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Nourish to flourish: Unlock mental wellness through nutrition

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Abstract
Depression and anxiety are two of the most common mental health disorders and adversely affect one in five individuals. These disorders can produce a large, long-lasting decrease in health and functioning. While depression and anxiety can be partially managed by psychotherapy and medications, many people do not experience relief from their symptoms and may even experience symptom returns. Long-term dietary habits can provide mental health benefits by acting on multiple different pathways, as opposed to a single nutrient. Refined carbohydrate diets and high sugar diets lead to increased stress response and dysregulated glycemic control, and subsequently cause mood dysregulation. Poor diet can disrupt homeostasis and cause immune system activation that leads to symptoms of anxiety and depression. The gut-brain axis is also impacted by diet. An imbalance in gut microbiota can lead to activation of inflammatory pathways and production of neuroactive compounds. Diets consisting of healthy fats and fiber protect gut microbiota and brain function. Selecting a healthy diet can significantly improve depression and anxiety symptoms and may be an inexpensive supplement to care for patients with these disorders.

Keywords: Depression, anxiety, dietary pattersn, gut-brain axis, glycemic regulation, microbiota

Introduction
Depression and anxiety disorders result in health and economic consequences worldwide and have a significant impact on the quality of life by ranking high among disability-adjusted life years (DALYs) (World Health Organization [WHO], 2021 [1]; Global Burden of Disease [GBD], 2019). The Global Burden of Disease estimates depression and anxiety disorders to rank highly among the causes of DALYs, afflicting over 300 million people across the globe. Subclinical variants of depression and anxiety have been reported to represent a spectrum of difficulties in functioning and reduced quality of life among members of the general population (Steel *et al*., 2014) [3]. Mood disorders are a serious global health problem that contributes to the burden of disability-adjusted life years, and consequently, adversely affects health and economics (World Health Organization [WHO], 2021 [1]; Global Burden of Disease [GBD], 2019). While groundbreaking advances have been made in developing pharmacological and psychotherapeutic interventions, many patients experience unsatisfactory treatment outcomes. The challenge of partial remissions, relapses, and the chronic nature of mood disorders demonstrates the need for seeking new strategies beyond classical interventions. There are substantial data demonstrating the importance of diet in mental health and overall wellness. There is a growing body of evidence based on dietary patterns that conveys a possible effect on mood disorders. Dietary patterns have the capability of influencing, inflammation, oxidation, dysfunction of the mitochondrion, and neuroplasticity, and gut-brain signaling. The integration of neuroscience, psychiatry, nutrition, and other relevant disciplines has led to the emergence of nutritional psychiatry. This enhanced understanding led to the emergence of nutritional psychiatry, a field that integrates insights from neuroscience, psychiatry, and nutrition to explore how diet quality relates to mental health outcomes across the lifespan (Marx *et al*., 2020) [4].

Mood Disorders: Definition and Classification
Mood disorders are characterized by disruptions in mood that affect everyday functioning. Persistent mood symptoms are included in the Diagnostic and Statistical Manual of Mental

Disorders, Fifth Edition (DSM-5). Mood disorders are classified as depressive disorders or bipolar and related disorders, depending on the patterns of symptoms. They may include persistently sad moods and the inability to experience pleasure (anhedonia), along with other neurovegetative and cognitive symptoms. Examples of depressive disorders are major depressive disorder, persistent depressive disorder (dysthymia), premenstrual dysphoric disorder, and seasonal affective disorder. Common symptoms are reduced energy, sleep and eating disturbances, changes in the speed of movements and thinking, difficulty paying attention, and problems with thinking and organizing plans and actions. Neuroinflammation, along with imbalances in monoamines and neurogenesis, and problems with the body's metabolism may cause these symptoms. It is now believed that these problems can be altered by diet.

Bipolar and Associated Disorders

Swings between depressive episodes and manic or hypomanic episodes repetitively characterize bipolar and associated disorders. Between episodes, individuals display fluctuations in depression, mania and/or hypomania, and energy levels and behaviors. Within the spectrum of disorders lie bipolar I, bipolar II, and cyclothymic disorders. Bipolar disorders, beyond their predisposition to cyclic episodes, are associated with a predisposition toward elevated cardiovascular and metabolic diseases and chronic systemic inflammation. Biological processes underlying these disorders share similarities with those of depressive disorders. There is growing evidence that underlying bipolar disorders are inflammation, oxidative stress, and disrupted neurotransmitters. This evidence supports the need for studying the role of diet in these disorders (Berk *et al*., 2013) [17].

Fad Diets and Mental Health Essay

Fad diets are characterized by a reduction of calories or the exclusion of particular food groups. They are intended to provide a rapid weight loss result but are based on little scientific evidence. This trend has gained popularity over the years, although there is growing evidence that fad diets can have detrimental effects on mental health and psychological well-being (Sarris *et al*., 2020) [5]. The first factor that explains the potential negative impact of fad diets is the development of nutrient deficiencies caused by their improper nutrition. It is known facts that restrictive diets lead to the depletion of several micronutrients essential for the proper functioning of neurotransmitters, synapses, mitochondria, and the brain as a whole. For example, a lack of B-complex vitamins, iron, magnesium, zinc, and omega-3 polyunsaturated fatty acids can lead to depression, anxiety, irritability, impaired learning and memory, and reduced resilience to stress (Zielińska *et al*., 2023) [6]. In addition, fad diets can cause mental disorders by disrupting the endocrine system's work and leading to dysfunction of the hypothalamic-pituitary-adrenal axis and imbalance of sex hormones (Marx *et al*., 2021) [57]. This can happen as a result of calorie restriction or the exclusion of certain food groups, such as carbohydrates. Consequently, fatigue, mood instability, increased stress sensitivity, and emotional reactivity may arise (Anderson *et al*., 2022) [7]. In addition, imbalances in glucose due to malnutrition or highly restrictive diets may trigger neuroendocrine stress reactions, such as the hypothalamic-pituitary-adrenal axis. This means fad diets are even more dangerous to mental health by exacerbating the symptoms of anxiety and depression (Benton *et al*., 2020) [8]. Psychologically, popular diets, such as fad diets, are likely to encourage rigidity in dietary control and dichotomous thinking about food. This approach is related to more preoccupation with eating, guilt about diet violations, and food-related anxiety. As a result, these elements are highly likely to have a negative influence on emotional regulation and are associated with higher psychological distress, poor body image, and disordered eating behaviors (Linardon *et al*., 2021) [9]. The cyclical pattern of food restriction and relapse is detrimental to self-efficacy and esteem that further worsen mood-related problems (Treasure *et al*., 2020) [10]. Additionally, many fad diets have a detrimental effect on the gut-brain axis by restricting dietary fiber and food diversity. These changes affect the structure and function of the gut microbiome, possibly promoting inflammation and impairing the production of neuroactive metabolites by microbes (Dash *et al*., 2022) [11]. This mechanism is widely considered a crucial mediator in the development of mood disorders. It can, therefore, be concluded that fad diets may have a detrimental effect on mental health by impairing nutritional status, increasing psychological stress and disrupting the interconnected metabolic, inflammatory, and neurobiological systems essential for proper mood regulation (Sarris *et al*., 2020; Marx *et al*., 2021) [5, 57].

Dietary Approaches to Support Mental Health Essay

There is accumulating evidence from nutritional neuroscience and psychiatric epidemiology that overall dietary quality, rather than any specific nutrients or calorie restriction, is critically implicated in mental health and well-being (Appleton *et al*., 2021) [12]. The balanced approach to nutrition characterized by diversity and sustainability was found to confer a decreased risk of depression, anxiety, and psychological distress through various physiological and psychological mechanisms. Healthy diets were associated with positive mood, reduced stress and mental fatigue, improved cognitive performance, and enhanced emotional regulation abilities (Lane *et al*., 2022) [20]. Diets that promote mental well-being are rich in minimally processed plant foods, including vegetables, fruits, whole grains, legumes, nuts, and seeds. Their regular consumption provides a wide array of dietary fiber, vitamins, minerals, antioxidants, and phytochemicals beneficial for neurotransmitter production and function, neuroplasticity, antioxidant defense, and gut microbiota modulation. Healthy fats, particularly polyunsaturated fatty acids, mainly omega-3, from fatty fish, walnuts, flaxseeds, and olive oil, are crucial for normal neuronal function and decreasing inflammation and are considered to play a protective role in mood regulation and depression. Finally, diets rich in protein from fish, legumes, dairy products, and lean meats provide essential amino acids involved in the biosynthesis of serotonin, dopamine, and GABA, neurotransmitters playing a key role in modulating mood, motivation, cognition, and behavior. Micronutrients, including B-complex vitamins, iron, zinc, and magnesium, are integral components of neurotransmitter synthesis enzymes and facilitate normal neuronal functioning; their deficiency disrupts numerous neurotransmission systems, resulting in depressed mood, impaired cognitive performance, and emotional

dysregulation (Berk *et al*., 2013) [17]. A balanced and healthy diet can impact mental health and well-being through several different mechanisms. There are a few key pathways connecting dietary intake with depression and anxiety. One of them includes the regulation of inflammatory responses and oxidative stress, both strongly implicated in the development and persistence of depression and anxiety. Pro-inflammatory cytokines and oxidative stress disrupt normal neurotransmission, induce neuroinflammation, and impair neuronal plasticity, while a diet rich in antioxidants helps reduce neuroinflammation and protect neurons from oxidative damage (Gibson-Smith *et al*., 2020) [19]. Another important connection between nutrition and mental health is regulation of the brain's glucose metabolism (O'Neil *et al*., 2022) [17]. Eating regular balanced meals throughout the day provides a sufficient amount of glucose to fuel the brain and prevent sudden drops of energy, hunger, and fatigue during the day. If glucose metabolism is impaired, a person may experience emotional instability and greater vulnerability to stressors, depression, and irritability (Pasco *et al*., 2012) [21]. Finally, recent discoveries have emphasized the gut-brain axis as a critical modulator of the diet-psychological state relationship. The food consumed affects the composition of the gastrointestinal microbiota and its impact on the immune system and the production of neurotransmitters and neural connections through the vagus nerve. Dysregulation of the microbiota has been associated with depression and anxiety-like behavior in both human and animal studies (Ríos-Hoyo and Gutiérrez-Salmeán, 2021) [22]. A number of observational and longitudinal studies have confirmed the association between diet quality and mental health. For example, in the study by Guo *et al*. (2022) [23], a pro-inflammatory dietary pattern characterized by the high consumption of fried food, sugar-sweetened beverages, and processed meats was associated with an increased risk of developing depression, whereas a prudent dietary pattern rich in fruits, vegetables, and fish was associated with a reduced risk. Molendijk *et al*. (2023) [24] performed a meta-analysis of data from more than 100,000 participants and found that an unhealthy diet was independently associated with an increased risk of depression in all analyzed population groups and age categories. On the other hand, a diet high in ultra-processed foods, added sugars, and saturated fatty acids and low in whole grains, fiber, and unsaturated fats is linked to systemic inflammation, metabolic disorders, dysbiosis, and mental health problems (Lassale *et al*., 2023) [26]. Therefore, the modern diet of people with mental disorders should be balanced, not depriving them of favorite foods but guiding them to choose healthy options and follow cultural habits, which would prevent the development of depression and anxiety and promote adherence to the diet, improving the patient's quality of life (Parletta *et al*., 2022) [27].

Mechanistic Pathways Linking Diet and Mood Disorders

Glycemic Regulation and Neuroendocrine Stress Responses

As noted earlier, the glycemic index (GI) and glycemic load (GL) indicate how quickly foods containing carbohydrates raise blood sugar. Consuming foods with a high glycemic index and load results in postprandial hyperglycemia, followed by reactive hypoglycemia. These alterations affect the neuro-endocrine stress pathway, which is triggered by elevated cortisol, adrenaline, and glucagon levels, potentially worsening depression and anxiety symptoms. This matters because sustained activation of the hypothalamus-pituitary-adrenal (HPA) axis leads to mood dysregulation and impaired brain function. A longitudinal cohort study, Whitehall II, showed over a decade that eating high-GI/GL foods is associated with the onset of depressive symptoms. Results from that study indicated that individuals following high GL and GI diets experienced faster progression of depressive symptoms (Gangwisch *et al*., 2015) [28]. Beyond observational research, controlled feeding trials have demonstrated that high-GI meals negatively affect mood, causing irritability and fatigue. Moreover, recent neuroimaging studies have shown that glucose variability affects functional connectivity and activity in the hippocampus and prefrontal cortex, areas essential for emotional regulation and cognition (Khalil *et al.*, 2022) [29]. It has also been recently discovered that glucose dysregulation triggers oxidative stress and mitochondrial dysfunction, leading to neurodegeneration and neuroinflammation that may contribute to depression (Schiavone *et al*., 2020) [30]. Interventions designed to stabilize glucose, such as low-GI diets and intermittent fasting, have shown potential for improving mood and cognitive function (Papamichou *et al*., 2022) [31]. Low-grade chronic systemic inflammation is a key factor in the development of depression (Raison and Miller, 2016) [32].

The anti-inflammatory effects of such diets are backed by meta-analyses of inflammatory biomarkers in depressed patients. In comparison to healthy controls, depressed participants consistently exhibited higher levels of IL-6 and CRP. Additionally, randomized controlled trials testing anti-inflammatory drugs, including non-steroidal anti-inflammatory drugs (NSAIDs) and cytokine inhibitors, reduced depressive symptoms, confirming inflammation as a therapeutic target (Su *et al*., 2021) [33]. Furthermore, several nutrients have anti-inflammatory properties. Omega-3 fatty acids, particularly EPA, decrease the production of pro-inflammatory eicosanoids and cytokines, and improve neuronal membrane fluidity, enhancing neurotransmission (Grosso *et al*., 2014) [34]. Polyphenols found in fruits, vegetables, and olive oil possess antioxidant properties and regulate pathways involved in inflammation and neuroprotection (Benton, 2011) [8]. A recent meta-analysis of omega-3 supplementation trials in depressed patients found some improvement, especially when inflammatory markers were elevated (Martins, 2020) [36]. Recent studies also suggest that the NLRP3 inflammasome, which regulates innate immunity, plays a role in inflammation associated with depression. The effect of diet on inflammasome activation has been shown (Alcocer-Gómez *et al.,* 2017) [37]. A diet high in antioxidants and low in processed foods inhibits NLRP3 activation, so proper eating habits may help ease depressive symptoms. The gut-brain axis, which involves neural (vagus nerve), immune, and endocrine signaling pathways, is crucial for mood regulation. Gut microbiota dysbiosis, marked by altered composition and reduced diversity, has been increasingly linked to depression and anxiety (Kelly *et al.*, 2016) [38]. Animal studies show that transferring fecal microbiota from depressed patients induces depressive behavior in rodents, indicating a causal relationship (Zheng *et al.*, 2016) [39]. Diet affects the diversity of gut microbes. Diets high in saturated fat and sugar but low in fiber reduce populations of bacteria

that produce SCFAs, including Faecalibacterium prausnitzii and Roseburia, which have anti-inflammatory and neuroprotective properties (Valdes *et al.*, 2018) [40]. Such gut microbiota imbalance can increase intestinal permeability, also called "leaky gut," allowing LPS to enter the bloodstream and trigger systemic inflammation and mood disorders (Kelly *et al.*, 2015) [41]. Conversely, diets following the Mediterranean pattern, rich in dietary fiber and polyphenols, enhance gut microflora diversity and increase SCFA production, helping maintain blood-brain barrier integrity and affect microglial activation (Johnson *et al.*, 2020) [42]. Butyrate, a key SCFA, has been demonstrated to reduce neuroinflammation and promote neurogenesis in preclinical studies (Stilling *et al.*, 2016) [44]. Recent human clinical trials using probiotics (Lactobacillus and Bifidobacterium species) and prebiotics have shown some efficacy in treating depression and stress responses, though results remain limited and inconsistent (Wallace and Milev, 2017) [43]. The 2022 systematic review and meta-analysis concluded that psychobiotics have a moderate effect on mood and anxiety in patients with mild-to-moderate symptoms (Huang *et al.*, 2022) [45]. Furthermore, research is exploring postbiotics (bacterial metabolic products) and synbiotics (combining probiotics and prebiotics) as next-generation therapies for the gut-brain axis (Vazquez-Moreno *et al*., 2023). Employing dietary strategies to modify gut microflora represents a promising alternative treatment for mood disorders.

Future Directions and Clinical Implications Personalized Nutrition and Integration into Psychiatric Care

The precision psychiatry paradigm represents an innovative strategy of individualizing treatment, including nutritional interventions, for persons diagnosed with mood disorders (Lin and Schmidt, 2023) [47]. Advances in genomic, metabolomic, and microbiome profiling enable the development of nutraceutical strategies targeting the unique biological and psychosocial characteristics of persons with mood disorders. For example, single nucleotide polymorphisms associated with increased inflammation and altered neurotransmission may dictate the most appropriate type and dose of omega-3 fatty acids or B vitamins for a person with depression (Berk *et al*., 2022) [18]. Similarly, stratification of patients on the basis of microbiome fingerprints or intestinal permeability may guide the selection of prebiotic or probiotic supplements (Kelly and Borre, 2021) [48]. The integration of multiomics data will promote the development of dietary guidelines that consider the heterogeneity of nutritional needs among psychiatric patients. A collaborative care model, wherein psychiatrists, clinical psychologists, dietitian/nutritionists, and primary care providers work together in concert, is critical for the successful implementation of precision psychiatry (Murphy *et al.*, 2023). A recent pilot study examining the effectiveness of a nutritional assessment tool found increased engagement from patients as well as reduced depressive symptoms in those who received services from dieticians as part of their mental health treatment team (Murphy *et al*., 2023). Digital health technologies offering continuous data collection and feedback on nutritional status, mood, and other domains are valuable tools in promoting personalized mental health nutrition care.

Addressing Barriers and Enhancing Adherence

Although the evidence on the effectiveness of nutritional interventions is growing, the challenge of improving adherence among persons with mood disorders remains paramount (Vancampfort *et al.*, 2019) [50]. Patients with mood disorders often experience executive dysfunction and reduced motivation to engage in behavior change, which can undermine nutritional interventions (Firth *et al.*, 2021) [52]. Furthermore, the risk for antidepressant-induced weight gain also contributes to treatment nonadherence (Firth *et al*., 2022) [52]. Future research and practice in mental health nutrition should prioritize the role of the physical and socioeconomic environments in influencing dietary behaviors and mental health outcomes. In particular, the role of poverty and food insecurity on the ability of persons with mood disorders to follow a healthy diet requires greater consideration (Walker *et al.*, 2020) [53]. Affordable access to nutritional items, healthy eating programs, and urban agriculture will be critical in bridging the gap between nutritional recommendations and population health needs. Behavioral economic interventions such as motivational interviewing (MI) and solution-focused brief therapy have been found to improve treatment engagement and adherence to nutritional recommendations (Hall *et al.*, 2021) [54]. For instance, a randomized controlled trial (RCT) examining the efficacy of MI plus counseling compared to counseling alone found that the former enhanced adherence to a Mediterranean-style diet while also improving depression symptoms (Nguyen *et al.*, 2022) [55]. Group and peer support interventions are also valuable in enhancing adherence to nutritional guidelines through increased social support and shared learning. Patients with severe mental disorders stand to benefit from such interventions given the high likelihood of isolation and reduced support networks (Adjibade *et al.*, 2021) [56]. Additionally, psychoeducation and basic nutritional counseling from mental health professionals can serve as a useful supplement to the care provided by dieticians when the latter are unavailable (Jacka *et al.*, 2021). Integrating nutritional screening and interventions into routine mental health practice will enhance early detection and management of unhealthy dietary patterns in this population.

Conclusion

Diet is an essential and multifaceted variable that plays a significant role in depression and anxiety via diverse mechanisms. Namely, it affects glycemic control and the neuroendocrine stress response, triggers inflammatory processes which intensify neurobiological dysfunction in mood disorders, and positively influences the gut-brain axis and microbiota. There is a growing body of evidence that diet is one of the key modifiable domains associated with mental health problems. It means that food intake and nutrition influence metabolic processes, proinflammatory pathways, and neurobiology. The consideration of nutritional factors in public health and mental health care may transform clinical practices and improve global health outcomes. Trials aiming to evaluate dietary interventions for depression and anxiety disorders were reviewed. They proved the notion that nutrition could be used as an adjunctive treatment for mental illnesses. The changes in diet observed positive effects on the core symptoms of the two conditions. Yet, the effect sizes were small, which prompts a need for additional trials and exploration of the

mechanisms that link diet, nutrition, and mental health. Moreover, there is a necessity to address the barriers to implementing dietary interventions as they are reported to have limited efficacy in patients due to multiple challenges. To conclude, nutrition is a key element of management and care for patients with psychological conditions that should be complemented by pharmacotherapy and psychotherapeutic interventions. This task is complex and multidimensional and involves health providers, policymakers, and individuals with mental health problems. Addressing the issues related to nutrition and mental health requires a more comprehensive approach to managing the condition and is of crucial importance. It demands interdisciplinary collaboration and the consideration of diverse individual aspects, ranging from biological to socioeconomic. Individuals with mental health disorders experience tremendous difficulties with adhering to dietary interventions. These barriers are diverse and vary from person to person, which makes it essential to analyze each case from several perspectives and address the main issues that prompt the failures to comply with dietitian's recommendations.

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