle-related factors.

In recent years, increasing attention has been directed toward the role of nutrition in mental health, leading to the emergence of the interdisciplinary field of nutritional psychiatry. This field investigates how dietary patterns, nutrient intake, and metabolic processes influence brain function and emotional regulation. A growing body of epidemiological and clinical evidence suggests that poor dietary habits-particularly those characterized by high consumption of ultra-processed foods, refined sugars, and saturated fats-are associated with an increased risk of depressive symptoms. Conversely, adherence to healthier dietary patterns, such as the Mediterranean diet, appears to exert a protective effect, potentially through anti-inflammatory, antioxidant, and neuroprotective mechanisms [2].

Beyond these associations, depression frequently coexists with a wide range of metabolic and inflammatory conditions, including obesity, insulin resistance, type 2 diabetes mellitus, and cardiovascular disease. These comorbidities are highly prevalent and often interdependent, suggesting the presence of shared pathophysiological mechanisms rather than simple coincidence.

Citation: Dumitrescu AM, Sava A, Hilițanu NL, Cozma LCD, Frâncu L, et al (2026). Depression in Nutrition-Related Pathologies: Mechanisms, Clinical Interactions and Emerging Therapeutic Strategies. Int J Health Sci Biomed. 3(2): 1-4. DOI: 10.5281/zenodo.19712842

Chronic low-grade inflammation, oxidative stress, endocrine dysregulation, and alterations in energy metabolism have been identified as key overlapping pathways linking these conditions [3]. Such mechanisms may influence central nervous system function by altering neurotransmitter synthesis, impairing neuroplasticity, and disrupting neural network connectivity.

The relationship between depression and metabolic disorders is increasingly recognized as bidirectional. On one hand, metabolic abnormalities-such as insulin resistance, dyslipidemia, and adipose tissue–driven inflammation-may contribute to the development and persistence of depressive symptoms. On the other hand, depression itself can promote maladaptive lifestyle behaviors, including poor dietary choices, physical inactivity, and sleep disturbances, thereby exacerbating metabolic dysfunction [4]. This reciprocal interaction creates a self-perpetuating cycle that complicates both prevention and treatment strategies.

In addition to systemic metabolic alterations, emerging research highlights the critical role of the gut–brain axis in mediating the effects of nutrition on mental health. The gut microbiota, influenced by dietary intake, interacts with the central nervous system through neural, immune, and endocrine pathways. Dysbiosis, or imbalance in microbial composition, has been associated with increased intestinal permeability, systemic inflammation, and altered neurotransmitter production, all of which may contribute to depressive symptomatology [5].

Furthermore, specific nutrition-related pathologies-such as gout, characterized by hyperuricemia and inflammation; obesity, marked by adipose tissue dysfunction; and type 2 diabetes, defined by impaired glucose metabolism-provide clinically relevant models through which the interaction between metabolic disturbances and depression can be examined. These conditions illustrate how dietary factors and metabolic pathways intersect with neurobiological processes involved in mood regulation [3], [6].

From a therapeutic perspective, these insights have significant implications. Traditional approaches to depression management, including pharmacotherapy and psychotherapy, may benefit from integration with nutritional and metabolic interventions. Strategies such as anti-inflammatory dietary patterns, micronutrient optimization, modulation of gut microbiota, and metabolic interventions like intermittent fasting have been proposed as potential adjunctive treatments. Although evidence supporting these approaches is still evolving, they represent promising avenues for more comprehensive and personalized care [7].

Material and Method

This study was conducted as a narrative review to synthesize current evidence on the relationship between depression and nutrition-related pathologies, focusing on pathophysiological mechanisms, clinical interactions, and therapeutic strategies. Boolean operators (“AND,” “OR”) were used to combine search terms and optimize the retrieval of relevant literature. Related keywords were grouped using parentheses to broaden the search strategy while maintaining specificity. For instance, search queries included combinations such as: (“depression” AND “nutrition”) OR (“depression” AND “inflammation”) OR (“gut–brain axis” AND “mental health”) OR (“obesity” OR “type 2 diabetes” AND “depression”).The initial search yielded 300 records. Following title and abstract screening, 110 articles were selected for full-text assessment. Of these, 16most relevant studies were included in the final analysis, including systematic reviews, meta-analyses, and clinical research, based on their contribution to understanding the link between metabolic, inflammatory, and nutritional factors in depression.

Findings were analyzed qualitatively and grouped into thematic categories, including biological mechanisms, associated pathologies, and emerging therapeutic approaches.

Results and Discussion

Pathophysiological Links Between Nutrition and Depression

Neuroinflammation and Diet

Chronic low-grade inflammation is a central feature of both depression and nutrition-related disorders. Diets high in processed foods and saturated fats increase inflammatory markers, whereas anti-inflammatory diets may mitigate this effect. Studies have shown that individuals consuming highly inflammatory diets have more than double the odds of depression compared to those with anti-inflammatory dietary patterns [8].

Gut–Brain Axis Dysfunction

The gut–brain axis represents a bidirectional communication system involving neural, endocrine, and immune pathways. Nutritional factors directly influence gut microbiota composition, which in turn affects neurotransmitter production and immune responses. Alterations in gut microbiota have been linked to depressive symptoms through mechanisms involving serotonin synthesis and HPA axis activation [9].

Dietary patterns rich in fiber, probiotics, and omega-3 fatty acids enhance microbial diversity and reduce systemic inflammation, potentially improving mood regulation [9].

Neurotransmitter and Metabolic Pathways

Nutritional deficiencies, particularly in essential fatty acids, vitamins, and amino acids, can impair neurotransmitter synthesis. For example, omega-3 fatty acids have demonstrated small-to-moderate antidepressant effects, particularly as adjunctive therapy [10].

Moreover, the brain’s high metabolic demand makes it especially vulnerable to nutritional imbalance, further linking dietary status with cognitive and emotional function [10].

Depression in Nutrition-Related Pathologies

Obesity and Metabolic Syndrome

Obesity is strongly associated with depression, forming a well-documented bidirectional relationship that involves both biological and behavioral mechanisms. From a pathophysiological perspective, adipose tissue is no longer considered a passive energy storage site but rather an active endocrine organ that secretes a wide range of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). These mediators contribute to chronic low-grade inflammation, which has been implicated in the development of depressive symptoms through its effects on neurotransmitter metabolism, neuroendocrine function, and synaptic plasticity [3].

In addition to inflammation, metabolic syndrome-characterized by central obesity, insulin resistance, dyslipidemia, and hypertension-further amplifies the risk of depression. Insulin resistance, in particular, has been associated with impaired glucose utilization in the brain, altered dopaminergic signaling, and reduced neurogenesis, all of which may negatively impact mood regulation. Moreover, psychosocial factors such as stigma, reduced self-esteem, and decreased physical activity often coexist in individuals with obesity, reinforcing the cycle

Citation: Dumitrescu AM, Sava A, Hiliţanu NL, Cozma LCD, Frâncu L, et al (2026). Depression in Nutrition-Related Pathologies: Mechanisms, Clinical Interactions and Emerging Therapeutic Strategies. Int J Health Sci Biomed. 3(2): 1-4. DOI: 10.5281/zenodo.19712842

between metabolic dysfunction and depression [3].

Eating Disorders and Nutritional Deficiency

Eating disorders, including restrictive eating patterns, anorexia nervosa, bulimia nervosa, and binge-eating disorder, represent a critical interface between nutrition and mental health. These conditions are frequently accompanied by depressive symptoms, which may arise both as a cause and a consequence of disordered eating behaviors [11, 12].
Nutritional deficiencies play a central role in this interaction. Inadequate intake of essential nutrients-such as omega-3 fatty acids, B vitamins, iron, and zinc-can impair neurotransmitter synthesis, particularly serotonin, dopamine, and norepinephrine, thereby contributing to mood disturbances. Additionally, severe caloric restriction may lead to hormonal imbalances, including alterations in leptin and cortisol levels, which further affect emotional regulation [11. 12].

Conversely, binge eating and excessive consumption of highly processed foods may promote systemic inflammation and metabolic dysregulation, exacerbating depressive symptoms. Behavioral factors, including loss of control over eating, body image dissatisfaction, and social withdrawal, further contribute to psychological distress, highlighting the complex and multifactorial nature of this relationship [11, 12].

Chronic Inflammatory Diseases

Chronic inflammatory diseases, such as cardiovascular disease and type 2 diabetes mellitus, are frequently accompanied by depressive symptoms, reflecting shared underlying biological pathways. These conditions are characterized by persistent immune activation, oxidative stress, and endothelial dysfunction, all of which may influence central nervous system function and emotional regulation [3].
In cardiovascular disease, endothelial dysfunction and reduced cerebral perfusion may impair brain function, while systemic inflammation contributes to alterations in neurotransmitter systems and neuroplasticity. Similarly, in type 2 diabetes, chronic hyperglycemia and insulin resistance lead to oxidative stress, mitochondrial dysfunction, and microvascular damage, which can affect brain regions involved in mood regulation, including the hippocampus and prefrontal cortex [13].
Diet plays a significant role in modulating these processes. Diets high in saturated fats, refined carbohydrates, and ultra-processed foods promote inflammation and metabolic imbalance, whereas diets rich in antioxidants, fiber, and unsaturated fatty acids may exert protective effects. The coexistence of depression with chronic inflammatory diseases not only worsens clinical outcomes but also complicates disease management, as depressive symptoms may reduce treatment adherence and lifestyle modification [8].

Gout and Hyperuricemia (Optional but Recommended Addition)

Gout, a metabolic disorder characterized by elevated serum uric acid levels and deposition of monosodium urate crystals, represents an additional example of a nutrition-related pathology associated with depression. The condition is strongly influenced by dietary factors, including high intake of purine-rich foods and fructose-containing beverages.
The inflammatory response in gout, mediated by activation of the NLRP3 inflammasome and release of interleukin-1β, contributes to systemic inflammation, which may also impact neurobiological processes involved in mood regulation. Clinically, recurrent episodes of severe pain, functional impairment, and lifestyle restrictions may increase the risk of depressive symptoms. Although the association between gout and depression is less extensively studied compared to other metabolic disorders, emerging evidence suggests a meaningful link that warrants further investigation [14].

Nutritional and Therapeutic Strategies

Dietary Patterns

Dietary patterns represent one of the most important modifiable factors influencing both physical and mental health. A growing body of evidence supports the role of whole-diet approaches, rather than isolated nutrients, in the prevention and management of depression. In particular, adherence to a Mediterranean dietary pattern-characterized by high intake of fruits, vegetables, whole grains, legumes, fish, nuts, and olive oil-has been consistently associated with a reduced risk of depressive symptoms [2].
The protective effects of such diets are likely mediated through multiple mechanisms, including reduction of systemic inflammation, improvement of metabolic parameters, and increased intake of essential micronutrients and bioactive compounds such as polyphenols and antioxidants. These components contribute to enhanced neuroplasticity, improved neurotransmitter synthesis, and reduced oxidative stress. In contrast, Western dietary patterns, rich in ultra-processed foods, refined sugars, and saturated fats, have been associated with increased risk of depression, possibly due to their pro-inflammatory and metabolically disruptive effects [2].

Anti-inflammatory Nutrition

Given the central role of chronic low-grade inflammation in the pathophysiology of depression, dietary strategies aimed at reducing inflammatory burden have gained significant attention. Anti-inflammatory nutrition focuses on the consumption of foods that modulate immune responses and reduce cytokine activity.Nutrients such as omega-3 fatty acids, found in fatty fish, have demonstrated anti-inflammatory properties and may support neuronal membrane integrity and neurotransmission. Similarly, diets rich in fruits, vegetables, and whole grains provide antioxidants and phytochemicals that counteract oxidative stress and inflammation. These dietary components may influence the production of pro-inflammatory cytokines, including IL-6 and TNF-α, which are implicated in depressive disorders [2],[10].
Furthermore, reducing the intake of pro-inflammatory foods-such as processed meats, refined carbohydrates, and trans fats-may contribute to improved mental health outcomes. Although evidence supports the association between anti-inflammatory diets and reduced depressive symptoms, further randomized controlled trials are needed to establish causality and optimal dietary interventions [10].

Microbiota-Based Interventions

The modulation of gut microbiota has emerged as a promising therapeutic strategy in the context of depression. The gut–brain axis provides a mechanistic framework through which dietary factors influence mental health, with the intestinal microbiota playing a central role in immune regulation, neurotransmitter production, and metabolic processes.Probiotics (live beneficial microorganisms), prebiotics (non-digestible fibers that stimulate microbial growth), and psychobiotics (microorganisms with potential mental health benefits) have been investigated for their role in improving depressive symptoms. These interventions may enhance gut barrier integrity, reduce systemic inflammation, and influence the synthesis of neurotransmitters such as serotonin and gamma-aminobutyric acid (GABA) [15]. Although early clinical

Citation: Dumitrescu AM, Sava A, Hiliţanu NL, Cozma LCD, Frâncu L, et al (2026). Depression in Nutrition-Related Pathologies: Mechanisms, Clinical Interactions and Emerging Therapeutic Strategies. Int J Health Sci Biomed. 3(2): 1-4. DOI: 10.5281/zenodo.19712842

studies suggest beneficial effects, the evidence remains heterogeneous, and further research is required to determine the most effective strains, dosages, and treatment durations. Nevertheless, microbiota-targeted therapies represent a promising adjunctive approach within the broader framework of nutritional psychiatry [15].

Intermittent Fasting and Metabolic Interventions

Intermittent fasting (IF) has gained increasing attention as a metabolic strategy with potential implications for mental health. IF encompasses various dietary patterns, including time-restricted feeding and alternate-day fasting, which aim to improve metabolic flexibility and reduce systemic inflammation. Several biological mechanisms may explain the potential benefits of IF in depression. Fasting periods have been associated with decreased inflammatory markers, enhanced mitochondrial function, and activation of autophagy, a cellular repair process that supports neuronal health. Additionally, IF may influence neurotransmitter systems by increasing levels of norepinephrine and dopamine, thereby improving mood, alertness, and cognitive performance. Moreover, intermittent fasting may positively affect the gut microbiota, promoting microbial diversity and improving gut–brain communication. Some evidence also suggests that IF may enhance stress resilience and regulate the hypothalamic–pituitary–adrenal (HPA) axis. However, clinical evidence remains limited, and the long-term effects and safety of IF, particularly in individuals with psychiatric conditions, require further investigation [7].

Integrative Treatment Models

Given the multifactorial nature of depression, integrative treatment approaches that combine nutritional, pharmacological, and psychotherapeutic strategies are increasingly recognized as optimal. Nutritional interventions should not be viewed as standalone treatments but rather as complementary components of a comprehensive care plan.Combining dietary modifications with antidepressant therapy and psychological interventions, such as cognitive-behavioral therapy, may enhance treatment efficacy and improve overall patient outcomes. Additionally, personalized approaches that consider individual metabolic profiles, lifestyle factors, and microbiota composition may further optimize therapeutic strategies.Such multidisciplinary models emphasize the importance of addressing both biological and behavioral determinants of depression, reflecting a more holistic understanding of the disorder [16].

Conclusion

Depression is increasingly recognized as a systemic disorder influenced by nutritional, metabolic, and inflammatory factors. The coexistence of depression with conditions such as obesity, diabetes, gout, and cardiovascular disease reflects shared pathophysiological mechanisms, including neuroinflammation, gut–brain axis dysfunction, and metabolic dysregulation. Nutritional interventions offer promising adjunctive strategies in the management of depression, particularly through anti-inflammatory dietary patterns and microbiota modulation. However, current evidence remains heterogeneous, and further high-quality randomized controlled trials are required.Future research should focus on personalized nutrition and integrative therapeutic approaches to improve clinical outcomes in patients with comorbid depression and nutrition-related pathologies.

References

1. World Health Organization (2017). Depression and other common mental disorders: Global health estimates. World Health Organization.
2. Firth J, Marx W, Dash S, Carney R, Teasdale SB, Solmi M et al. (2019). The effects of dietary improvement on symptoms of depression and anxiety: A meta-analysis of randomized controlled trials. Psychosom Med. 81:265–280.
3. Miller AH, Raison CL (2016). The role of inflammation in depression: From evolutionary imperative to modern treatment target. Nat Rev Immunol. 16:22–34.
4. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW et al. (2010). Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 67:220–229.
5. Cryan JF, O'Riordan KJ, Cowan CSM, Sandhu KV, Bastiaanssen TFS, Boehme M et al. (2019). The microbiota-gut-brain axis. Physiol Rev. 99:1877–2013.
6. Dandona P, Aljada A, Bandyopadhyay A (2004). Inflammation: The link between insulin resistance, obesity and diabetes. Trends Immunol. 25:4–7.
7. Mattson MP, Longo VD, Harvie M (2017). Impact of intermittent fasting on health and disease processes. Ageing Res Rev. 39:46–58.
8. Lucas M, Chocano-Bedoya P, Schulze MB, Mirzaei F, O'Reilly EJ, Okereke OI et al. (2014). Inflammatory dietary pattern and risk of depression among women. Brain Behav Immun. 36:46–53.
9. Mayer EA, Knight R, Mazmanian SK, Cryan JF, Tillisch K (2014). Gut microbes and the brain: Paradigm shift in neuroscience. J Neurosci. 34:15490–15496.
10. Grosso G, Galvano F, Marventano S, Malaguarnera M, Bucolo C, Drago F et al. (2014). Omega-3 fatty acids and depression: Scientific evidence and biological mechanisms. Oxid Med Cell Longev. 2014:313570.
11. Giel KE, Bulik CM, Fernandez-Aranda F, Hay P, Keski-Rahkonen A, Schag K et al. (2022). Binge eating disorder. Nat Rev Dis Primers. 8:16.
12. El Ghoch M, Soave F, Calugi S, Dalle Grave R (2013). Eating disorders, physical fitness and sport performance: A systematic review. Nutrients. 5:5140–5160.
13. Whooley MA (2006). Depression and cardiovascular disease: Healing the broken-hearted. JAMA. 295:2874–2881.
14. Du L, Zong Y, Li H, Wang Q, Xie L, Yang B et al. (2024). Hyperuricemia and its related diseases: Mechanisms and advances in therapy. Signal Transduct Target Ther. 9:212.
15. Cryan JF, Dinan TG (2012). Mind-altering microorganisms: The impact of the gut microbiota on brain and behaviour. Nat Rev Neurosci. 13:701–712.
16. Kris-Etherton PM, Petersen KS, Hibbeln JR, Hurley D, Kolick V, Peoples S et al. (2021). Nutrition and behavioral health disorders: Depression and anxiety. Nutr Rev. 79:247–260.

Citation: Dumitrescu AM, Sava A, Hiliţanu NL, Cozma LCD, Frâncu L, et al (2026). Depression in Nutrition-Related Pathologies: Mechanisms, Clinical Interactions and Emerging Therapeutic Strategies. Int J Health Sci Biomed. 3(2): 1-4. DOI: 10.5281/zenodo.19712842