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Nutritional Psychiatry: Dietary Interventions for Mood Disorders

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Abstract

Background: The global prevalence of mood and anxiety disorders is rising, exacerbated by modern lifestyles and diets high in processed foods. This has stimulated the emergence of nutritional psychiatry, a field investigating the link between diet and mental health. Concurrently, limitations in traditional psychiatric treatments highlight the need for complementary, modifiable lifestyle interventions.

Aim: This narrative review aims to synthesize current evidence on the role of dietary patterns and specific nutrients in the prevention and management of psychiatric disorders, to provide guidance for psychoprophylaxis and dietary intervention.

Methods: A comprehensive literature search was conducted using PubMed for English-language articles published after 2005. From 3,473 identified records, 110 high-quality sources were selected based on predefined criteria, including peer-reviewed journals with an impact factor.

Results: The review establishes that pro-inflammatory, Western-style diets are associated with an increased risk of depression and anxiety. In contrast, whole-food dietary patterns like the Mediterranean and MIND diets demonstrate protective effects. Specific nutrients—including omega-3 fatty acids, B vitamins, vitamin D, zinc, and probiotics (psychobiotics)—show promise in modulating key pathways like inflammation, oxidative stress, and the gut-brain axis. However, trials on single-nutrient supplementation for depression prevention have largely yielded null results, underscoring the superiority of holistic dietary changes.

Conclusion: Diet is a critical, modifiable factor in mental health. Integrating nutritional counseling and evidence-based dietary patterns into standard psychiatric care offers a powerful, complementary strategy for improving mental well-being and preventing disorders.

Keywords: Nutritional Psychiatry, Diet, Mental Health, Depression, Gut-Brain Axis, Psychobiotics, Mediterranean Diet, Prevention

Introduction

In the context of accelerating urbanization and rapid technological, economic, and cultural development, contemporary lifestyles are undergoing profound transformation. The increasing pace of life, constant pursuit of self-actualization, and chronic overstimulation, combined with a perceived lack of time, have markedly altered dietary patterns,

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promoting reliance on energy-dense, highly processed, and convenience foods at the expense of traditional, nutrient-rich diets (1). These changes are recognized as key contributors to so-called civilization diseases, including obesity, cardiovascular disease, type 2 diabetes, and certain cancers, which together represent a major burden from a public health perspective (1). Importantly, the same environmental and behavioral determinants that drive somatic noncommunicable diseases also appear to influence mental health, suggesting a shared etiological background involving lifestyle, diet quality, and chronic psychosocial stress (1,2). Among civilization diseases, depressive and anxiety disorders have emerged as particularly concerning due to their rapidly increasing prevalence and profound social and economic consequences (2). Depressive and anxiety disorders are now frequently described as a global epidemic, with a continuously rising number of individuals requiring mental health support in both high-income and low- and middle-income countries (2,3). According to estimates from the International Health Metrics Evaluation (IHME), as of the end of 2017 approximately 13% of the world's population was affected by mental disorders, underscoring the scale of the problem on a global level (3). Data from Europe indicate an even higher burden: the study by Wittchen et al. demonstrated that mental disorders affect as many as 38% of the European population, confirming that these conditions are among the most common health problems in the region (4). Similar trends have been observed in Poland, whereby the end of 2019 approximately 1.6 million individuals had received psychiatric treatment, illustrating a substantial and growing demand for specialist care within the national health system (5). These figures likely underestimate the true prevalence, given persistent stigma, underdiagnosis, and limited access to care, particularly in underserved and rural areas (3,4,5).

The COVID-19 pandemic has further exacerbated the burden of mental disorders worldwide. In addition to the direct health threat posed by SARS-CoV-2 infection, stringent sanitary restrictions, social distancing measures, and periods of quarantine or isolation contributed to increased feelings of loneliness, insecurity, sadness, anxiety, and mistrust, frequently intensified by misinformation and inconsistent communication in the public sphere (6). For many individuals, disruption of daily routines, economic uncertainty, and reduced access to in-person healthcare services acted as powerful stressors, precipitating new-onset mental health problems or worsening pre-existing conditions (6). As a consequence, psychological and psychiatric support has become one of the most sought-after forms of health assistance in contemporary societies, with demand frequently outstripping available resources (2,5,6). In Poland, as in many other countries, mental health services face considerable structural and workforce constraints. It is estimated that there are only about 4,300 practicing psychiatrists, a number insufficient to meet the current and projected needs of the population (7). The situation is even more challenging in child and adolescent psychiatry, where only around 455 specialists are in practice, leading to long waiting times and significant barriers to care for younger patients (8). Although psychological and psychotherapeutic services may be somewhat more accessible, public opinion remains divided regarding their effectiveness, and the absence of comprehensive national registers of psychologists and psychotherapists hampers systematic planning and quality assurance (7,8). These limitations collectively contribute to a gradual transformation of the mental healthcare model, with increasing emphasis on community-based care, integration of mental health into primary care, and exploration of complementary and adjunctive interventions beyond conventional pharmacotherapy and psychotherapy (2,9).

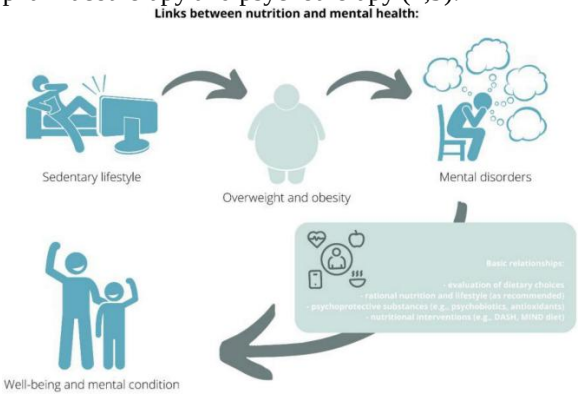

Fig. 1: Link between nutrition and mental health.

Despite advances in psychopharmacology and evidence-based psychotherapies, treatment outcomes for many patients remain suboptimal. A considerable proportion of individuals with depressive or anxiety disorders experience only partial remission, frequent relapses, or treatment resistance, despite adherence to guideline-concordant therapies (9). This therapeutic gap has stimulated growing interest in modifiable lifestyle factors—such as diet, physical activity, sleep, and substance use—as additional targets for prevention and management. In this context, nutrition has emerged as a particularly promising area of research. Over the past decade, there has been a dramatic increase in studies examining the influence of dietary patterns, specific nutrients, and overall diet quality on mental health outcomes, including depression, anxiety, and cognitive function (1,9). These investigations suggest that poor-quality diets rich in processed foods, added sugars, and saturated fats may contribute to the onset and maintenance of mental disorders, whereas dietary patterns characterized by high consumption of vegetables, fruits, whole grains, legumes, nuts, and

unsaturated fats may exert protective effects (1,2,9). The concept of "nutritional psychiatry" has therefore gained prominence as a field that integrates principles of clinical nutrition, neuroscience, and psychiatry to explore how dietary interventions may complement existing treatments for mental disorders (9). From a public health perspective, this line of inquiry is particularly important, as it offers the possibility of primary prevention strategies that are scalable, cost-effective, and aligned with recommendations for the prevention of other noncommunicable diseases (1,3). Furthermore, incorporating nutritional assessment and counseling into standard mental healthcare may help reduce the overall prevalence and severity of mental disorders by targeting shared pathophysiological pathways such as chronic inflammation, oxidative stress, altered gut microbiota, and dysregulated neuroendocrine function (1,2,9). In summary, the convergence of rising mental health needs, limitations of current therapeutic modalities, and accumulating evidence on the role of diet in mental well-being provides a strong rationale for further investigation and integration of nutritional strategies into comprehensive mental health care and prevention frameworks (2,3,9).

Review Data:

The review aimed to identify nutritional recommendations relevant to the use of diet as psychoprophylaxis and in the dietary management of psychiatric disorders. Given that current knowledge in this area remains limited despite numerous studies, the authors undertook a broad narrative review to collate and synthesize the most up-to-date evidence. The process followed recommended good practices for evidence-based reviews. A team of researchers, supported by a librarian trained in literature searching, EBM, and HTA, first conducted a preliminary scan of the literature to define the research field and refine a set of keywords consistent with the review's objectives. Eligibility criteria included language, publication period, publication status, and author expertise. Only English-language articles were selected, and studies published after 2005 were included to ensure both recency and maturity of the research field. Preference was given to full-text, open-access articles published in journals with an impact factor, reflecting the rapid development of both dietetics and mental health sciences. The search strategy employed PubMed, using MeSH-consistent terms combined with Boolean operators, including phrases such as "psychodietetics," "nutripsychiatry," "diet," "mental health," "obesity," "depression," and "mental disorders," ensuring breadth, transparency, and methodological consistency. The initial search identified 3,473 records, from which 356 were deemed directly relevant, and ultimately 110 high-value sources were included based on predefined criteria and GRADE-consistent questions assessing reliability, validity, and relevance. An additional 11 sources were used for background and theoretical context. Critical appraisal emphasized publication in peer-reviewed, impact-factor journals, while recognizing limitations such as exclusion of non-English and grey literature and the known drawbacks of impact factor as a quality metric.

Correlations between nutrition and mental health

The relationship between nutrition and mental health is increasingly recognized as bidirectional, complex, and clinically significant. Excess body weight has become a major social and medical challenge, with more than 0.7 billion people worldwide currently classified as obese, representing approximately 30% of the global population; mortality attributable to obesity continues to rise in parallel with this epidemic (10). Contemporary dietary habits, characterized by high intakes of ultra-processed, energy-dense products and sugar-sweetened beverages, coexist with insufficient consumption of nutrient-dense foods such as vegetables, fruits, and whole grains. As a consequence, many individuals simultaneously experience caloric excess and micronutrient deficiency, a phenomenon often described as quantitative malnutrition (11). This pattern is particularly detrimental for the nervous system, which depends on an adequate supply of B vitamins, zinc, magnesium, and other micronutrients that support neurotransmitter synthesis, myelination, and neuronal energy metabolism (10, 11). At the same time, fiber-rich plant foods and whole cereals, which contribute to gut microbiota diversity and short-chain fatty acid production, are consumed in amounts far below recommended levels in many populations (10, 11). When these adverse dietary patterns are compounded by other lifestyle risk factors—such as cigarette smoking, sedentary behavior, and harmful alcohol consumption—the cumulative effect on cardiometabolic and mental health is profound. Epidemiological studies consistently demonstrate that such behaviors increase the risk not only of obesity and type 2 diabetes but also of depressive and anxiety disorders (10). The literature on nutritional prevention of depression indicates that individuals adhering to healthy dietary patterns, including Mediterranean-style diets rich in plant foods, fish, and unsaturated fats, exhibit lower rates of depressive symptoms and better overall psychological well-being (12). These associations suggest that diet exerts both direct and indirect effects on brain function, through mechanisms that include modulation of inflammatory pathways, oxidative stress, neurotrophic signaling, and metabolic regulation (10–13).

A key mechanistic link between nutrition and psychiatric disorders is the antioxidant system, which plays a central role in the neutralization of reactive oxygen species and the maintenance of redox homeostasis in neural tissue (13). Oxidative stress has been repeatedly implicated in the

pathophysiology of mood and psychotic disorders, and the proper functioning of endogenous antioxidant defenses is critically dependent on dietary intake of vitamins, minerals, and other bioactive compounds (13). Another crucial mediator is brain-derived neurotrophic factor (BDNF), a neurotrophin involved in synaptic plasticity, neurogenesis, and neuroprotection. Nutritional status and specific nutrients influence BDNF expression and activity, thereby affecting vulnerability to neurodegenerative and affective disorders (14). Observational data indicate that adherence to healthy dietary patterns is associated with reduced incidence of depression and even lower suicide risk, pointing to the potential psychoprotective role of diet across the life course (15, 16). Building on this foundation, randomized controlled trials have begun to evaluate dietary modification as an adjunctive or stand-alone intervention in the treatment of depression, with promising results for symptom reduction and functional improvement (15–17). Within this emerging field, selective supplementation with specific nutrients has attracted growing interest as a potential strategy to augment standard pharmacological and psychotherapeutic treatments. Compounds such as S-adenosylmethionine, N-acetylcysteine, zinc, and B-complex vitamins—including folic acid—as well as vitamin D and long-chain omega-3 polyunsaturated fatty acids, have been singled out for their neurobiological relevance (18). Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), participate in synaptogenesis and modulate receptor turnover, while also exerting anti-inflammatory and anti-apoptotic effects. They influence membrane fluidity, support BDNF signaling, and affect neurotransmitter synthesis and reuptake, thereby contributing to mood regulation and cognitive processes (18). S-adenosylmethionine (SAM), synthesized from adenosine and methionine, is a universal methyl-group donor involved in epigenetic regulation and neurotransmitter metabolism; clinical trials have demonstrated its antidepressant properties, particularly as an adjunct to conventional antidepressants (19).

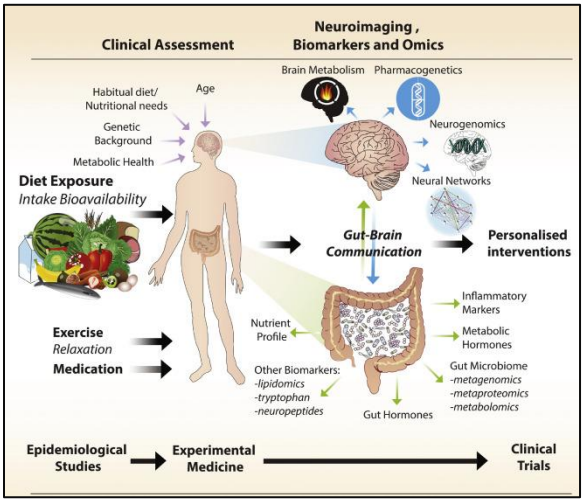

Fig. 2: Nutritional Psychiatry.

N-acetylcysteine (NAC), a precursor of the antioxidant glutathione, has shown beneficial effects in several psychiatric conditions, including schizophrenia, bipolar affective disorder, and trichotillomania (20). Its mechanisms of action encompass anti-inflammatory and antioxidant properties, modulation of glutamatergic transmission, and neuroprotection against oxidative and excitotoxic damage (20). Trace elements such as zinc further exemplify the tight coupling between micronutrient status and mental health. Zinc deficiency has been associated with greater severity of depressive symptoms, and supplementation—when combined with antidepressant therapy—appears to facilitate mood stabilization and accelerate clinical response (21). Zinc participates in cytokine modulation, influences neurogenesis, and alters BDNF levels, thereby integrating inflammatory and neurotrophic pathways relevant to depression (21). B-group vitamins, crucial cofactors in one-carbon metabolism and neurotransmitter synthesis, are likewise essential for optimal neural function. Folic acid (vitamin B9) deficiency has been repeatedly linked to depressive symptomatology and to suboptimal response to antidepressant medications (22). Mechanistically, folate insufficiency may lead to elevated homocysteine levels, impaired methylation reactions, and altered monoamine metabolism, all of which can negatively affect mood and cognition (22). Vitamin D has also emerged as a key player at the interface of nutrition and mental health. Low serum vitamin D concentrations are associated with an increased risk of both schizophrenia and depression, suggesting that deficiency may constitute a modifiable risk factor for these conditions (23). Interventional work in adolescents diagnosed with depression demonstrated that three months of vitamin D supplementation, administered as 4,000 IU/day for one month followed by 2,000 IU/day for two months, significantly reduced the severity of depressive symptoms, irritability, fatigue, mood lability, sleep disturbances, weakness, and concentration difficulties (24). Animal

studies complement these findings, revealing that vitamin D promotes synaptic plasticity, exerts neuroprotective effects, enhances the production of neurotrophic factors such as nerve growth factor (NGF), and modulates the dopaminergic system, thereby offering a plausible biological basis for its antidepressant and antipsychotic potential (24).

Evidence synthesized in the reviewed table further illustrates the diverse psychoprotective properties of bioactive food components. For example, Gazerani (96) examined populations struggling with migraine headaches and highlighted the role of folate in the form of folic acid (vitamin B9). Adequate folate intake, by supporting the addition of methyl groups via DNA methyltransferase during methylation processes and maintaining appropriate serum homocysteine levels, appears to contribute to migraine prevention, which is clinically relevant given the high comorbidity between migraine and mood or anxiety disorders (96). Cater et al. (97) and Parikh et al. (98) focused on docosahexaenoic acid, demonstrating its neurotherapeutic properties in healthy adults and newborns. DHA was shown to stimulate neurotransmission and support the development of the cerebral cortex and visual system by efficiently crossing the blood–brain barrier, thereby enhancing the neuro-efficiency of both verbal and non-verbal communication processes (97, 98). Parikh et al. (98) also investigated a broader set of bioactive compounds, including alpha-lipoic acid, lignans, soluble fiber, and the phytoestrogen secoisolariciresinol diglucoside, in populations with nervous system conditions such as depression and in newborns with encephalopathy. These components were associated with favorable influences on the development and size of cortical cells during pre- and postnatal periods, neuromodulation of cognitive-behavioral functioning, and protection against depressive symptoms in offspring, as well as reduced risk of hypoxic-ischemic encephalopathy in neonates (98). A crucial mechanism underpinning these benefits was the reduction of oxidative stress parameters and attenuation of inflammatory processes within the nervous system, reinforcing the centrality of redox balance in mental health (98).

Further support for the role of dietary phytochemicals comes from clinical and experimental research on flavonoids. Park et al. (99) conducted a blinded randomized trial in depressed patients, while Mulati et al. (100) used an obese mouse model of neuronal impairment. Both studies indicated that flavonoid supplementation improved brain-derived neurotrophic factor levels and alleviated depressive symptoms, illustrating how modulation of BDNF can translate into clinical benefit (99, 100). Additionally, changes in PSD-95 protein expression, a marker of synaptic integrity, suggested that flavonoids may counteract synaptic dysfunction and neuronal damage, mechanisms that are increasingly recognized as central to the pathogenesis of depression and related disorders (99, 100). Amino acids and minerals also play important roles in the nutrition–mental health nexus. Mittal et al. (101) reviewed evidence on tryptophan, an exogenous amino acid and precursor of serotonin, in the context of symptom reduction and disease progression in Parkinson's disease. Their analysis showed that metabolic transformations of tryptophan into serotonin help regulate circadian rhythms, emotional stability, and overall mood, while participation in catecholamine metabolism links tryptophan to processes occurring at the level of the brain–gut axis (101). These findings dovetail with broader research indicating that disturbances in tryptophan–serotonin pathways contribute to depression, anxiety, and sleep disorders. Fernández et al. (102), Dogan-Sander et al. (103), and Godos et al. (104) synthesized review and meta-analytic data demonstrating that adequate intake of minerals such as magnesium, calcium, selenium, zinc, manganese, and copper, together with antioxidant vitamins D, E, C and carotenoids, improves neuronal and cognitive function in patients with Parkinson's disease, schizophrenia, and depression. These nutrients reduce oxidative stress, restore systemic homeostasis, and diminish chronic low-grade inflammation, as reflected by decreases in C-reactive protein (CRP), interleukin-6 (IL-6), white blood cell indices, and somato-psychological symptoms in depressed individuals (102–104).

Complex carbohydrates and additional bioactive substances, including eicosapentaenoic acid, the amino acid glycine, polyphenols, and anthocyanins, have been studied primarily in relation to Alzheimer's disease and neuroinflammation (104, 105). Godos et al. (104) and Burton-Freeman et al. (105) reported that these components modulate the expression of neuromodulators and neurotransmitters and attenuate activation of the hypothalamic–pituitary–adrenal (HPA) axis, thereby lowering endogenous stress and cortisol levels. Proper insulin secretion and glucose uptake into cells, mediated by adequate GLUT receptor functionality, were also enhanced, linking metabolic control to cognitive resilience (104, 105). Furthermore, these nutrients influenced neurogenesis, synaptic plasticity, and microglial activation in the central nervous system, contributing to the prevention of inflammation and neurodegenerative changes. At the biochemical level, they decreased oxidation of low-density lipoprotein (LDL) particles and lipid peroxidation, while activating antioxidant enzymes such as catalase and superoxide dismutase, thus further reinforcing antioxidant defenses (104, 105). Taken together, these findings indicate that the correlation between nutrition and mental health is not restricted to single nutrients but arises from complex interactions between overall dietary patterns, specific bioactive components, and individual vulnerability factors.

Diets rich in whole plant foods, high-quality proteins, and unsaturated fats provide synergistic combinations of vitamins, minerals, polyphenols, and fatty acids that collectively support neurochemical balance, anti-inflammatory signaling, and structural integrity of neural circuits (12, 15, 18). At the same time, excess intake of refined carbohydrates, saturated fats, and processed foods can promote systemic and neuroinflammation, oxidative stress, insulin resistance, and dysbiosis of the gut microbiota, each of which has been implicated in the development or exacerbation of mood and cognitive disorders (10–13, 18). The gut–brain axis, mediated by microbial metabolites, immune signaling, and vagal pathways, likely constitutes an important route through which diet influences emotional and cognitive functioning, although this area remains under intensive investigation (13, 20).

From a clinical perspective, the observed correlations suggest that comprehensive management of mental disorders should consider nutritional status alongside pharmacotherapy and psychotherapy. Screening for obesity, micronutrient deficiencies, and unhealthy dietary patterns can identify modifiable risk factors that may hinder recovery or predispose to relapse (10, 11, 21–23). Nutritional counseling aimed at adopting evidence-based dietary patterns, combined with targeted supplementation where deficiencies are documented, holds promise as an adjunct to standard psychiatric care. However, while the reviewed evidence is compelling, it is also heterogeneous, and not all trials have yielded positive results. Differences in study design, population characteristics, intervention duration, and dosages complicate direct comparisons and highlight the need for larger, well-controlled randomized trials to clarify causal relationships and determine optimal therapeutic protocols (15–17, 19–21). The synthesis of studies on bioactive dietary components, including those summarized in the compiled table, underscores the breadth of mechanisms through which nutrition can modulate mental health, ranging from epigenetic regulation and neurotransmitter metabolism to anti-inflammatory and antioxidant actions (96–105). Nevertheless, nutritional strategies should not be viewed as a replacement for evidence-based psychiatric treatments but rather as a complementary dimension of holistic care. As research in psychodietetics and nutritional psychiatry continues to expand, integrating high-quality dietary assessment and intervention into clinical practice may contribute substantially to reducing the global burden of mental disorders and improving long-term outcomes for patients across diverse settings (12, 15, 18, 24).

Psychoprotective food ingredients

The concept of psychoprotective food ingredients is rooted in the recognition that the gastrointestinal tract and the central nervous system are linked through a dense network of neural, endocrine, immune, and metabolic signaling pathways collectively termed the gut–brain axis. The gut microbiota, estimated at around 10^{14} microorganisms and harboring approximately 3.3 million genes—about 150 times more than the human genome—constitutes a key regulator within this axis, with more than a thousand microbial species forming a complex and dynamic ecosystem (25). Through continual cross-talk with intestinal epithelial cells, immune cells, and the enteric nervous system, the microbiota can modulate central neural circuits involved in stress reactivity, mood regulation, and cognition. Communication occurs via multiple routes, including the autonomic nervous system and particularly the vagus nerve, which conveys afferent sensory information from the gut to limbic and cortical regions implicated in emotional processing (26). Experimental and clinical data indicate that many of the mental health benefits observed with probiotic supplementation are at least partly mediated by vagal signaling, since vagotomy abolishes several psychotropic effects in animal models (27). Evidence from germ-free (GF) mice raised in sterile conditions underscores the pivotal role of the microbiota in the maturation of neuroendocrine pathways. GF animals exhibit exaggerated activation of the hypothalamic–pituitary–adrenal (HPA) axis in response to stress, reflected in significantly elevated glucocorticosteroid and adrenocorticotropic hormone concentrations; colonization of the gastrointestinal tract with Bifidobacterium infantis can normalize these responses, demonstrating a direct influence of specific bacterial strains on stress physiology (28). Conversely, exposure to stress in early life or adulthood has been shown to disrupt microbial composition and diversity, suggesting that stress–microbiota interactions are bidirectional and self-reinforcing (29). The immune system is another crucial communication channel: intestinal microbiota are essential for the appropriate development and function of the gut-associated lymphoid tissue, shaping local and systemic immune responses (30). Bacterial antigens such as polysaccharide A, lipopolysaccharides, and teichoic or thymic acids modulate immune tolerance, cytokine production, and inflammatory signaling, all of which are relevant to the pathophysiology of psychiatric disorders in which low-grade inflammation is frequently observed (31).

Beyond structural and immunological roles, the microbiota functions as a metabolic “organ” that synthesizes numerous neuroactive compounds. Commensal bacteria produce γ-aminobutyric acid (GABA), short-chain fatty acids such as butyrate, acetate and propionate, as well as serotonin, dopamine, and other metabolites that can influence brain function through local effects on enteroendocrine cells, modulation of systemic

cytokines, and direct or indirect actions on neural pathways (32). Short-chain fatty acids in particular have been implicated in maintaining blood–brain barrier integrity, regulating microglial activation, and modulating gene expression via epigenetic mechanisms. These observations provide a mechanistic basis for the idea that specific microbial configurations or microbial-derived metabolites may confer psychoprotective effects and that they can be targeted through diet. Within this framework, it is reasonable to consider whether probiotic, prebiotic, and synbiotic preparations can be used as nutritional interventions aimed at improving or maintaining mental health. Probiotics are classically defined as live microorganisms which, when administered in adequate amounts, confer a health benefit on the host (33). Since the early work of Ilya Metchnikov, who received the Nobel Prize in 1908 for demonstrating the health benefits of lactic acid–producing bacteria, lactic acid bacteria such as Lactobacillus and Bifidobacterium species have become the most widely studied probiotics. These organisms are naturally present in fermented dairy products, pickled vegetables, and other traditionally preserved foods, forming an important component of many cultural diets (34). Prebiotics, in contrast, are nondigestible food ingredients that selectively stimulate the growth or activity of beneficial bacterial species in the colon, thereby improving host health (35). Compounds such as inulin, fructooligosaccharides, and galactooligosaccharides are common prebiotics; they not only promote beneficial microbiota but may also inhibit pathogenic bacteria and reduce inflammation by altering microbial composition and metabolic output (35, 36). Synbiotics combine prebiotics and probiotics into a single formulation designed to maximize survival and functional impact of the administered microbes.

The term psychobiotics has been introduced to denote those probiotics (or in some definitions, prebiotics) that confer mental health benefits in individuals with psychiatric symptoms or disorders (37). Psychobiotics exert their effects through multiple mechanisms, including the synthesis of neurotransmitters such as GABA and serotonin, production of short-chain fatty acids with neuroactive properties, modulation of tryptophan metabolism and the kynurenine pathway, and regulation of systemic inflammatory tone (36, 37). Early experimental work demonstrated that oral administration of Lactobacillus helveticus and Bifidobacterium longum in animal models over approximately one month was associated with reduced anxiety- and depression-like behaviors and lower stress-induced corticosterone levels, highlighting the potential of these strains as psychobiotic candidates (38). At present, standard treatments for psychiatric disorders rely primarily on antidepressants, antipsychotics, mood stabilizers, and structured psychotherapies; however, the possibility of augmenting these approaches with psychobiotic strategies is increasingly attractive, particularly in light of the observation that many psychotropic medications themselves can disturb the gut microbiome and reduce microbial diversity, potentially offsetting some of their therapeutic benefits (39). An expanding body of clinical research evaluates psychobiotic interventions in healthy individuals exposed to stress as well as in patients with depression, Alzheimer's disease, chronic fatigue syndrome, and mild cognitive impairment. One of the earliest randomized trials in healthy adults, conducted by Diop et al. (106), investigated a 12-week supplementation with Lactobacillus acidophilus Rosell-52 and Bifidobacterium longum Rosell-175 at a dose of 3×10^9 CFU per day. Participants receiving this probiotic combination experienced a significant reduction in gastrointestinal complaints compared with placebo, particularly under conditions of heightened stress, and showed a marked decrease in the severity of stress-induced nausea and abdominal pain. Although the primary outcomes were somatic, the results underscore how modulation of gut function in stressed individuals may secondarily influence psychological well-being, given the strong bidirectional links between visceral discomfort and mood (106).

Messaoudi et al. (37) advanced this line of inquiry by conducting a double-blind randomized trial in 55 healthy adults who consumed Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 (3×10^9 CFU/day) for 30 days. This study is often cited as the first to demonstrate that a psychobiotic formulation can alleviate stress-induced psychiatric symptoms in humans. Participants receiving the probiotic showed significant reductions in anxiety symptoms on the HSCL-90 scale, as well as measurable decreases in both anxiety and depressive symptom clusters. Urinary cortisol, a biomarker of HPA axis activation, was also reduced, confirming attenuation of physiological stress responses. Interestingly, individuals with lower baseline cortisol levels derived particular benefit in terms of anxiety and depression scores on tools such as the Perceived Stress Scale (PSS), Hospital Anxiety and Depression Scale (HADS), and HSCL-90, suggesting that individual stress responsivity may moderate psychobiotic efficacy (37). In clinical populations with diagnosed depression, similar psychobiotic formulations have demonstrated adjunctive therapeutic potential. Wallace et al. (107) examined depressed patients not currently receiving antidepressants in a double-blind, randomized 16-week trial using Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 at a daily dose of 6×10^9 CFU. After four weeks, participants in the probiotic group displayed significant reductions in scores on multiple assessment scales, including the Montgomery–Åsberg Depression Rating Scale (MADRS), the Quick Inventory of Depressive Symptomatology (QIDS-SR16), the Pittsburgh Sleep

Quality Index (PSQI), and the Snaith–Hamilton Pleasure Scale (SHAPS), which measures anhedonia. Anxiety symptoms, assessed via the Generalized Anxiety Disorder-7 (GAD-7) scale and the State–Trait Anxiety Inventory (STAI), also improved, indicating broad effects on mood and anxiety dimensions (107).

In a related study, Kazemi et al. (108) evaluated the same bacterial combination in depressed patients who were concurrently taking antidepressants such as sertraline, escitalopram, fluoxetine, or amitriptyline. Over eight weeks, those receiving Lactobacillus helveticus and Bifidobacterium longum showed greater reductions in Beck Depression Inventory scores compared with patients taking placebo or prebiotic galactooligosaccharides. Biochemical analyses indicated increased serotonin production from tryptophan and a decreased kynurenine/tryptophan ratio, supporting the hypothesis that psychobiotics may shift tryptophan metabolism away from neurotoxic kynurenine pathways toward serotonin synthesis, thereby enhancing antidepressant response (108). Rudzki et al. (109) explored psychobiotic augmentation using Lactobacillus plantarum 299v in a double-blind randomized study of 60 patients with major depressive disorder receiving standard SSRI treatment. Over eight weeks, the combined SSRI plus Lactobacillus plantarum 299v group exhibited improved cognitive performance and reduced levels of kynurenine (KYN) compared with SSRI plus placebo. The decrease in KYN levels may have contributed to cognitive gains, as elevated kynurenine metabolites have been implicated in cognitive dysfunction and neurotoxicity; this finding highlights a potential mechanism through which psychobiotics can mitigate both emotional and cognitive symptoms in depression (109). Additional smaller trials such as the double-blind randomized study by Wallace et al. (107) in 10 patients with depression and the post hoc analysis by Heidarzadeh-Rad et al. (110) in 78 depressed patients both support an antidepressant effect of combinations of Lactobacillus helveticus Rosell-52 and Bifidobacterium longum Rosell-175. In these investigations, eight weeks of supplementation improved depressive symptoms, possibly mediated by increases in serum BDNF, reinforcing the idea that nutritional modulation of neurotrophic signaling has clinically relevant consequences (107, 110).

Psychobiotic interventions have also been tested in neurodegenerative conditions. Aghai et al. (111) conducted a double-blind randomized trial in 48 patients with Alzheimer's disease (AD), using a multi-strain probiotic mixture containing Lactobacillus fermentum, Lactobacillus plantarum, Bifidobacterium lactis, Lactobacillus acidophilus, Bifidobacterium bifidum, and Bifidobacterium longum at 3×10^{10} CFU/day for 12 weeks. Cognitive and biochemical outcomes suggested that patients with severe AD were relatively insensitive to probiotic supplementation, and the authors emphasized that disease severity, probiotic composition, dose, and timing may all determine responsiveness (111). In contrast, Akbari et al. (112) administered 200 mL/day of probiotic milk containing Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum, and Lactobacillus fermentum (2×10^9 CFU/day) to 52 patients with AD over 12 weeks. Although no significant effects were observed on markers of oxidative stress and inflammation, probiotic consumption had a positive impact on cognitive test performance and certain metabolic parameters, indicating that cognitive benefits may occur even in the absence of overt changes in systemic oxidative markers (112). Tamtaji et al. (113) evaluated a combination of Lactobacillus acidophilus, Bifidobacterium bifidum, and Bifidobacterium longum (6×10^9 CFU/day) together with 200 µg selenium for 12 weeks in 79 AD patients. This co-supplementation improved cognitive function and some metabolic indices, suggesting that synergistic interactions between probiotics and antioxidant micronutrients may be particularly beneficial in neurodegenerative contexts (113).

Beyond classical mood and dementia disorders, psychobiotic strategies have been explored in conditions characterized by chronic fatigue and cognitive complaints. Wallis et al. (114) investigated patients with chronic fatigue syndrome in an open-label study involving 44 participants over six weeks. The intervention combined erythromycin with Lactobacillus rhamnosus, Bifidobacterium lactis, Bifidobacterium breve, and Bifidobacterium longum in specified CFU doses. The authors reported that particular microbial strains interacted with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) symptoms and offered promise for therapeutic approaches targeting intestinal dysbiosis, although larger controlled trials are needed for confirmation (114). Cognitive dysfunction associated with aging and mild cognitive impairment (MCI) has likewise become an important target for psychoprotective food ingredients. Hwang et al. (115) conducted a double-blind randomized controlled trial in 92 individuals with MCI, supplementing Lactobacillus plantarum C29 at 1.25×10^{10} CFU/day combined with powdered fermented soybeans (DW2009) for 12 weeks. The results indicated that DW2009 could be safely administered and improved cognitive performance, pointing to the potential of combining traditional fermented foods with concentrated probiotic strains in early cognitive decline (115). Kobayashi et al. (116) performed an open-label study in 27 participants with MCI receiving Bifidobacterium breve A1 at 2×10^{10} CFU/day for six months. Oral supplementation improved cognitive function and quality of life,

suggesting a favorable impact on daily functioning in elderly individuals (116). A subsequent double-blind randomized controlled trial by the same group in 117 patients with MCI confirmed the safety of Bifidobacterium breve A1 and supported its potential role in maintaining cognitive function in elderly individuals with memory impairment over 12 weeks (117).

Collectively, these studies underscore that specific bacterial strains, delivered through foods or supplements, may exert psychoprotective effects ranging from mood stabilization and anxiety reduction to cognitive enhancement and mitigation of neurodegenerative processes. Nevertheless, there are important limitations that must temper enthusiasm. Many trials are relatively small, vary in probiotic composition, dosage, and duration, and use heterogeneous outcome measures, making direct comparison and meta-analysis difficult. Placebo effects, dietary confounders, and interindividual variability in baseline microbiota composition further complicate interpretation. Moreover, the long-term durability of psychobiotic effects and their interaction with standard pharmacotherapies remain incompletely understood, especially given the potential for antidepressants and antipsychotics to disrupt microbiome structure (39). From a nutritional standpoint, psychoprotective food ingredients encompass not only isolated probiotic strains but also the broader dietary matrices that support their survival and activity, including fermented dairy products, fermented soy, pickled vegetables, and prebiotic-rich plant foods. The rational design of psychobiotic therapies will likely require a personalized approach that accounts for baseline microbiota profiles, host genetics, dietary patterns, and clinical diagnosis. Future research should aim to identify the most effective strain combinations, clarify dose–response relationships, and determine which patient subgroups are most likely to benefit. Despite current uncertainties, the accumulated evidence suggests that targeted modulation of the gut microbiota through probiotic, prebiotic, and synbiotic interventions represents a promising and biologically plausible avenue for enhancing mental health and preventing or attenuating psychiatric and neurocognitive disorders (25–39, 96–117).

A wide spectrum of biological and environmental factors, including genotype, intrauterine infections, early developmental disturbances, later traumatizing life events, and the use of harmful psychoactive substances, shape both the onset and the longitudinal course of psychiatric disorders. These determinants interact in complex ways across the life span, influencing not only whether a disorder emerges but also its severity, chronicity, and response to treatment. Clinical and epidemiological data indicate that early recognition and intervention in emerging psychiatric conditions are associated with superior treatment outcomes, reduced symptom burden, and better social and occupational functioning, an effect that is particularly evident in research on prodromal and first-episode psychosis (40). Consequently, prevention in psychiatry, as in other branches of medicine, relies on the availability of valid tools to detect heightened risk, to monitor nascent psychopathological changes, and to guide timely intervention before full syndromal illness becomes established. Within this preventive framework, McGorry et al. (41) proposed a four-stage developmental model of mental disorders that has become highly influential in early intervention psychiatry. According to this model, severe mental illness emerges gradually from earlier states of vulnerability. Stage 0 represents a high-risk but asymptomatic phase, followed by stage 1, in which undifferentiated, non-specific symptoms such as mild anxiety, restlessness, low-grade depressive features, or somatic complaints begin to appear. Stage 1 can be further subdivided into stages 1A and 1B, reflecting increasing symptom intensity and functional decline (41). Progression to stage 2 marks the occurrence of the first discrete episode of a diagnosable disorder, often accompanied by persistent symptoms and frequent relapses, particularly in psychotic illnesses. Stage 3 is characterized by incomplete remission between episodes and recurrent, often predictable relapses, while stage 4 denotes chronic, treatment-resistant illness with entrenched disability (41). This staging approach underscores that psychiatric disorders worsen over time in a manner strongly shaped by environmental influences superimposed on genetic liability, and it is precisely these environmental factors that represent the key target for preventive interventions.

Several candidate biomarkers that are tightly linked to environmental and lifestyle exposures, including nutrition, have been proposed as early indicators of risk. One of the most extensively studied systems is the hypothalamic–pituitary–adrenal (HPA) axis, which regulates stress responses. A diminished capacity to cope with stress is a well-recognized contributor to the development of psychiatric conditions (42). Traumatic experiences in childhood, such as abuse, neglect, or chronic family adversity, exert long-lasting effects on HPA axis reactivity, thereby increasing vulnerability to stress-related disorders later in life (43). In many psychiatric illnesses, including affective and psychotic disorders, dysregulation of the HPA axis is evident, often manifesting as hypercortisolemia and impaired feedback inhibition (42, 44). Pharmacological studies suggest that antipsychotic medications may partially normalize HPA axis overactivity, which could contribute to their therapeutic effects, particularly on agitation and stress sensitivity (44–47). Strikingly, even psychiatrically healthy first-degree relatives of individuals with psychotic disorders have been found

to exhibit subtle HPA axis abnormalities, including elevated basal cortisol levels, indicating that HPA dysfunction may serve as a biological marker of inherited vulnerability before overt illness has developed (48). In light of emerging data on the influence of diet and gut microbiota on HPA axis regulation, these findings invite further investigation of nutritional strategies as modulators of stress-related risk (42, 48).

Beyond neuroendocrine dysregulation, inflammatory and oxidative pathways have been implicated as key biological processes in the pathophysiology of major psychiatric disorders (49). The inflammatory hypothesis of depression posits that increased levels of pro-inflammatory cytokines perturb monoamine neurotransmission, neuroplasticity, and glucocorticoid signaling, thereby contributing to the onset and persistence of depressive symptoms (50). Elevated concentrations of cytokines such as interleukin-6 and tumor necrosis factor-α have been documented not only in depressive episodes but also in psychotic and manic states, suggesting shared inflammatory mechanisms across diagnoses (50, 51). Importantly, longitudinal studies indicate that raised inflammatory markers can precede the first onset of depression or psychosis, supporting their role in disease genesis rather than being merely epiphenomena of established illness (52). Parallel evidence points to increased oxidative stress in psychotic disorders, including reductions in glutathione and other endogenous antioxidant enzymes, which may compromise neuronal integrity and synaptic function (53). Therapeutic observations further strengthen the clinical relevance of these pathways. The adjunctive use of selective cyclooxygenase-2 (COX-2) inhibitors has shown promising effects in reducing symptom severity in bipolar affective disorder and schizophrenia, presumably through targeted anti-inflammatory actions (51, 54). Likewise, treatment with statins, which combine lipid-lowering properties with anti-inflammatory and antioxidant effects, has been associated with a decreased risk of developing depressive disorders in epidemiological studies (55). Such data indicate that anti-inflammatory and antioxidant strategies could complement traditional psychopharmacology, and they highlight the importance of lifestyle factors, including diet, which strongly influence systemic inflammation and redox balance (49–55).

Polyunsaturated fatty acids, particularly omega-3 series, have emerged as additional biomarkers and potential therapeutic agents in psychiatry. These lipids are integral components of neuronal membranes, modulating fluidity, receptor function, and signal transduction. Several lines of evidence suggest that omega-3 polyunsaturated fatty acids may play a role in the pathogenesis of affective and psychotic disorders (56, 57). Deficiencies in omega-3 levels have been reported in individuals at ultra-high risk of psychosis, corresponding to stage 1B in McGorry's model, as well as in patients with first-episode and chronic psychotic disorders (56–58). A landmark randomized controlled trial demonstrated that supplementation with omega-3 polyunsaturated fatty acids in high-risk individuals significantly reduced the transition rate to full-blown psychotic disorders compared with placebo, indicating that modifying lipid status may exert a genuine preventive effect (58). These findings are consistent with broader research linking dietary patterns rich in fish and plant-based sources of omega-3 fatty acids to lower rates of depression and better cognitive outcomes, underscoring the nutritional dimension of psychiatric risk (56–58). An additional interface between nutrition, immunity, and psychiatric vulnerability is provided by the intestinal barrier. This barrier is a multilayered structure comprising the gut microbiota, an overlying mucus layer, the intestinal epithelial lining, and subepithelial components of the circulatory, immune, nervous, and lymphatic systems. Among these, the epithelial layer of tightly interconnected enterocytes is the central determinant of barrier integrity (59). Its primary task is to regulate the selective absorption of nutrients, electrolytes, and water from the lumen while preventing translocation of pathogens and toxins into the systemic circulation (59). A range of external factors, many of them modifiable, can compromise this barrier, including psychological stress, systemic pro-inflammatory states, dysbiosis of the intestinal microbiota, excessive alcohol consumption, and repeated or inappropriate use of antibiotics (60–62). Disruption of tight junctions and increased intestinal permeability ("leaky gut") allow luminal bacteria and their products to cross into the lamina propria and beyond, activating immune cells and triggering inflammatory cascades that can influence endocrine and neural systems as well (61, 62).

Current research has highlighted the microbiota and its diversity as major determinants of low-grade systemic inflammation, which in turn is implicated in the pathogenesis of depression and other psychiatric conditions (61). In line with the leaky gut hypothesis, patients with depression have been observed to exhibit elevated IgA and IgM antibodies directed against lipopolysaccharides from Gram-negative gut bacteria, suggesting increased exposure of the immune system to bacterial antigens as a result of barrier dysfunction (63). To capture the inflammatory potential of dietary patterns, investigators have developed the dietary inflammatory index (DII), which quantifies the expected effect of the whole diet or individual food components on circulating inflammatory markers based on prior literature (64). In a comprehensive systematic review, Chen et al. (64) found that higher DII scores, reflecting more pro-inflammatory diets,

were associated with an increased risk of common psychiatric outcomes, including depressive symptoms, anxiety, psychological distress, and schizophrenia. A particularly important insight from their dose–response analysis was that each 1-point increase in DII corresponded to a 6% higher risk of depressive symptoms, illustrating that even modest shifts toward pro-inflammatory eating patterns may have measurable mental health consequences (64). Similar associations have been reported by Firth et al. (63), who observed that individuals with schizophrenia consuming diets rich in pro-inflammatory foods and poor in anti-inflammatory components showed more pronounced psychiatric symptoms and worse overall outcomes. These findings reinforce the notion that dietary patterns not only shape systemic inflammation but also may contribute directly to the trajectory of severe mental illness. Given that pro-inflammatory diets are characterized by high intakes of refined carbohydrates, saturated fats, and ultra-processed foods and low intake of fruits, vegetables, whole grains, and omega-3-rich foods, they are also likely to compromise the structure and function of the intestinal barrier (61, 64). Indeed, growing evidence indicates that Western-style diets dominated by fast food and highly processed products are associated with increased intestinal permeability, altered microbiota composition, and heightened endotoxemia (65, 66). These changes may, in turn, propagate systemic inflammation, disturb HPA axis function, and amplify oxidative stress, thereby linking dietary behavior to the biological processes that underlie psychiatric vulnerability and chronicity (49–53, 60–66).

Taken together, the converging lines of evidence from genetic, neuroendocrine, inflammatory, and gut-related research support a developmental model of psychiatric disorders in which early environmental exposures—particularly stress and diet—interact with biological vulnerability to shape both onset and course. The HPA axis, inflammatory and oxidative markers, omega-3 fatty acid status, and indices of intestinal barrier integrity are emerging as promising, nutrition-sensitive biomarkers that may help identify individuals at risk, track disease progression, and guide targeted preventive and therapeutic strategies. By integrating these biomarkers into the staged model of mental illness proposed by McGorry et al. (41), and by recognizing the pivotal role of diet in modulating them, psychiatry can move toward a more preventive, personalized, and nutritionally informed paradigm of care (40–66).

Nutritional interventions with proven preventive potential for mental disorders

The field of nutritional psychiatry has developed rapidly over the last two decades, largely driven by epidemiological observations that dietary patterns are associated with the risk, course, and prognosis of common mental disorders. Large cohort studies show that individuals consuming diets rich in minimally processed, nutrient-dense foods tend to have better mental health outcomes, whereas those whose diets are dominated by ultra-processed, energy-dense products show higher rates of depression, anxiety, and cognitive decline (17). Intervention studies, though still relatively few, have begun to confirm that these associations are at least partly causal, indicating that specific dietary patterns can be used as preventive or adjunctive strategies in the management of mental disorders (17, 67–70). The central challenge for nutritional psychiatry is now to generate methodologically robust, adequately powered randomized controlled trials that define the role of diet and individual nutrients in prevention across different diagnostic groups and life stages, and that clarify the mechanisms linking dietary change to improvements in mental health (67–70). To date, only a limited number of randomized controlled trials have evaluated whole-diet interventions for the treatment or prevention of depression. One of the seminal studies in this area examined the effects of a 12-week Mediterranean-style diet in adults with major depressive disorder. Participants receiving structured dietary support to adopt a Mediterranean diet showed significant improvements in mood and reduced anxiety compared with those receiving social support alone, suggesting that changing overall dietary pattern, rather than simply adding a supplement, can meaningfully influence depressive symptomatology (71). Subsequent trials such as HELFIMED and PREDI_DEP have strengthened this evidence base, again demonstrating that adherence to a Mediterranean-style diet is associated with better outcomes in depression and reduced psychological distress (72, 73). These studies collectively support the notion that complex dietary patterns rich in fruits, vegetables, whole grains, legumes, nuts, olive oil, and fish—foods that provide a broad spectrum of fiber, antioxidants, polyphenols, and unsaturated fatty acids—can have clinically relevant effects on mental health (71–73).

In contrast to the positive results observed with whole-diet interventions, trials focusing on multinutrient supplementation have generally been disappointing with respect to the primary prevention of depression. The MooDFOOD randomized controlled trial provides an important example. In this large study of overweight or obese adults with subsyndromal depressive symptoms, supplementation with a multinutrient formula containing omega-3 polyunsaturated fatty acids, vitamin D, folic acid, and selenium over a prolonged period did not reduce the incidence of major depressive episodes compared with placebo (74). Nor did the supplement improve depressive or anxiety symptoms or health-related quality of life indices, despite including nutrients that had previously been implicated in mood regulation (74). Similar null findings have emerged from

systematic reviews and meta-analyses focusing on single nutrients. For vitamin D, a comprehensive review concluded that supplementation did not consistently improve mood or prevent depression, even in individuals with low baseline levels (75). An RCT investigating omega-3 polyunsaturated fatty acids in people with mild to moderate depression likewise found no significant advantage of omega-3 treatment over placebo in reducing depressive symptoms (76). Evidence for B-vitamin supplementation as a preventive strategy is similarly weak. Large trials in older men and women revealed no protective effect of folic acid combined with vitamins B_6 and B_{12} on the onset of depression over follow-up periods, despite successful reductions in homocysteine concentrations (77, 78). Selenium, another micronutrient with theoretical antioxidant and neuroprotective properties, also failed to demonstrate mood benefits in a randomized study of older adults, where selenium supplementation did not improve depressive symptoms or general mood indices (79). Taken together, these findings suggest that isolated nutrient supplementation, at least with the combinations and doses tested to date, cannot be recommended as an evidence-based strategy for the prevention of depression at the population level. Instead, they underscore the likely importance of complex dietary matrices and food synergy, as well as the possibility that supplements may only be effective in targeted subgroups with specific deficiencies (74–79).

While depression prevention via supplementation remains uncertain, stronger evidence supports a protective role of dietary quality for cognitive aging and dementia. Multiple longitudinal studies have demonstrated that higher adherence to healthy dietary patterns in adulthood is associated with a reduced risk of cognitive decline and better performance on neuropsychological tests over time (17). Older adults who consume diets abundant in vegetables, fruits, whole grains, nuts, and fish exhibit slower trajectories of cognitive deterioration than those whose diets are dominated by refined carbohydrates, saturated fats, and ultra-processed foods (17). A key mechanistic hypothesis is that such diets are richer in antioxidant and anti-inflammatory compounds, including polyphenols, which counteract oxidative stress and neuroinflammation implicated in neurodegenerative processes. Indeed, higher intake of antioxidant polyphenols in older adults has been linked with improved cognitive capacity and slower progression of mild cognitive impairment (80–82). The Mediterranean diet, characterized by high consumption of plant foods, moderate intake of fish and poultry, low intake of red and processed meats, and regular use of extra-virgin olive oil and nuts, has received particular attention in this context. In one influential trial, a Mediterranean diet supplemented with either extra-virgin olive oil or mixed nuts was associated with improved cognitive function and reduced risk of cognitive decline in an older population, compared with a control low-fat diet (83). These findings suggest that adherence to Mediterranean dietary principles may confer neuroprotective effects, potentially through a combination of vascular, metabolic, anti-inflammatory, and direct neurobiological mechanisms, including improved endothelial function, reduced oxidative damage, and modulation of amyloid metabolism (80–83).

Against this background, specific dietary patterns have been proposed to optimize brain health and potentially prevent or delay the onset of mental disorders. Among these, the MIND diet, the Mediterranean diet, and the ketogenic diet have attracted particular interest as nutritional interventions with potential psychoprotective effects. The MIND (Mediterranean–DASH Intervention for Neurodegenerative Delay) diet was developed explicitly to counteract neurodegenerative brain changes and support nervous system function (84). It synthesizes key elements of the Mediterranean diet and the DASH (Dietary Approaches to Stop Hypertension) diet, both of which favor high intakes of vegetables, fruits, nuts, whole grains, and olive oil, as well as regular consumption of fish and moderate amounts of red wine with meals (85). The DASH and Mediterranean diets have already demonstrated beneficial effects in reducing risk for diabetes, cancer, cardiovascular disease, and obesity, emphasizing their broad systemic impact (86–89). What differentiates the MIND diet from its parent patterns is its targeted focus on foods and nutrients most strongly associated with cognitive protection. It places particular emphasis on leafy green vegetables and berries, which are rich in flavonoids and other neuroprotective phytochemicals, and these components are not specifically highlighted in the classical Mediterranean or DASH formulations (90). The MIND diet does not stress high consumption of fruit in general, nor of dairy products or potatoes, reflecting evidence that not all food groups considered “healthy” in other contexts exert equal benefits on brain aging (90). Regarding fish intake, the MIND diet is less demanding: individuals consuming as little as one portion of fish per week can still meet the criterion for high adherence, whereas the Mediterranean and DASH diets typically require higher frequencies of fish consumption to be considered compliant (91). This lower threshold may make the MIND diet more feasible and acceptable in populations where fish is consumed infrequently.

Longitudinal observations indicate that adherence to the MIND diet significantly slows age-related cognitive decline and lowers the risk of developing Alzheimer’s disease, even after adjusting for other lifestyle factors (92). Moreover, adherence to the MIND diet has been significantly associated

with reduced odds of depression and psychological distress, although the relationship with anxiety appears weaker or non-significant in some cohorts (90). These findings suggest that the MIND diet may exert broad beneficial effects on both cognitive and emotional dimensions of mental health, potentially via shared mechanisms such as enhanced vascular health, reduced inflammation, and improved synaptic plasticity (84, 90, 92). The Mediterranean diet itself has also been associated with a protective effect on anxiety and perceived mental stress, further supporting the notion that plant-forward, minimally processed dietary patterns may bolster resilience to psychological adversity (83, 93). A different, but complementary, line of research focuses on the ketogenic diet, an intervention with a long history in neurology as an effective treatment for drug-resistant epilepsy. Mental illnesses frequently coexist with metabolic disturbances in the brain and are accompanied by systemic metabolic conditions such as obesity, insulin resistance, and cardiovascular disease, all of which may exacerbate psychopathology and complicate treatment. The ketogenic diet, in which up to 80% of total energy is derived from fat and carbohydrate intake is markedly restricted, induces a metabolic state in which the liver produces ketone bodies—primarily β-hydroxybutyrate and acetoacetate—as alternative energy substrates for the brain (83). Although such a macronutrient profile appears at odds with conventional dietary guidelines, extensive clinical experience has established that ketones can reduce seizure frequency and severity in patients with epilepsy who are unresponsive to standard anticonvulsant therapies (83).

Evidence for ketogenic interventions in mitochondrial epilepsy and other refractory seizure disorders is more mixed. In a study by El Sabbagh et al. (94), none of the patients on a ketogenic diet achieved a clinically significant reduction in seizure frequency, suggesting that underlying mitochondrial pathology may limit responsiveness to ketosis. Conversely, Kang et al. (95) reported more favorable results in a series of 14 patients: ten individuals experienced a greater than 50% reduction in seizure frequency, and seven became seizure-free during ketogenic treatment. Notably, beyond seizure control, improvements were observed in mood, cognitive function, communication skills, energy levels, anxiety, and even psychotic symptoms such as auditory and visual hallucinations (90, 95). These findings imply that altering brain energy metabolism through ketosis may modulate neurotransmitter systems and neuroinflammatory pathways relevant to both neurological and psychiatric symptom domains. Furthermore, ketogenic regimens have been associated with beneficial biometric changes, including improvements in lipid profiles, weight reduction, better glycemic control, and decreases in glycated hemoglobin (HbA1c) levels (93, 95). Given that many individuals with severe mental illness experience metabolic syndrome, antipsychotic-induced weight gain, and type 2 diabetes, such metabolic benefits may indirectly enhance mental health by reducing somatic comorbidity, improving self-esteem, and increasing physical functioning (93). Nevertheless, the ketogenic diet is intensive, restrictive, and requires close medical supervision due to potential adverse effects such as micronutrient deficiencies, dyslipidemia, and kidney stones. Its long-term safety and efficacy as a primary or adjunctive intervention in psychiatric populations remain to be established.

Taken together, the current evidence suggests that among nutritional interventions, whole-diet patterns such as the Mediterranean diet and the MIND diet have the most convincing preventive potential for common mental disorders, particularly depression and cognitive decline, while the ketogenic diet shows promise in specific neurological and possibly psychiatric conditions but requires much more rigorous evaluation (71–73, 83–95). In contrast, the accumulated data do not support routine use of multinutrient or single-nutrient supplementation—for example, vitamin D, omega-3 fatty acids, B-vitamins, or selenium—as stand-alone preventive measures for depression in the general population, although such supplements may still have a role in correcting documented deficiencies or in carefully selected subgroups (74–79). Despite these advances, substantial gaps in knowledge remain. Many of the existing trials are limited by small sample sizes, relatively short intervention periods, heterogeneous outcome measures, and lack of long-term follow-up. The mechanisms by which dietary patterns exert their mental health effects—whether through modulation of inflammation, oxidative stress, neurotrophic factors, gut microbiota, or metabolic and vascular pathways—are only partly understood. Furthermore, individual variability in genetic makeup, microbiome composition, and psychosocial context likely modifies response to dietary interventions, indicating that "one-size-fits-all" recommendations may be insufficient (67–70, 118–121).

For nutritional psychiatry to progress from promising associations to robust clinical recommendations, it will be crucial to replicate, refine, and scale up dietary intervention studies targeting both prevention and treatment of common mental disorders. Future trials should employ rigorous randomized designs with adequate power, carefully characterize baseline nutritional and metabolic status, integrate biological biomarkers alongside clinical endpoints, and follow participants over extended periods to assess durability of effects (118–121). There is also a pressing need to compare whole-diet interventions directly with supplementation strategies, to identify cost-effective, culturally adaptable dietary prescriptions, and to explore how nutritional interventions can be

integrated into multidisciplinary mental health services. Only through such comprehensive and coordinated research efforts can nutritional interventions with proven preventive potential be fully harnessed to reduce the global burden of mental disorders.

Conclusion:

In conclusion, the evidence synthesized in this review firmly establishes nutrition as a pivotal, modifiable determinant of mental health, giving rise to the promising field of nutritional psychiatry. The findings demonstrate that overall dietary patterns exert a more significant influence on mental well-being than isolated nutrients. Specifically, whole-food diets such as the Mediterranean and MIND diets, rich in fruits, vegetables, whole grains, and healthy fats, are consistently associated with a reduced risk of depression and cognitive decline. Conversely, diets high in ultra-processed foods promote inflammation and oxidative stress, thereby increasing psychiatric vulnerability. The mechanisms underlying this diet-mental health connection are multifaceted, involving the modulation of inflammation, oxidative stress, neurotrophic factors like BDNF, and the gut-brain axis through psychobiotics. While supplementation with specific nutrients (e.g., omega-3s, vitamin D) may benefit individuals with deficiencies, their standalone use for primary prevention in the general population is not strongly supported. This underscores the principle of food synergy, where the combined effect of a nutrient-dense diet is greater than the sum of its parts. Therefore, moving forward, mental healthcare must evolve to systematically incorporate nutritional assessment and dietary intervention. Promoting evidence-based, anti-inflammatory dietary patterns represents a scalable, empowering, and effective strategy for both preventing and adjunctively treating mood disorders, ultimately reducing the global burden of mental illness.

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