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MEDITERRANEAN DIET AND DEPRESSION: A LITERATURE REVIEW OF HUMAN STUDIES

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ABSTRACT

With depression as a major cause of disability worldwide, the need for risk reduction and improving treatment outcomes is pressing. This narrative review summarizes human evidence on the association between adherence to the Mediterranean diet (MD) and depressive disorders or depressive symptoms, and on the effects of Mediterranean-style dietary interventions in reducing depressive symptoms. A literature search was conducted in PubMed, Cochrane, and Google Scholar databases, using keywords such as "Mediterranean diet", "Depression" among others, and studies were selected and reviewed. Overall, observational evidence from multiple cross-sectional studies and several prospective cohorts indicates that higher MD adherence is associated with fewer depressive symptoms and a modestly reduced risk of incident depression across diverse populations. Randomized and cluster-randomized trials in clinical and at-risk groups further suggest that Mediterranean-style dietary interventions can reduce depressive symptom severity and improve mental health–related quality of life when used alongside usual care. Meta analyses and systematic reviews consistently show statistical significance of the findings. Potential mechanisms include anti-inflammatory and antioxidant effects, neurotrophic and neurotransmitter pathways, gut–brain interactions, and improvements in cardiometabolic health. The MD appears to be a safe and feasible adjunctive lifestyle recommendation for adults with depression, although heterogeneity in exposure measurement and limited long-term trial data warrant larger, multi-centre studies with longer follow-up and mechanistic assessments, across different populations.

KEYWORDS

Mediterranean Diet, Depression, Dietary Interventions, Mental Health and Nutrition

CITATION

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Introduction

Depression is a highly prevalent and disabling mental disorder and a major contributor to global non-fatal health loss [1]. Despite advances in pharmacological and psychological treatments, many patients do not achieve full remission after first-line care and may require multiple treatment steps, which has increased interest in adjunctive, modifiable lifestyle approaches [2]. In this context, "lifestyle psychiatry" has highlighted diet—alongside physical activity and sleep—as a potentially important, scalable target for prevention and complementary treatment of depressive disorders [3].

The Mediterranean diet (MD) is a dietary pattern traditionally characterized by high consumption of vegetables, fruits, legumes, nuts, and whole grains; olive oil as the primary fat source; moderate intake of fish and fermented dairy products; and lower intake of red/processed meats and refined foods [4]. The MD has well-established cardiometabolic benefits and reduces cardiovascular events in high-risk adults, supporting its feasibility as a long-term, health-promoting eating pattern [5]. Given the frequent co-occurrence and bidirectional links between depression and cardiometabolic dysregulation, it is plausible that dietary patterns that improve metabolic and vascular health may also influence depression risk and symptom burden [3,5].

Over the past two decades, an expanding body of human research has examined whether higher MD adherence is associated with fewer depressive symptoms and whether Mediterranean-style dietary interventions can improve outcomes in adults with depression. The objective of this review is to summarize and critically assess evidence from human studies on the relationship between MD adherence (and Mediterranean-style interventions) and depressive disorders or depressive symptoms.

Methodology

Search strategy

A literature search was conducted in PubMed, Cochrane and Google Scholar databases to identify human studies examining the Mediterranean diet in relation to depression. Search terms included combinations of “Mediterranean diet”, “Mediterranean dietary pattern”, “MedDiet”, “Diet, Mediterranean”, “depression”, “depressive symptoms”, “depressive disorder”, “major depressive disorder”, and “Depressive Disorder”. For interventional studies, the terms “randomized/randomised”, “trial”, and “intervention” were added.

Results

Systematic reviews and meta-analyses

Of the recent large systematic reviews Eliby et al. (2023) found that Mediterranean Diet interventions significantly reduced depressive symptom severity. 44 studies were examined that met inclusion criteria, moreover, other dietary patterns were included in the study, and of them MD showed the most promise [6]. The findings were in line with previous meta-analyses and reviews [6-9]. One systematic review and meta-analysis by Shafiei et al. (2019) contradicts those findings, in the study the researchers pooled observational studies on MD adherence and depression, cross-sectional analyses showed significantly lower odds of depression among individuals with higher Mediterranean diet adherence, but data from prospective cohort studies found no link between MD and risk of depression. [10]. However despite this outlier, the majority of literature points towards a highly beneficial role of MD [6-9]. Additionally Bizzozero-Peroni et al. (2025) conducted a meta-analysis of 5 randomised controlled studies which focused on applying MD interventions in patients with diagnosed or self reported major depressive disorder or mild to major depressive symptoms [11]. While a reduction in depressive symptoms was observed the study highlighted the need for more RTCs with larger populations and longer follow up times [11].

Cross-sectional studies

In Spanish primary care, Oliván-Blázquez et al. (2021) showed on a population of 3062 subjects that adherence to a “proper Mediterranean diet”, based on a validated index, was associated with lower PHQ-9 depressive symptom scores [12]. The diet criteria included, among others, less than 1 red meat serving per day, less than 1 sugary drink per day, more than 2 vegetables cooked in olive oil per week and more than 3 servings of nuts per week [12]. Analyses of US NHANES data by Oddo et al. indicated that adults in the highest quartile of adherence to alternate Mediterranean Diet (aMED) score had substantially lower odds of moderate-to-severe depressive symptoms (PHQ-9 $\geq$10) compared with those in the lowest quartile [13]. Fan et al. also working on US NHANES data, observed a non-linear inverse relationship between aMED and depressive symptoms, suggesting diminishing returns beyond moderate adherence [14]. In Korea, Hwang et al. found that higher adherence to an adapted MD index was associated with lower odds of depression in both men and women in a population of 5,849 adults [15].

Among adults with obesity, Menichetti et al. reported that higher MD adherence, validated by MEDAS score, was associated with lower risk of anxiety and depression, 7% of odds reduction per 1 point of increase of MEDAS score, indicating possible benefits in metabolically at-risk populations [16].

Several cross-sectional studies focused on older people, Masana et al. reported that higher MD adherence was associated with lower GDS scores in older adults living across many Mediterranean islands [17]. Hernández-Galiot and Goñi found that non-institutionalised elderly Spaniards with higher MedDietScore values had fewer depressive symptoms and better perceived health [18]. In an Italian cohort, Vicinanza et al. observed that Mediterranean diet adherence attenuated the association between multimorbidity and depressive symptoms, suggesting that diet may buffer the mental health impact of multiple chronic conditions [19]. Conti et al. used data from the NutBrain study which looked at adults over 65 living in the Lombardy region of Italy, and observed that higher adherence to MD correlated with lower odds of depression, however when the analysis was stratified by sex, it was found that the correlation was statistically significant only in women [20].

Multiple studies assessed university students, Pennisi et al. studied Italian university students and observed that higher Medi-Lite MD scores were associated with lower PHQ-9 depressive symptom severity [21]. In a national survey of Greek university students, Alexatou et al. found that low Mediterranean diet adherence (KIDMED index) was associated with higher prevalence of depression (BDI-II) and anxiety [22]. Among Chilean university students, Morales et al. found that moderate-to-high Mediterranean diet adherence was associated with lower odds of depressive, anxiety and stress symptoms (DASS-21), whereas high ultra-processed food intake was associated with worse mental health [23]. In Lebanese university students, El Mikkawi et al. showed that higher Mediterranean diet adherence (MEDAS score) was associated with lower

levels of anxiety and perceived stress, while associations with depressive symptoms (PHQ-4) were far weaker [24]. In Spanish university students, Alfaro-González et al. reported that high Mediterranean diet adherence (MEDAS ≥9) was associated with lower BDI-II and GAD-7 scores. However, mediation analyses suggested that lean mass and muscle strength mediated the association between MD and depression [25].

Prospective cohort studies

In the SUN cohort which covered Spanish university graduates, Sánchez-Villegas et al. (2009) followed over 10,000 non-depressed participants while asessing adherence to MD using a validated score [26]. Over a median 4.4-year follow-up, participants in the group with highest adherence had a greatly reduced risk of developing depression compared with those who did not follow the dietary guidelines, even after adjustment for numerous confounding variables [26].

In the Chicago Health and Aging Project, Skarupski et al. found that higher MD scores were associated with fewer depressive symptoms (CES-D) over an avarage time of 7.2 years of observation, among community-dwelling older adults in the USA [27].

In a large Swedish cohort of middle-aged and older women, over a period of over 20 years, Yin et al. observed that higher Mediterranean-style dietary pattern adherence was associated with reduced risk of first-time clinical depression, particularly severe depression, after adjustment for a broad set of confounders [28].

The HELIAD (Hellenic Longitudinal Investigation of Aging and Diet) study showed that greater adherence to the Mediterranean diet was associated with fewer depressive symptoms and lower probability of depression, even after accounting for cognitive status and its progression among older Greek adults [29].

In Eastern China, Zhang et al. used an alternate Mediterranean Diet (aMED) score adapted to local eating patterns and found that each 1-point increase in aMED was associated with approximately 5% lower risk of incident depression, with stronger associations in participants aged ≥65 years [30].

Randomized and cluster-randomized trials

The SMILES trial (Supporting the Modification of lifestyle In Lowered Emotional States) randomised adults with moderate-to-severe major depression and poor diet quality to a modified MD intervention (seven individual sessions with a dietitian over 12 weeks) or a befriending control condition [31]. All participants received usual clinical care. The MD group demonstrated a large and clinically meaningful improvement in MADRS scores compared with the control group, with remission rates of 32.3% versus 8.0%, respectively [31].

In the HELFIMED trial, adults with depression were randomized to a Mediterranean-style diet plus fish oil intervention with group education and cooking workshops, or to a social group control [32]. Over 3 months, the intervention group showed significantly greater improvements in depressive symptoms, anxiety and stress (DASS-21), and mental health–related quality of life than the control group [32].

The AMMEND trial (A Mediterranean Diet in MEN with Depression) enrolled young men (18–25 years) with moderate-to-severe depressive symptoms [33]. Participants received either a MD counselling intervention or a befriending session. At 12 weeks, the MD group exhibited significantly greater reductions in BDI-II scores and higher remission rates than the control group [33].

The PREDIMED trial, a large cardiovascular prevention trial, randomised high-risk adults to a MD supplemented with extra-virgin olive oil, a MD supplemented with nuts, or a low-fat control diet [34]. In a secondary analysis, Sánchez-Villegas et al. reported that among participants with type 2 diabetes, assignment to the MD plus nuts was associated with a lower risk of incident depression compared with the low-fat control diet [34].

The PREDIDEP trial, conducted in Spanish primary care, targeted adults with previous depression and cardiovascular risk factors. Cabrera-Suárez et al. found that a MD intervention enriched with extra-virgin olive oil improved health-related quality of life, including mental health domains, compared with usual diet advice [35].

In Iran, Radkhah et al. randomised adults with stress, anxiety and depressive symptoms to receive structured MD instructions or control dietary advice for 12 weeks [36]. The MD group had greater reductions in DASS-21 depression, anxiety and stress scores, and improvements in anthropometric indices, compared with the control group [36].

Discussion

Potential mechanisms

MD is rich in anti-inflammatory and antioxidant constituents, including omega-3 fatty acids, monounsaturated and polyunsaturated fats, polyphenols, and antioxidant vitamins (e.g., C and E) [37]. Depressive disorders have been linked to elevated inflammatory activity and oxidative stress [38,39]. Accordingly, reductions in inflammation and oxidative stress observed with higher-quality dietary patterns may plausibly contribute to improvements in mood [38–39].

Nutrients abundant in the MD (e.g., B vitamins, folate, and omega-3 fatty acids) participate in pathways relevant to monoamine synthesis and regulation [40,41]. Mediterranean-style dietary patterns have also been examined in relation to neurotrophic signaling, including brain-derived neurotrophic factor (BDNF), which is implicated in synaptic plasticity and stress resilience [42].

High intakes of fiber and polyphenol-rich plant foods typical of the MD support a more diverse gut microbiome and beneficial microbial functions [43]. Microbiome-derived metabolites, including short-chain fatty acids, can influence immune, endocrine, and neural signaling relevant to brain function [44]. These pathways are commonly described within the broader microbiota–gut–brain axis framework linking diet to mental health outcomes [45].

The MD improves cardiometabolic risk factors and reduces cardiovascular events [5]. Cardiometabolic disease and depression show bidirectional associations, suggesting that metabolic and vascular dysregulation may contribute to depressive risk and burden [46,47]. Therefore, MD-related improvements in cardiometabolic health may indirectly reduce depression risk and symptom severity over time [46,47].

Mediterranean-style dietary interventions often include behavioral and social components (e.g., cooking workshops, group sessions, shared meals) that can increase engagement and adherence [32]. Such components may also enhance social support and self-efficacy—factors relevant to depression management [31–33]. Trials using active social comparators (e.g., befriending/social groups) suggest that dietary change can produce benefits beyond non-specific support alone [31–33].

Limitations of the studies

This review indicates a quite consistent inverse relationship between MD adherence and depressive symptoms and risk of developing depression, supported by cross-sectional studies, prospective cohorts, and randomized dietary interventions. The strength of inference varies substantially by study design.

Cross-sectional studies dominate the literature and consistently show that higher MD adherence is associated with fewer depressive symptoms in general adult populations, older adults, and students. While this consistency across settings improves confidence that the association is not population-specific, cross-sectional evidence remains vulnerable to reverse causation and cannot establish temporal order.

Prospective cohorts provide stronger support for a potential protective effect, with several studies reporting modest reductions in incident depression risk or lower symptom trajectories among those with higher MD adherence. However, effect sizes are typically small, and residual confounding is a persistent concern. Individuals with higher MD adherence often differ systematically from low-adherence participants in education, income, physical activity, smoking, sleep, social support, and health-service access—factors that are themselves associated with depression risk. Although cohorts adjust for many covariates, measurement error in both diet and confounders may leave meaningful residual confounding. In addition, cohort studies vary in outcome definitions (clinical diagnosis, antidepressant use, symptom thresholds), follow-up duration, and baseline mental health exclusion criteria, which limits comparability and contributes to heterogeneity across findings.

Randomized and cluster-randomized trials offer the most direct evidence for causality. Trials that targeted clinically depressed participants and delivered structured MD-oriented support generally reported clinically meaningful reductions in depressive symptom severity and/or improvements in mental health–related quality of life when compared with active social controls or usual care. Yet important limitations remain. Most trials have modest sample sizes, short intervention periods (commonly ~12 weeks), and limited post-intervention follow-up, leaving uncertainty about long-term maintenance of dietary changes and durability of antidepressant effects. Moreover, MD interventions are complex and typically include counseling, goal-setting, education, and sometimes cooking workshops or food provision. Even when active controls are used, it is difficult to fully separate the effect of diet quality from non-specific therapeutic factors such as increased attention, expectancy, behavioral activation, and social support. Adherence assessment is also heterogeneous: some trials rely on self-reported checklists or short screeners, and fidelity to specific MD components may vary.

Across all designs, heterogeneity in how the MD is defined and quantified is a major barrier to synthesis. Studies use multiple indices (e.g., MEDAS, aMED, MedDietScore, MeDi-Lite) with different scoring rules and cut-offs, and some adapt MD scores to non-Mediterranean contexts. These differences may lead to misclassification and reduce the precision of pooled estimates. Dietary intake is most often assessed using FFQs or recalls, which are prone to reporting bias; this may be particularly relevant in depressed participants, who may have impaired recall or altered perceptions of diet. Depression assessment also varies widely (PHQ-9, CES-D, BDI-II, GDS, diagnostic interviews), and symptom scales capture transient distress as well as clinical syndromes. As a result, some studies may be measuring general psychological distress rather than major depressive disorder.

The generalizability of findings is another consideration. Many observational studies are conducted in specific subgroups (older adults, students, clinical samples, cardiometabolic risk cohorts), and trial participants often have poor baseline diet quality and moderate-to-severe symptoms—conditions under which dietary improvement may yield larger benefits. It remains unclear whether the MD provides similar mental health benefits in populations with already high diet quality or in low-resource settings where access to core MD foods is limited. Conversely, the MD may be particularly valuable for individuals with comorbid obesity, diabetes, or cardiovascular risk, where improvements in inflammation and metabolic health may indirectly benefit mood.

Finally, mechanistic evidence in humans is suggestive but still incomplete. Proposed pathways—reduced inflammation and oxidative stress, improved cardiometabolic profile, modulation of the gut–brain axis, and support for neurotrophic signaling—are biologically plausible, yet few depression-focused trials include comprehensive biomarker panels, microbiome measures, or mediation analyses to confirm these mechanisms. Future research should prioritize adequately powered, multi-centre RCTs with longer follow-up, robust adherence measures, and mechanistic endpoints, and should test pragmatic implementation models in primary care and community settings.

Conclusions

Across different study designs, higher adherence to a MD is generally associated with fewer depressive symptoms and a reduced risk of incident depression. Randomized and cluster-randomized trials further suggest that such dietary interventions can reduce severity of depressive symptoms and improve mental health–related quality of life when delivered as an adjunct to usual care. From a clinical and public health perspective, promotion of MD appears to be a safe, feasible and potentially effective lifestyle recommendation for adults with depression. It should complement, rather than replace, evidence-based pharmacotherapy and psychotherapy. Future research should prioritize larger, multi-centre trials with longer follow-up, implementation studies in routine care settings and differences in effectiveness across patient populations. standardized outcome measures, assessing individual components of MD, underlying mechanisms (e.g., inflammatory markers, microbiome, neuroimaging).

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