

DIETARY PATTERNS AS MODIFIABLE RISK FACTORS FOR DEPRESSION: A NARRATIVE REVIEW

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SUMMARY

Background: The role of nutrition in treating clinical depression has been widely discussed. Unhealthy lifestyle patterns, like lack of physical activity, junk food consumption, and irregular sleep patterns are common in depressed patients. Considering the mental and physical side-effects, the daily nutrition of these patients seems to be a plausible option for reducing depressive symptoms and enhancing treatment results.

Methods: A PubMed search was done for meta-analyses published from January 2018 to June 2023 with the query: (diet) AND (psychiatric disorder) AND (depression). We selected meta-analyses that met specific criteria like including the entire diet or specific diet patterns and having depression or depressive symptoms as a primary or secondary outcome.

Results: Out of 28 papers found, the 9 meta-analyses, selected for review, revealed different types of correlation between dietary patterns and the symptoms of depression and anxiety.

Healthy diets were associated with higher intake of fruits, vegetables, nuts, and lower intake of pro-inflammatory food items like processed meats and trans fats. Adherence to such diets showed a negative association with incident depression in cross-sectional and longitudinal studies. A diet mostly including ultra-processed foods was associated with higher odds of depressive and anxiety symptoms. Women were found to be more susceptible than men both in developing the depressive symptoms with unhealthy diet and in reducing the symptoms of depression and anxiety with improvement of diet quality. Statistically significant improvement in symptoms of depression and anxiety in both sexes was observed in study groups assigned for individual consultations of a dietician and a psychotherapist when compared with group sessions or general recommendations.

Conclusions: Research on the correlation of healthy dietary patterns and symptoms of depression and anxiety has mainly focused on non-clinical populations. The evidence supports an inverse association between healthy eating habits and symptoms of depression. Further research should be encouraged on the eating habits of clinically depressed individuals and the underlying physiological mechanisms of uncontrolled food intake.

Key words: nutrition - dietary pattern – depression - psychiatric disorder - modifiable risk factor

Abbreviations: MDD - major depressive disorder; RCTs - randomized controlled trials

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INTRODUCTION

The role of nutrition in the treatment of clinically depressed individuals has been widely discussed for the recent decade. The unhealthy life patterns such as the lack of physical activity, the “junk food” choice, alcohol and tobacco consumption, irregular sleep habits are prevalent in depressed patients (Bourke et al. 2022, Orlando et al. 2021, Mills et al. 2020). The hypothesis of the inter-related nature of the patient’s life-style and depression pushed the research on the daily-life habits as the modifiable risk factors for depression. At the same time, the side-effects of the pharmacotherapy for depression are reported to provoke weight-gain and development of metabolic syndrome that aggravate the patients’ daily living and adherence to treatment (El Asmar et al. 2018). For better patient’s management, the guided daily nutrition seems to be one of the plausible options to reduce the symptoms of depression and anxiety and enhance the treatment results.

In our review we analyze the existing data on the dietary patterns in correlation with the symptoms of depression and anxiety. We addressed the recent meta-analyses as the reliable source of evidence comprising the data from controlled and observational studies of the last two decades.

METHODS

The PubMed database was searched for the meta-analyses published in the period of January, 2018 – June, 2023, with the following query: (diet) AND (psychiatric disorder) AND (depression). The inclusion criteria were: 1) the meta-analysis included the whole-of-diet or specified diet pattern, assessed with validated scales; 2) depression or depressive symptoms were the primary or secondary outcome, assessed with validated scales; 3) the meta-analysis or sub-group analysis presented comprehensive data on relation between nutrition and depression/depressive symptoms; 4) the presence/absence

of clinically diagnosed depression in the studied population was described. The meta-analyses were not included for the review, if: 1) a single nutritional component was analyzed or a diet was not adequately assessed; 2) depression or depressive symptoms were not the outcome, or their assessment was questionable in terms of our review; 3) the comprehensive data on the relation between nutrition and depression/depressive symptoms was not provided in the meta-analysis/sub-group analysis results; 4) the presence or absence of clinically diagnosed depression in the population was not mentioned.

RESULTS

Our search resulted in 28 papers, with 13 remaining after the title and abstract survey. After the full-text analysis, 9 articles were selected for the review as complying for inclusion criteria. The Table 1 contains the summary of the recent meta-analyses focused on the correlation of dietary patterns with symptoms of depression and anxiety.

Three meta-analyses were using the data from randomized controlled trials (RCTs) in adolescents and adults (Bourke et al. 2022, Firth et al. 2019, Varace et al. 2023). Six meta-analyses included the data from observational studies, mainly having cross-sectional design, in children, adolescents, and adults (Iguacel et al. 2021, Lane et al. 2022, Lassale et al. 2018, Li et al. 2022, Orlando et al. 2021, Shafiei et al. 2019, 2023). Clinically depressed population ($n = 100$) was reported in two studies (Firth et al. 2019, Bourke et al. 2022) along with the populations without mental disorders.

The diet patterns and dietary interventions included in the scope of the recent meta-analyses revealed different strength of association with the symptoms of depression and anxiety. Despite the significant statistical and methodological heterogeneity between the studies reported by the authors, the review of the selected meta-analyses helped identifying several trends summarized below. Table 2 provides brief information on the scope of dietary patterns and their association with the symptoms of depression and anxiety. Table 3 highlights the findings on the effect of the dietary patterns on the symptoms of depression and anxiety.

Healthy diets and dietary patterns

The healthy dietary patterns share common elements: higher fruits, vegetables, and nut intake, lower intakes of pro-inflammatory food items such as processed meats and trans fats, and moderate alcohol intake. Free-living adolescent and adult individuals reporting high scores in adherence to Mediterranean diet, Dietary approaches to stop hypertension (DASH) and pro-vegetarian diet, high Healthy Eating Index (HEI) and other national diet indices, and low Dietary Inflammatory Index (DII) had demonstrated a negative association between higher healthy diet score and incident

depression in longitudinal studies (Lassale et al. 2018). A meta-analysis focused on children and adolescents (Orlando et al. 2021) revealed a small, statistically significant negative association between healthy dietary patterns and depressive symptoms along with small, significant positive association between unhealthy dietary patterns and depressive symptoms.

Firth et al. (2019) had outlined several associations between a diet and depressive symptoms in the meta-analysis of RCTs, including all types of diet and diet as a part of multicomponent life-style interventions aimed at improving nutrient intake, or decreasing fat intake, or reducing bodyweight in adults (Firth et al. 2019). A meta-analysis of 16 RCTs found dietary interventions significantly reducing depressive symptoms in comparison to controls, with a small pooled effect (g [95% CI] = 0.275 [0.10; 0.45], $p=0.002$), both in clinically and non-clinically depressed samples. No overall effect of dietary interventions on anxiety was detected, probably due to the absence of clinical anxiety disorder samples. A significant positive effect of the dietary interventions on the symptoms of depression and anxiety was observed in the studies that involved a nutritional professional or in the studies with female samples >75%. At the same time, significant negative effect of dietary interventions on depressive symptoms and nonsignificant negative effect on anxiety symptoms were found in the studies with male samples >75%.

A healthy diet as a part of multicomponent life-style intervention

The meta-analysis by Bourke et al. (2022) included the data from 15 RCTs with adolescent participants, predominantly overweight. Among them, 33 individuals had a diagnosis of current major depressive episode or dysthymia. The life-style interventions were targeting physical activity/sedentary behaviors, nutrition/diet in all the RCTs. Additionally, several trials were aimed at sleep behaviors and substance use. The overall effect size after intervention for symptoms of depression and anxiety was nonsignificant, in favor of the intervention group. In line with Firth et al. (2019), personalized interventions had a significant effect for depression symptoms ($k = 9$, $n = 1278$, $g = -0.28$ [-0.52; -0.05]), when compared to universal interventions (Firth et al. 2019).

Vegetarian or vegan diets

For vegetarian or vegan (animal products completely excluded) diets, no statistically significant differences between vegetarian/vegan diets and omnivores in the incidence of depression (MD = -0.532 [-2.047; 0.984]) were revealed in population aged 18-70 years, predominantly female, without chronic diseases. Remarkably, the vegetarian/vegan diets were associated with lower levels of anxiety (MD = -0.847 [-1.677; -0.018]). The subgroup analysis for depression showed that vegans/vegetarians were at increased risk for depression (odds

Table 1. The key findings of meta-analyses published during the last 5 years (January, 2018 – June, 2023) on effect of dietary patterns on symptoms of depression and anxiety

Source	Source type	Participants, (n)	Intervention / Dietary pattern	Control	Outcome, (measure)	Main findings	Limitations
Bourke et al. (2022)	Meta-analysis	15 RCTs, adolescents aged 14-24 years, (n=2,902) predominantly overweight. Current major depressive episode or dysthymia (n=33).	Interventions targeting physical activity/sedentary behaviors, nutrition/diet; additionally, in 3 studies: sleep behaviors, and substance use	'inactive' controls (waitlist, no intervention, treatment as usual) and 'active' controls (attention or alternative interventions that did not target modifiable health behaviors)	Depression (CES-D, DASS, BDI, BYI, PHQ-9, RSES, K-SADS), anxiety (BYI, DASS, GAD-7)	The overall effect size after intervention for symptoms of depression and anxiety was nonsignificant, in favor of the intervention group. For depression: $g = -0.07$, 95% CI = -0.17 to 0.03 , with between-study heterogeneity 95% PI = $[-0.30, 0.17]$. For anxiety: $g = -0.07$, 95% CI = -0.19 to 0.05 , with between-study heterogeneity 95% PI = $[-0.24, 0.10]$. Personalized interventions had a significant effect for depression symptoms ($k = 9$, $n = 1278$, $g = -0.28$, 95% CI = $[-0.52, -0.05]$), when compared to universal interventions. No significant subgroup differences were observed based on type of control group, age, or intervention modality (face-to-face or remote)	High heterogeneity between the studies Small sample of clinically depressed individuals
Firth et al. (2019)	Meta-analysis	16 RCTs, adults (45,826). Clinical depression (67), the rest of participants with comorbid, subclinical, or secondary symptoms of depression/anxiety	"Whole-of-diet" dietary interventions; all "types" of diet; multicomponent life-style interventions	Nondietary control interventions (active control). No intervention (inactive control)	Depression (CES-D, BDI, HAM-D, MADRS, GDS), anxiety (TMAS), depression/anxiety (subscales of HADS, SF-36, BSI, POMS, GWB Schedule)	Types of diet interventions: primarily aimed at improving nutrient intake ($n = 9$), aimed to decrease fat intake ($n = 4$), designed to reduce bodyweight ($n = 4$). Duration from 10 days to 3 years. No significant differences between interventions. A random-effects meta-analysis of 16 RCTs: dietary interventions significantly reduced depressive symptoms in comparison to controls, with a small pooled effect ($g = 0.275$, 95% CI = 0.10 to 0.45 , $p=0.002$), both in clinically and non-clinically depressed samples. A random-effects meta-analysis of 11 RCTs ($n = 2270$): no overall effect of dietary interventions on anxiety compared with controls ($g = 0.100$, 95% CI = -0.036 to 0.235 , $p=0.148$, $Q = 18.5$, $I^2 = 46.1$). No clinical anxiety disorder samples. Studies that involved a nutritional professional observed a significant effect on depressive symptoms ($n = 12$, $n = 45,508$, $g = 0.329$, 95% CI = 0.12 to 0.54 , $p=0.002$) and anxiety symptoms ($n = 9$, $n = 2235$, $g = 0.273$, 95% CI = 0.02 to 0.53 , $p=0.034$) Studies with female samples $>75\%$ ($n = 8$) observed significant positive effects of dietary interventions on depressive symptoms ($g = 0.195$, 95% CI = 0.06 to 0.37 , $p=0.007$) and anxiety symptoms ($n = 6$, $n = 965$, $g = 0.211$, 95% CI = 0.09 to 0.34 , $p=0.001$) Studies with male samples $>75\%$ ($n = 4$) observed significant negative effects of dietary interventions on depressive symptoms ($g = -0.208$, 95% CI = -0.45 to 0.03 , $p = .091$) and nonsignificant negative effect on anxiety symptoms ($g = -0.19$, 95% CI = -0.42 to 0.04 , $p=0.107$).	Publication bias Small sample of clinically depressed individuals Significant heterogeneity in the meta-analyses due to broad inclusion criteria

Note: RCTs - randomized controlled trials; CES-D - Center for Epidemiological Studies-Depression; DASS - Depression Anxiety Stress Scale; BDI - Beck Depression Inventory; BYI - Beck Youth Inventory; PHQ - Patient Health Questionnaire; RSES - Rosenberg Self-Esteem Scale; K-SADS - Schedule for Affective Disorders and Schizophrenia for School-Age Children; GAD-7 - Generalized Anxiety Disorder Assessment; HAM-D - Hamilton Rating Scale for Depression; MADRS - Montgomery-Åsberg Depression Rating Scale; GDS - Geriatric Depression Scale; TMAS - Taylor Manifest Anxiety Scale; HADS - Hospital Anxiety and Depression Scale; SF-36 - Short-Form Health Survey; BSI - Brief Symptom Inventory; POMS - Profile of Mood States; GWB Schedule - General Well-Being Schedule; non-RCTs - non-randomized controlled trials; FFQs - food-frequency questionnaires; 24HR - 24-hour Dietary Recall; DHO - Diet History Questionnaire; HEI - Healthy Eating Index; DASH - Dietary approaches to stop hypertension; DIH - Dietary Inflammatory Index; DQES - Dietary Questionnaire for Epidemiological Studies; DSM-IV-TR - Diagnostic and Statistical Manual of Mental Disorders; GHQ-12 - General Health Questionnaire 12 items; K10 - Kessler Psychological Distress Scale; MFO - Moods and Feelings Questionnaire (range 0-66); PHQ-9 - Patient Health Questionnaire 9 item depression module; SDS - Zung Self-Rating Depression Scale; DSS - depressive symptoms scale; CDI - Child Depression Inventory; RADS - Reynolds Adolescent Depression Scale; DSRSC - Depression Self-rating Scale for Children; SAI - Spielberger State Anxiety Inventory; TMDS - Total Mood Disturbance Score; PAID - Diabetes-39 dimensions and Problem Areas in Diabetes; STAI-T - State-Trait Anxiety Inventory-Trait anxiety; QOL -Quality Of Life; BAI - Beck Anxiety Inventory

Table 1. Continues

Source	Source type	Participants, (n)	Intervention / Dietary pattern	Control	Outcome, (measure)	Main findings	Limitations
Iguacel et al. (2021)	Systematic review with meta-analysis	10 observational studies with a comparison group, 2 RCTs, 1 non-RCT, population aged 18-70 years, without chronic diseases following vegetarian or vegan diets (17, 809)	Vegetarian or vegan (animal products completely excluded) diets	Omnivores	In mental health: depression, anxiety, stress, neuro-psychiatric, psychological health and well-being (DASS, CES-D, SF-36).	No statistically significant differences between vegetarian/vegan diets and omnivores in the incidence of depression (MD = -0.532; 95% CI: -2.047, 0.984). High heterogeneity between-the studies (I ² = 92.53; p=0.040). Vegetarian/vegan diets were associated with lower levels of anxiety (MD = -0.847; 95% CI: -1.677, -0.018) High heterogeneity between-the studies (I ² = 92.08; p=0.001). Subgroup analysis for depression: Vegans/vegetarians were at increased risk for depression (odds ratio = 2.142; 95%CI, 1.105-4.148), statistically significant higher depression level in vegetarians/vegans under 26 years old (MD= 1.737; 95% CI: 0.757, 2.717), in female vegetarians/vegans (MD= 2.910; 95% CI: 0.876, 4.944). Subgroup analysis for anxiety: Lower anxiety level in studies including predominantly women (MD= -0.744; 95% CI: -1.461, -0.026); Higher levels of anxiety in vegetarian/vegans younger than 26 years (MD= 0.901; 95% CI: 0.143, 1.658).	Flawed methodology of mixing mean differences for different scales. High statistical heterogeneity between the studies. No clinically depressed individuals. Population overrepresented by women
Lane et al. (2022)	Systematic Review and Meta-Analysis	17 observational studies, children, adolescents, adults, (n = 385,541)	Consumption of ultra-processed food (NOVA4 group)	Minimal vs maximal ultra-processed food consumption score	Ultra-processed food consumption (FFQs, 24HR, DHQ 2-weeks), depression and anxiety (not specified)	Depression and anxiety: greater ultra-processed food consumption was associated with higher odds of depressive and anxiety symptoms (odds ratio: 1.53, 95% CI: 1.43 to 1.63, p<0.001, I ² = 8.9%);	The majority of studies used a cross-sectional design (88%) No population with clinically diagnosed depression Self-report bias, heterogeneity between outcome assessment tools
Lassale et al. 2018	Systematic Review and Meta-Analysis	41 observational studies, adolescents, adults, general free-living populations, naturally adherent to any diet pattern: Mediterranean diet (n = 46,584); HEI (n = 52,450); DASH (n = 20,472); DII (n=65,666); other diet patterns, (n = 106,904)	Diet adherence score: Mediterranean diet, HEI, DASH, DII, other national diet indices, pro-vegetarian diet	Minimal vs maximal diet adherence score	A dietary score (24HR, DHQ, DQES, FFQ); clinical depression and depressive symptoms (BDI, CES-D, DASS, GDS, HADS, DSM-IV-TR, GHQ-12, K10, MFQ (range 0-66), PHQ-9)	A general trend towards an inverse association between higher healthy diet score and depression was observed in longitudinal studies The dietary scores share common elements: higher fruits, vegetables, and nut intake, lower intakes of pro-inflammatory food items such as processed meats and trans fats, and alcohol in moderation	Diet self-report bias High heterogeneity between the studies

Note: RCTs - randomized controlled trials; CES-D - Center for Epidemiological Studies; DASS - Depression Anxiety Stress Scale; BDI - Beck Depression Inventory; BYI - Beck Youth Inventory; PHQ - Patient Health Questionnaire; RSES - Rosenberg Self-Esteem Scale; K-SADS - Schedule for Affective Disorders and Schizophrenia for School-Age Children; GAD-7 - Generalized Anxiety Disorder Assessment; HAM-D - Hamilton Rating Scale for Depression; MADRS - Montgomery-Åsberg Depression Rating Scale; GDS - Geriatric Depression Scale; TMAS - Taylor Manifest Anxiety Scale; HADS - Hospital Anxiety and Depression Scale; SF-36 - Short-Form Health Survey; BSI - Brief Symptom Inventory; POMS - Profile of Mood States; GWB Schedule - General Well-Being Schedule; non-RCTs - non-randomized controlled trials; FFQs - food-frequency questionnaires; 24HR - 24-hour Dietary Recall; DII - Diet History Questionnaire; HEI - Healthy Eating Index; DASH - Dietary approaches to stop hypertension; DII - Dietary Inflammatory Index; DQES - Dietary Questionnaire for Epidemiological Studies; DSM-IV-TR - Diagnostic and Statistical Manual of Mental Disorders; GHQ-12 - General Health Questionnaire 12 items; K10 - Kessler Psychological Distress Scale; MFQ - Moods and Feelings Questionnaire (range 0-66); PHQ-9 - Patient Health Questionnaire 9 item depression module; SDS - Zung Self-Rating Depression Scale; DSS - depressive symptoms scale; CDI - Child Depression Inventory; RADS - Reynolds Adolescent Depression Scale; DSRSC - Depression Self-Rating Scale for Children; SAI - Spielberger State Anxiety Inventory; TMDS - Total Mood Disturbance Score; PAID - Diabetes-39 dimensions and Problem Areas in Diabetes; STAI-T - State-Trait Anxiety Inventory-Trait anxiety; QOL -Quality OfLife; BAI - Beck Anxiety Inventory

Table 1. Continues

Source	Source type	Participants, (n)	Intervention / Dietary pattern	Control	Outcome, (measure)	Main findings	Limitations
Li et al. 2022	Meta-Analysis	17 observational studies, adults, (157,409)	Dietary inflammatory potential	Minimal vs maximal dietary inflammatory index or blood inflammatory markers	Dietary inflammatory potential (DII, blood cytokine level), clinical depression, depressive symptoms, anxiety (CES-D, PHQ-9, HADS, DASS, SDS)	Compared with the lowest inflammatory diet group, the highest group was significantly associated with the incidence of depression and anxiety: (95% CIs): 1.45 (1.30 ~ 1.62) for depression and 1.66 (1.41 ~ 1.96) for anxiety A subgroup analysis. For depression, the increased risk was 49% in women (OR 1.49, 95% CI 1.28 ~ 1.74) and 27% in men (OR 1.27, 95% CI 1.06 ~ 1.52). For anxiety, the increased risk was 80% in women (OR 1.80, 95% CI 1.30 ~ 2.49) and 47% in men (OR 1.53, 95% CI 0.81 ~ 2.89).	Heterogeneity of measurement methods and inclusion criteria in the studies Small number of studies on anxiety (n = 4)
Orlando et al. 2021	Meta-analysis	39 observational studies, children and adolescents aged 4–18 years (116,546)	Healthy/unhealthy dietary patterns	Present, not specified	Dietary pattern (FFQ, 24HR, 4-day diet diary); depression and anxiety (Kandel and Davies DSS, PHQ-9, GAD-7, CDI, CES-D, BDI, RADS, DASS-21, DSRSC)	Small, significant negative association between healthy dietary patterns and depressive symptoms (k = 19, r = -0.13, p<0.001, 95% CI [-0.18, -0.08]) with significant heterogeneity between studies (Q = 375.775, p<0.0001, I ² = 94.944) Small, significant positive association between unhealthy dietary pattern and depressive symptoms (k = 13, r = 0.11, p=0.001, 95% CI [0.05, 0.17]) with significant heterogeneity between studies (Q = 657.387, p<0.0001, I ² = 98.175)	High heterogeneity between the studies Report bias between children and parents on the diet quality No population with clinically diagnosed depression
Shafiei et al. 2019, 2023	Systematic Review and Meta-Analysis	14 observational studies, free-living adult population, (56,043)	Adherence to Mediterranean diet	Diet adherence score, minimal vs maximal	Diet score (FFQ, 9-, 11- component Mediterranean dietary patterns); Depression (CES-D, K10, GDS, HADS, SDS)	In cohort studies, inverse significant association between adherence to the Mediterranean diet and risk of depression (overall hazard ratio = 0.81; 95% CI, 0.70–0.94) In cross-sectional studies, an inverse significant association between adherence to the Mediterranean diet and risk of depression (overall odds ratio = 0.81; 95% CI, 0.71–0.92) No significant heterogeneity between the studies.	Heterogeneity between diet assessment methods and tools
Varaee et al. (2023)	Systematic Review and Meta-Analysis	8 RCTs, adults without mood disorders, overweight, with obesity, (590)	Low carbohydrate diet (LCD or keto-genic diet, <26% carbohydrates)	High carbohydrate diet, energy-restricted diet, regular diet pattern	Depression and anxiety (SAI, BDI, POMS, TMDS, PAID, STAI-T, QOL, HADS, BAI)	No significant association between a LCD diet and anxiety (SMD = 0.19, 95% CI - 0.10, 0.47; p = 0.20) and depression (SMD = 0.06, 95% CI - 0.11, 0.24; p=0.49). LCD increases anxiety in studies with <26% carbohydrate intake (SMD = 0.31; 95%CI 0.10, 0.52; P≤0.0001; I ² = 0.00, P=0.52)	Blinding bias (people under intervention) Studies published only in English

Note: RCTs - randomized controlled trials; CES-D - Center for Epidemiological Studies-Depression; DASS - Depression Anxiety Stress Scale; BDI - Beck Depression Inventory; PHQ - Patient Health Questionnaire; RSES - Rosenberg Self-Esteem Scale; K-SADS - Schedule for Affective Disorders and Schizophrenia for School-Age Children; GAD-7 - Generalized Anxiety Disorder Assessment; HAM-D - Hamilton Rating Scale for Depression; MADRS - Montgomery-Åsberg Depression Rating Scale; GDS - Geriatric Depression Scale; TMAS - Taylor Manifest Anxiety Scale; HADS - Hospital Anxiety and Depression Scale; SF-36 - Short-Form Health Survey; BSI - Brief Symptom Inventory; POMS - Profile Of Mood States; GWB Schedule - General Well-Being Schedule; non-RCTs - non-randomized controlled trials; FFQs - food-frequency questionnaires; 24HR - 24-hour Dietary Recall; DHQ - Diet History Questionnaire; HEI - Healthy Eating Index; DASH - Dietary approaches to stop hypertension; DII - Dietary Inflammatory Index; DQES - Dietary Questionnaire for Epidemiological Studies; DSM-IV-TR - Diagnostic and Statistical Manual of Mental Disorders; GHQ-12 - General Health Questionnaire 12 items; K10 - Kessler Psychological Distress Scale; MFQ - Moods and Feelings Questionnaire (range 0–66); PHQ-9 - Patient Health Questionnaire 9 item depression module; SDS - Zung Self-Rating Depression Scale; DSS - depressive symptoms scale; CDI - Child Depression Inventory; RADS - Reynolds Adolescent Depression Scale; DSRSC - Depression Self-rating Scale for Children; SAI - Spielberger State Anxiety Inventory; TMDS - Total Mood Disturbance Score; PAID - Diabetes-39 dimensions and Problem Areas in Diabetes; STAI-T - State-Trait Anxiety Inventory-Trait anxiety; QOL - Quality Of Life; BAI - Beck Anxiety Inventory

Table 2. The association of dietary patterns with the symptoms of depression and anxiety

Type of diet	Association with depressive symptoms	Association with anxiety symptoms
Healthy diets and dietary patterns	Negative	None
A healthy diet as a part of multicomponent life-style intervention	No information	No information
Vegetarian or vegan diets	None	Negative
The Mediterranean diet	None (in cohort studies) Negative* (in cross-sectional studies)	No information
A low carbohydrate diet and ketogenic diet	None	None
Dietary patterns with high inflammatory potential	Positive*	Positive*

Note: Statistically significant associations are marked by *

Table 3. The effect of dietary patterns on the symptoms of depression and anxiety

Type of diet	Effect on depressive symptoms	Effect on anxiety symptoms
Healthy diets and dietary patterns	Reducing* in females Increasing* in males Reducing* with personalized mode	Reducing* in females Increasing in males Reducing* with personalized mode
A healthy diet as a part of multicomponent life-style intervention	Reducing Reducing* with personalized mode	Reducing
Vegetarian or vegan diets	Increasing* in females Increasing* under 26 years-old	Reducing in females Increasing under 26 years-old
The Mediterranean diet	No information	No information
A low carbohydrate diet and ketogenic diet	None	Increasing with <26% carbohydrate intake
Dietary patterns with high inflammatory potential	No information	No information

Note: Statistically significant effects are marked by *

ratio (OR) = 2.142 [1.105; 4.148]), with statistically significant higher depression level in vegetarians/vegans under 26 years old (MD = 1.737 [0.757; 2.717]) and in female vegetarians/vegans (MD = 2.910 [0.876; 4.944]). The subgroup analysis for anxiety found lower anxiety level in studies including predominantly women (MD = -0.744 [-1.461; -0.026]) and higher levels of anxiety in vegetarian/vegans younger than 26 years (MD = 0.901 [0.143; 1.658]) (Iguacel et al. 2021). Nevertheless, this meta-analysis has flawed methodology of calculating mean differences instead of standardized mean differences for different outcomes, and hence its results should be considered with caution.

The Mediterranean diet

A healthy diet in which consumption of vegetables and fruits, nuts and seeds, whole grains, dairy products, olive oil, fish, and fresh seafood is encouraged, while consumption of red and processed meats is restricted. Analyzed by Shafiei et al. in free-living adult population, the adherence to Mediterranean diet had significant inverse association with the risk of depression (overall hazard ratio (HR) = 0.81 [0.70; 0.94]) in cohort studies. Simultaneously, an inverse significant association between adherence to the Mediterranean diet and risk of depression (OR = 0.81 [0.71; 0.92]) was revealed in cross-sectional studies (Shafiei et al. 2019, 2023). These findings were in line with the earlier meta-analysis (Lassale et al. 2018).

A low carbohydrate diet and ketogenic diet

A low carbohydrate diet is a dietary approach that restricts the intake of carbohydrates, typically to less than 130 grams per day or less than 10% of total daily energy intake (Tinsley & Willoughby 2016). This diet focuses on reducing the consumption of foods high in carbohydrates such as grains, starchy vegetables, and sugary foods. The main goal of a low carbohydrate diet is to control blood sugar levels and promote weight loss. On the other hand, a ketogenic diet is a high-fat, low-carbohydrate diet that induces ketosis by restricting carbohydrate intake to less than 50 grams per day or less than 5% of total daily energy intake (Zhang et al. 2018). The main goal of a ketogenic diet is to shift the body's primary energy source from carbohydrates to fat, leading to the production of ketone bodies. This metabolic state has been shown to have various health benefits, including weight loss, improved glycemic control, and metabolic parameters in type 2 diabetes (T2DM) (Zhang et al. 2018).

The meta-analysis by Varace et al. (2023) included RCTs with adult participants without mood disorders seeking treatment for overweight, obesity, and T2DM. A low carbohydrate diet (<26% carbohydrates) or ketogenic diet were mainly compared to low-fat/high carbohydrate diets, energy-restricted diet, regular diet pattern. No significant associations were found between low carbohydrate/ketogenic diets and depression (standardized mean difference (SMD) = 0.06 [-0.11; 0.24]; p=0.49) or anxiety

(SMD = 0.19 [-0.10; 0.47], $p=0.20$). An additional analysis revealed the association of carbohydrate intake <26% with increased anxiety (SMD = 0.31 [0.10; 0.52]; $p\leq 0.001$; $I^2 = 0.00$) (Varaee et al. 2023).

Dietary patterns with high inflammatory potential

The diet inflammatory index (DII) was developed by Shivappa et al. (2014). The authors had identified and analyzed studies that investigated the effects of various foods and nutrients on inflammation markers, such as C-reactive protein (CRP), tumor necrosis factor-alpha (TNF- α), and interleukins. Using this information, they developed a scoring system that assigns positive scores to foods and nutrients with pro-inflammatory effects and negative scores to those with anti-inflammatory effects. By summing the scores of all the foods and nutrients consumed, the DII provides an overall measure of the inflammatory potential of an individual's diet (Shivappa et al. 2014).

Among the 45 food parameters of the DII classification, the pro-inflammatory potential was assigned to the intake of carbohydrate, cholesterol, ferrum, protein, saturated fat, trans fat, overall energy (kcal) and total fat consumption (Shivappa et al. 2014). Li et al. (2022) analyzed 17 observational studies in adult populations for the dietary inflammatory potential and its correlation with the symptoms of depression and anxiety. The group with the highest DII was significantly associated with the incidence of depression and anxiety: OR = 1.45 [1.30; 1.62] for depression, OR = 1.66 [1.41; 1.96] for anxiety, when compared with the lowest DII group. A subgroup analysis revealed that pro-inflammatory diet is significantly associated with both depression and anxiety in women (OR = 1.49 [1.28; 1.74] and OR = 1.80 [1.30; 2.49], respectively) but not in men (OR = 1.27 [1.06; 1.52] and OR = 1.53 [0.81; 2.89], respectively).

A diet mostly including ultra-processed foods was specifically analyzed by Lane et al. (2022) for the association with the symptoms of depression and anxiety. The NOVA food classification distinguishes the ultra-processed foods as industrial formulations that undergo extensive processing and contain five or more ingredients, which typically include artificial food additives rarely or never used in home kitchens such as preservatives, colors, texturizing agents, and olfactory and taste enhancers (Lane et al. 2022). The nutrient profile of ultra-processed foods, characterized by high levels of added sugars, unhealthy fats, and low nutritional value, has been linked to inflammation and altered gut microbiota (Mariath et al. 2022). These foods may also contribute to oxidative stress and the expression of inflammatory biomarkers (Mariath et al. 2022). The meta-analysis of 17 observational studies in children, adolescents, and adults revealed that greater ultra-processed food consumption was associated with consistently higher odds of depressive and anxiety symptoms (OR = 1.53 [1.43; 1.63],

$I^2 = 8.9\%$). The cause-effect relationships between the ultra-processed foods consumption and incidents of depression and anxiety could not be irrevocably identified since most studies (88%) used a cross-sectional design (Lane et al. 2022). Nevertheless, healthy dietary patterns and low dietary inflammatory index had demonstrated a negative association between higher healthy diet score and incident depression in longitudinal studies (Lassale et al. 2018).

DISCUSSION

The potential of daily nutrition in prevention and treatment of depression is still disputable. The meta-analyses of healthy dietary patterns rich in natural foods revealed the negative association with the symptoms of depression and anxiety both in cross-sectional and longitudinal studies. The healthy diets with higher fruits, vegetables, and nut intake, lower intake of pro-inflammatory food items such as processed meats and trans fats were reported to reduce the symptoms of depression and anxiety in free-living populations of all age groups. Our analysis has revealed the lack of studies in clinically depressed individuals. The majority of the studies, included in the recent meta-analyses, focused on the self-reported symptoms of depression and anxiety in general population or people seeking treatment for obesity. Nevertheless, the outlined general trends in eating behaviors and diet quality contribute to the existing hypotheses of problematic eating habits in persons with major depressive disorder (MDD).

Specifically, the recent meta-analyses found the diet susceptibility to be sex-related. The statistically significant effect of diet quality and change of diet on the symptoms of depression was different in strength (Li et al. 2022) and opposite in its direction (Firth et al. 2019) in male and female participants. In general adult population, women were reported having approximately twice higher risk for developing the symptoms of depression and anxiety than men when following a highly pro-inflammatory diet (Li et al. 2022). At the same time, the use of a healthy diet as an intervention had statistically significant positive effect in reducing the symptoms of depression and anxiety in women, and significantly aggravated the symptoms of depression and anxiety in men in the studies on the populations with clinical, comorbid or subclinical symptoms of depression and anxiety (Firth et al. 2019).

In case of diagnosed mood disorder, the risk for developing an unhealthy dietary pattern is quite high. The atypical MDD with increased appetite provoking the weight-gain has become more prevalent than melancholic depression characterized by low appetite and weight-loss (Mills et al. 2020). The mood state can contribute for the highly palatable food choice forming an uncontrolled eating behavior similar to substance addiction (Mills et al. 2020, Orlando et al. 2021, Burrows et al. 2018). Food addiction is currently

measured using the Yale Food Addiction Scale, with the prevalence of food addiction ranging from 5-10% in general population, 15-25% in people with obesity, and 25-28% in patients with MDD (Mills et al. 2020). Food addiction as eating behavior in individuals seeking for weight-loss treatment is correlating with the symptoms of depression and anxiety (Burrows et al. 2018). The food addiction symptoms, such as tolerance and cravings, are directly linked with the depressive symptom severity and are more common in females than in males (Mills et al. 2020).

Mills et al. (2020) have investigated the role of peripheral dopamine in abnormal eating behavior (overeating or food addiction) in patients with MDD. Their findings suggest that peripheral dopamine may be specifically related to eating patterns in MDD, rather than all depressive symptoms. Depressed males with food addiction had significantly lower plasma dopamine levels compared to depressed males without food addiction and control males. At the same time, plasma dopamine levels did not differ between females with MDD by presence or absence of food addiction and controls. The relationships observed between plasma dopamine levels and problematic eating behaviors differed between sexes. In females, plasma dopamine levels were positively correlated with emotional eating, restrained eating, a failure to quit food intake and withdrawal symptoms. In males however, dopamine levels correlated negatively with restrained eating only (Mills et al. 2020).

Some types of foods and their additives, generally referred as “highly palatable foods”, were recently considered as provoking uncontrolled eating and food addiction. These highly palatable foods were reported to activate elevated dopamine release in the *Nucleus accumbens*, trigger the behavioral indicators of addiction such as loss of control and cravings for its consumption (Hebebrand & Gearhardt 2021). The food is highly palatable when having an ability to deliver reinforcing ingredients (refined carbohydrates, fat) into the organism through the removal of ingredients that slow absorption (fiber) (Hebebrand and Gearhardt 2021). From this point of view, the ultra-processed food containing more sugar, fat and additives than natural food may be both pro-inflammatory and highly palatable. The greater ultra-processed food consumption was positively associated with the symptoms of depression and anxiety (Lane et al. 2022).

Relying on these findings, the introduction of a healthy dietary pattern in the treatment plan for MDD, suggesting the control of food intake and restriction of highly palatable and ultra-processed foods, may require special attention of a psychotherapist. The control of plasma dopamine level as related to eating patterns in patients with atypical MDD presents scientific interest. Given that women with higher plasma dopamine level are more susceptible to emotional

eating and fail to control their food intake, the balancing of physiological, emotional and nutritional factors may positively contribute to treatment outcome. The restraint of habitual unhealthy dietary patterns in males with food addiction and its correlation with low plasma dopamine level requires further investigation. In such patients, we hypothesize that a withdrawal from highly palatable foods while following a healthy diet may aggravate the symptoms of depression and anxiety due to the plasma dopamine deficit.

It is worth noting that a personalized mode of intervention for healthy life-style seems to have a high potential. Statistically significant improvement in symptoms of depression and anxiety in both sexes was observed in study groups assigned for individual consultations of a dietician and a psychotherapist when compared with group sessions or general recommendations (Firth et al. 2019, Bourke et al. 2022). A patient’s individual motivation for physical activity along with healthy diet may also contribute to favorable prognosis of depression treatment outcome (Bourke et al. 2022). In this case, a collaboration of a psychotherapist, a nutritionist and a fitness coach may be required for targeting the unhealthy life patterns as modifiable risk factors for depression. For achieving the synergistic effect in treatment of depression, the participating dieticians and fitness coaches need some education on the specific traits of depressed persons such as being less likely to engage in healthy eating behaviors and having low motivation for daily-life activities in comparison with healthy individuals.

CONCLUSION

In the last decade, the research on the correlation of healthy dietary patterns and symptoms of depression and anxiety focused mainly on the non-clinical populations. The nine meta-analyses under review have provided the evidence for inverse association between healthy eating habits and symptoms of depression. The highly pro-inflammatory diets and ultra-processed foods consumption were reported to increase the risk for depression. Women were found to be more susceptible than men both in developing the depressive symptoms with unhealthy diet and in reducing the symptoms of depression and anxiety with improvement of diet quality. Interventions targeting low physical activity may enhance the positive effect of healthy diet. Further research should be encouraged on the eating habits of clinically depressed individuals and the underlying physiological mechanisms of uncontrolled food intake.

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Dmitrii Gorbachev, Natalia Borisova & Timur Syunyakov have composed the primary idea and specified the hypothesis.

Dmitrii Gorbachev & Natalia Borisova wrote the first draft of the manuscript.

Dmitrii Gorbachev & Timur Syunyakov managed the research documents formalization, detailed manuscript editing and revision.

Ekaterina Markina, Oxana Chigareva & Anna Gradinar have been responsible for the literature data collection, its systematization and analysis.

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