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The role of olive oil and its constituents in mental health: a scoping review

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Scoping Review

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Abstract

Mounting evidence suggests that the Mediterranean diet has a beneficial effect on mental health. It has been hypothesised that this effect is mediated by a variety of foods, nutrients and constituents; however, there is a need for research elucidating which of these components contribute to the therapeutic effect. This scoping review sought to systematically search for and synthesise the research on olive oil and its constituents and their impact on mental health, including the presence or absence of a mental illness or the severity or progression of symptoms. PubMed and OVID MEDLINE databases were searched. The following article types were eligible for inclusion: human experimental and observational studies, animal and preclinical studies. Abstracts were screened in duplicate, and data were extracted using a piloted template. Data were analysed qualitatively to assess trends and gaps for further study. The PubMed and OVID MEDLINE search yielded 544 and 152 results, respectively. After full-text screening, forty-nine studies were eligible for inclusion, including seventeen human experimental, eighteen observational and fourteen animal studies. Of these, thirteen human and four animal studies used olive oil as a comparator. Observational studies reported inconsistent results, specifically five reporting higher rates of mental illness, eight reporting lower and five reporting no association with higher olive oil intake. All human experimental studies and nine of ten animal studies that assess olive oil as an intervention reported an improvement of anxiety or depression symptoms. Olive oil may benefit mental health outcomes. However, more experimental research is needed.

Mental illnesses, including depression, anxiety, schizophrenia and bipolar disorder, are widely prevalent across the globe. In Canada, one in five individuals are affected by mental illness every year, and it remains one of the leading causes of disability in Canada[1,2]. Mood and anxiety disorders in particular have continued to drastically rise in prevalence in Canada within the past decade[3]. Mental illnesses have detrimental impacts on quality of life, commonly equivalent or greater than that of other illnesses[4], through an impact on social support, marital status, occupation and disability. With this increase in mental illness and its substantial impact, there is a need for more research that targets not only treatment options for mental illness but also preventative measures that reduce the global burden of disease.

There is currently abundant research demonstrating the positive effect of the Mediterranean diet on physical health. The Mediterranean diet has been known to have substantial benefits on the prevention of cancer, CVD and metabolic disease[5]. Other studies found that the Mediterranean diet reduces the risk of Parkinson's disease, Alzheimer's disease and overall mortality[6]. There is also emerging evidence that it may protect against the development of mental health disorders, as demonstrated by multiple prospective cohort studies[7]. The Mediterranean diet is rich in fruits, vegetables, nuts, fish, white meat and unsaturated fats, namely olive oil. It has also been highly regarded as a palatable and sustainable diet[8]. Clinical trials using the Mediterranean diet have demonstrated the ability to significantly reduce depressive symptoms[9]. One systematic review of observational studies found that higher adherence to the Mediterranean diet was associated with lower rates of Axis I disorders (depression, anxiety, bipolar disorders, schizophrenia, psychosis, eating disorders, obsessive–compulsive disorders, trauma and stress-related disorders, substance abuse and attention-deficit/hyperactivity disorder), with the lowest rates seen in depression and anxiety[10]. Although the evidence is mounting for a protective and therapeutic effect of the Mediterranean diet on mental health, it is not fully understood how each of the individual components of this diet contributes to this benefit.

Olive oil, a staple in the Mediterranean diet, is mainly composed of oleic acid (an omega 9 [*n*-9] fatty acid), and oleuropein, a phenolic compound that gives olives their bitter taste[11]. It makes up 20–25 % of the total energy intake in the traditional Mediterranean diet[12]. Olive oil is known to have a beneficial association with cardiovascular disease, type 2 diabetes and all-cause mortality[12]. Specific compounds in olive oil, such as oleocanthal, oleacein and oleuropein, have been found to be directly associated with reduced risk of cancer due to their anti-inflammatory and antioxidant properties[13,14]. Another study observed significant reductions in oxidative stress biomarkers associated with the high phenolic content of olive oil, providing further support for its antioxidant

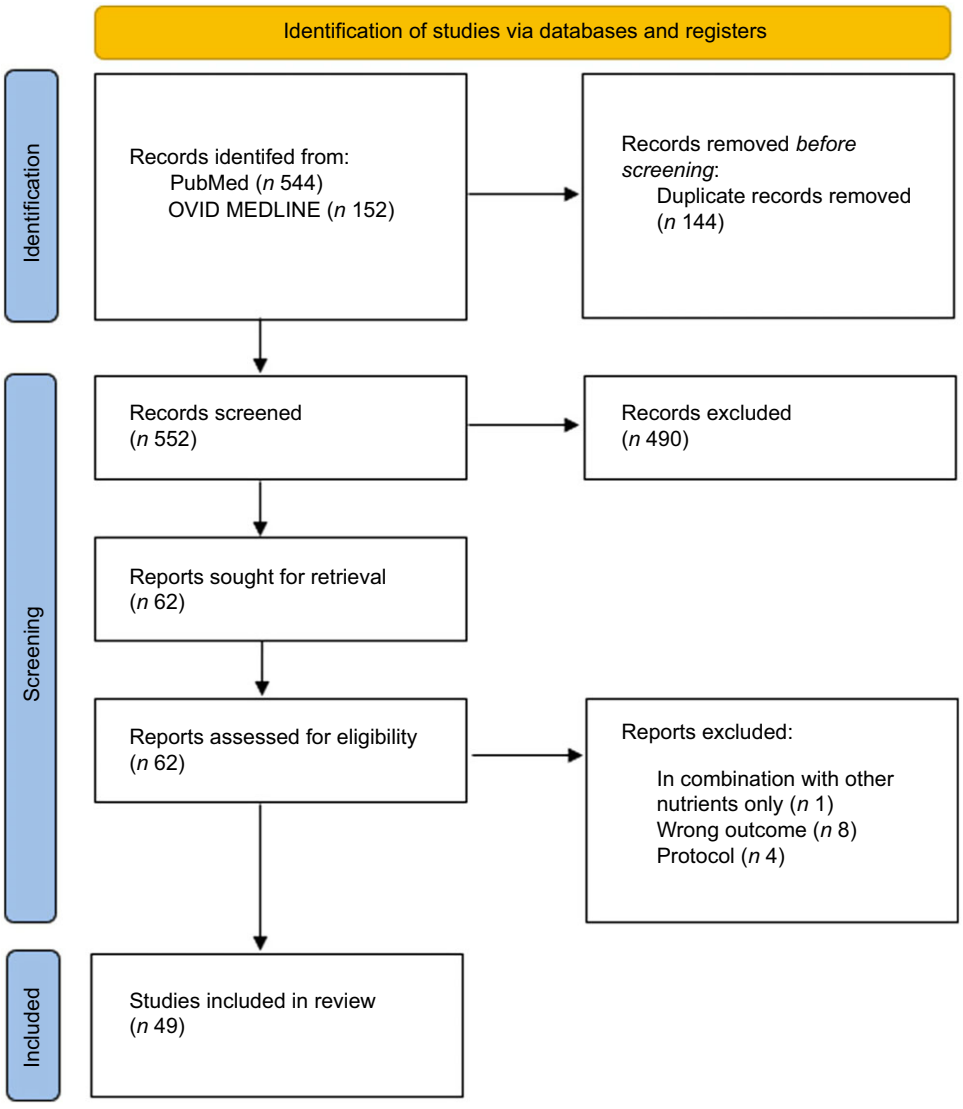

Figure 1. PRISMA flow diagram.

effects[15]. One study found significant reductions in symptoms associated with immune-mediated inflammatory diseases, specifically due to the anti-inflammatory and immunomodulatory effects of polyphenols in olive oil[16]. Inflammation and oxidative stress have both been proposed as mechanisms which mediate the impact of diet on mental health[17]; these mechanisms might explain how olive oil could benefit mental health. To date, the effect of olive oil consumption on mental health has not been thoroughly studied. Due to the limited experimental research and no prior synthesis on the effects of olive oil on mental health, a scoping review is warranted. The objective of this scoping review is to systematically search for and synthesise the research on olive oil and mental health.

Methods

Eligibility criteria

The following eligibility criteria were applied.

Inclusion criteria:

Human experimental or observational studies, animal studies and meta-analyses.

Delivery of olive oil or one of its constituents (oleic acid and oleuropein) or assessment of intake of olive oil or measurement of tissue levels of constituents.

Assessment of any mental health outcome (incidence of mental disorder, severity of mental disorder, treatment or progression of a mental disorder). Eligible mental disorders included: depressive disorders, anxiety disorders, psychotic disorders, bipolar and related disorders, obsessive–compulsive and related disorders, attention-deficit disorders, trauma- and stressor-related disorders, substance use disorders and eating disorders. Any year of publication, language or publication status.

Exclusion criteria:

Narrative reviews, editorials or opinion articles.

Delivery or assessment of olive oil in combination with other fatty acids, nutrients or foods

Assessment of neurodegenerative disorders.

Information sources and search strategy

PubMed and OVID MEDLINE databases were searched on 10 November 2023. The following search strategies were used. No filters or limits were used.

Table 1. Intervention studies designed to assess the impact of olive oil supplementation

Author	Population	Study Design	Sample Size	Intervention	Control	Duration	Outcome of Interest	Results
Foshati *et al.* 2022	Diagnosed MDD	Double-blind randomised control trial	73	EVOO 25 ml/d (not combined with any other treatments or advice)	Sunflower oil 25 ml/d	52 d	Depression (BDI-II, HAMD-7)	Decrease in HAMD-7 score of 9 points ($P = 0{\cdot}006$), reduction in BDI-II did not reach statistical significance.
Rus *et al.* 2017	Diagnosed Fibromyalgia	Double-blind randomised control trial	23	EVOO 50 ml/d (not combined with any other treatments or advice)	Refined olive oil 50 ml/d	3 weeks	Mental Health Status (MCS-12)	Increase (improvement) in MCS-12 score by 11·228 ($P < 0{\cdot}035$).
Canheta *et al.* 2021	Obese individuals	Randomised control trial	129	EVOO 52 ml/d (not combined with any other treatments or advice)	Traditional Brazilian diet	12 weeks	Anxiety & Depression (HADS)	38·23 % reduction in symptoms of anxiety ($P = 0{\cdot}019$), 55·17 % reduction in symptoms of depression ($P = < 0{\cdot}001$), 57·69 % reduction in symptoms of anxiety and depression combined ($P = < 0{\cdot}001$)
Mitsukura *et al.* 2021	Healthy individuals	Randomised control trial	17	EVOO 15 g and bite-sized white bread	Bite-sized white bread only	1 d	Stress (Cerebral blood flow)	Decrease in oxyhemoglobin concentration in the frontal lobe and occipital lobe which was interpreted as lower mental stress

EVOO, extra virgin olive oil; MDD, major depression disorder; BDI-II, Beck Depression Inventory II; HAMD-7, Hamilton Depression Rating Scale 7; MCS-12, Mental Component Score 12; HADS, Hospital Anxiety and Depression Scale.

PubMed: (Olive oil OR ("Oleic Acid"[Mesh]) OR "Olive Oil"[Mesh] OR *n*-9 OR Oleuropein) AND ("Anxiety"[Mesh] OR "Anxiety Disorders"[Mesh] OR depression OR "Depressive Disorder"[Mesh] OR "Depression"[Mesh] OR mental health OR psychiat* OR mental illness)

OVID Medline: (Olive oil or *n*-9 or oleuropein) and (anxiety or anxiety disorder or depression or depressive disorder or mental health or psychiat* or mental illness)

Record screening and selection

Titles and abstracts were screened independently in duplicate by the two authors using the eligibility criteria. The program Abstrackr[18] was used for organisation. In cases of disagreement, the authors discussed the study until consensus was reached. Studies were then reviewed in full text to confirm eligibility.

Data collection process and data items

Data were extracted using piloted templates. Extraction was completed by one author and checked by the second author. The data extracted included: study design, participant/subject population, sample size, intervention or exposure (including duration), outcome and results.

Data analysis

Data were analysed qualitatively to assess trends and gaps for further study.

Results

The PubMed and OVID MEDLINE search yielded 544 and 152 results, respectively (Fig. 1). After deduplication, 552 results remained. After full-text screening, forty-nine studies were eligible for inclusion, including seventeen human experimental, eighteen observational and fourteen animal studies. Of the studies found, thirteen human intervention studies and four animal studies were designed to assess the impact of a different intervention on mental health outcomes and used olive oil as the comparator. Four human intervention studies that were designed to assess the impact of olive oil on mental health were identified (Table 1)[19–22]. All four were randomised controlled trials. Sample size ranged from seventeen to 129 and duration ranged from three to 12 weeks. The patient populations involved included people with major depressive disorder, fibromyalgia, obesity and healthy subjects. All four studies reported an improvement in mental health outcomes, including symptoms of depression[19,21], anxiety[21], stress[22] and overall mental health status[20].

Eighteen observational studies met criteria for inclusion (Table 2)[23–40]. Twelve studies were cross-sectional in design and of these, five assessed olive oil intake using a self-reported diet data collection instrument[23–27] while seven measured tissue levels of oleic acid[28–34]. The six prospective studies assessed olive oil or oleic acid intake[35–40]. Of the six prospective studies, five reported an association between higher baseline olive oil intake and lower risk of developing a mental health disorder or symptoms at a later time point[35,36,38–40]. The outcomes included diagnosis of anorexia or bulimia nervosa[35], symptoms of depression[36], incident depression diagnosis[38], development of severe depressed mood[39] and positive affect[40]. The remaining study found no association between intake and depression symptom severity[37]. Among the cross-sectional studies, the results were less consistent. Two cross-sectional studies measuring olive oil intake reported significant reductions in symptoms of mental illness (depression and binge eating disorder)[26,27] with higher intake, while three cross-sectional studies measuring olive oil intake reported a significant increase in symptoms of mental illness (depression and anxiety)[23–25]. Of the seven cross-sectional studies that assessed tissue levels of oleic acid, one reported that higher levels were associated with greater plasticity among children with attention deficit hyperactivity disorder[34]. Four of the seven cross-sectional

Table 2. Observational studies

Author	Study Design	Population	Sample Size	Exposure	Comparator	Outcome of Interest	Results
Vuckovic *et al.* 2021	Cross-sectional	Kidney transplant recipients	115	Higher olive oil intake	Lower olive oil intake	Depressive symptoms (BDI-II)	Positive correlation between BDI-II score and olive oil intake (R = 0·189, *P* = 0·049)
Daley *et al.* 2015	Cross-sectional	Young Australian women	7635	High oleic acid intake	Low oleic acid intake	Anxiety (self-reported)	Higher intake associated with increased likelihood of self-reported diagnosis of anxiety (OR = 1·02, 95 % CI 1·00, 1·05 *P* = 0·046). No association with self-reported depression (OR = 1·0 95 % CI 0·98, 1·01, *P* = 0·523)
Li *et al.* 2020	Cross-sectional	Perimenopausal women	2793	Highest quartile of oleic acid intake (> 32·26 g/d)	Lowest quartile of oleic acid intake (< 17·28 g/d)	Depression (Center for Epidemiologic Studies Depression Scale)	Higher intake associated with increased risk of depressive symptoms (OR: 1·994 (95 % CI 1·298, 3·063)
Pagliai *et al.* 2018	Cross-sectional	Ages 90–99	388	Highest olive oil intake (daily consumption)	Lowest olive oil intake (not daily consumption)	Depression (Geriatric Depression Scale)	Higher intake associated with lower risk of depression (OR = 0·34 95 % CI 0·20, 0·59 *P* < 0·001)
Bertoli *et al.* 2015	Cross-sectional	High risk of binge eating disorder	1472	Olive oil intake of >/= 4 tbsp per day	Olive oil intake of < 4 tbsp per day	Risk of developing binge eating disorder	Higher intake associated with decreased risk of eating disorder
Cocchi et Tonello 2010	Cross-sectional	Clinical diagnosis of MDD and healthy controls	84	Oleic acid levels among individuals with depression	Oleic acid levels among healthy controls	Difference in oleic acid levels	No significant difference (22·19 +/–2·08 and 21·14 +/–4·134, *P* = NS)
Kim *et al.* 2016	Cross-sectional	Ultra-high risk for psychosis	80	Higher oleic acid levels	Lower oleic acid levels	Psychosis symptoms and depression (PANSS, MADRS, GAF)	No association between oleic acid levels and total PANSS (correlation coefficient –0·029), MARDS (0·106) and GAF (0·023), *P* > 0·05 for all
Virkkunen *et al.* 1987	Cross-sectional	Male, imprisoned violent offenders with alcohol abuse and non-violent control persons	50	Oleic acid levels among prisoners	Oleic acid levels among controls	Difference in plasma phospholipid oleic acid levels	Higher oleic acid levels (13·30 +/–1·62 *v.* 11·39 +/–1·09, *P* < 0·001) among offenders compared to controls
Assies *et al.* 2004	Cross-sectional	Recurrent depression	44	Oleic acid levels among individuals with recurrent depression	Oleic acid levels from laboratory reference values (plasma: 1035–2025 umol, erythrocyte: 58–115 pmol/10e6)	Difference in plasma and erythrocyte oleic acid	Among individuals with depression, plasma oleic acid higher than reference range (2607·9 95 % CI 2342·8, 2902·7), erythrocyte oleic acid within the reference range (83·1 95 % 80·7, 85·4).
Assies *et al.* 2001	Cross-sectional	Medicated young people with schizophrenia and matched control subjects	33	Oleic acid levels in individuals	Oleic acid levels in control subjects	Difference in erythrocyte oleic acid	No difference in oleic acid (71·7 pmol/10e6 +/–10·61 *v.* 75·5 +/–4·48 *P* = 0·181)
Kim *et al.* 2014	Cross-sectional	Ultra-high risk for psychosis	80	Oleic acid levels among participants with the highest cognitive impairment	Oleic acid levels among participants with the least cognitive impairment	Cognitive factor of the Positive and Negative Syndrome Scale	No difference in oleic acid levels 22·72 *v.* 23·25 (*P* = 0·445)

(*Continued*)

Table 2. (*Continued*)

Author	Study Design	Population	Sample Size	Exposure	Comparator	Outcome of Interest	Results
Sumich *et al.* 2013	Cross-sectional	Adolescent boys with ADHD	20	High erythrocyte oleic acid levels	Low erythrocyte oleic acid levels	Personality traits (NEO-FFI Personality Questionnaire)	Higher levels associated with greater plasticity in personality assessment (Pearson correlation = 0·668, $P = < 0·001$)
Leone *et al.* 2018	Prospective	General population	11 800	Highest tertiles of olive oil intake (mean 30 g/d)	Lower tertile of olive oil intake (mean of 8 g/d)	Diagnosis of anorexia or bulimia nervosa during the follow-up period	Lower likelihood of diagnosis (HR: 0·47 95 % CI 0·29, 0·76, $P = 0·005$)
Kyrozis *et al.* 2009	Prospective	Healthy men and women 60 years or older	610	Higher olive oil intake	Lower olive oil intake	Depression (Geriatric Depression Scale)	Higher intake associated with fewer depression symptoms (beta coefficient −0·37, $P = 0·042$)
Elstgeest *et al.* 2019	Prospective	Adults	1058	Highest quartile of olive oil intake	Lowest quartile of olive oil intake	Depression (Center for Epidemiologic Studies Depression Scale)	No association between olive oil intake and depression scores ($P = 0·628$)
Sanchez-Villegas *et al.* 2011	Prospective	University graduates free from depression at baseline	12 059	Highest quintile of olive oil intake (mean 28·0 g/d)	Lowest quintile of olive oil intake (mean 2·8 g/d)	Incident depression diagnosis	Olive oil intake inversely associated with risk of depression HR 0·78 (95 % CI 0·60, 1·01) ($P = 0·03$); after adjusting for the Mediterranean diet pattern 0·80 (0·62, 1·04) $P = 0·06$)
Wolfe *et al.* 2009	Prospective	Healthy adults	4856	Highest tertile of oleic acid intake (mean 38·97 g/d for women, mean 60·49 g/d for men)	Lowest tertile of oleic acid intake (mean 12·40 g/d for women, mean 19·39 g/d for men)	Development of severe depressed mood (Center for Epidemiologic Studies Depression Scale)	Higher intake associated with a lower likelihood of diagnosis (OR 0·48 (95 % CI 0·25, 0·95) for women with high intake, P for trend = 0·03) No significant trend for men
Ford *et al.* 2013	Prospective	Adventist church attendees	9255	Highest olive oil intake	Lowest olive oil intake	Positive affect (Positive and Negative Affect Schedule Questionnaire)	Increased intake associated with positive affect $\beta = 0·070$ (95 % CI 0·029, 0·111) $P = 0·001$

TBSP, tablespoon; BDI-II, Beck Depression Inventory II; MDD, major depressive disorder; NS, not significant; PANSS, Positive and Negative Syndrome Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; GAF, Global Assessment of Functioning; NEO-FFI, NEO Five-Factor Inventory; HR, hazard ratio.

studies measuring tissue levels of oleic acid found no association[28,29,32,33], while two reported an association between higher levels and worse mental health: higher levels were found in criminal offenders compared with control subjects and increased levels were associated with increased diagnosis of depression[30,31].

Ten animal studies designed to assess the effect of olive oil met criteria for inclusion (Table 3)[41–50]. All of these studies used rodent models. Five studies measured the impact of olive oil supplementation while five assessed the impact of oleuropein supplementation. Nine of ten animal studies reported significant improvements in mental health outcomes with higher olive oil consumption[41–47,49,50]. Three studies reported a decrease in anxiety-like behaviour[42,44,49], two studies reported a decrease in depression-like behaviour[43,50] and three studies reported a decrease in both anxiety and depression-like behaviours[41,45,46]. One study reported a decrease in cognitive impairments associated with post traumatic stress disorder (PTSD)[47], while one study reported no improvement in anxiety-like behaviour[48].

Thirteen interventions studies using olive oil as a comparator were eligible for inclusions (Table 4)[51–63]. Of the thirteen studies, twelve compared olive oil supplementation to omega 3 (*n*-3) fatty acids[51–57,59–63] and one compared olive oil supplementation to flax oil[58]. Sample size ranged from 30 to 132. Olive oil dose ranged from 280 mg to 8 g per day and duration ranged from 35 d to 44 weeks. Populations included individuals diagnosed with major depressive disorder[51,53,63], individuals being treated for a current depressive episode[56], individuals with bipolar disorder[54,58], renal transplant recipients[52], children with attention deficit/hyperactivity disorder-like symptoms[55], individuals diagnosed with schizophrenia[57], adolescents with Tourette's disorder[59], community members reporting chronic work stress[60], pregnant women[61] and healthy subjects[62]. Primary outcomes include

Table 3. Animal studies

Author	Animal model	Intervention	Results
Kokras *et al.* 2020	Mice	Olive oil total phenolic content	Decreased anxiety and depression behaviours
Pitozzi *et al.* 2010	Male rats	High phenolic olive oil	Decreased anxiety-like behaviour
Xu *et al.* 2021	Mouse LPS model of depression	Oleuropein	Decreased depression behaviour
Mikami *et al.* 2021	Physically inactive mice fed a high-fat diet	Olive leaf extract (containing oleanolic acid and oleuropein)	Decreased depression behaviour
Nakajima *et al.* 2020	Obese rats exposed to high-fat, high-sugar diet	Olive oil as the source of fat in a high fat diet (*v.* lard)	Decreased anxiety-like behaviour
Badr *et al.* 2020	Mice with corticosterone induced depression	Oleuropein	Decreased anxiety and depression
Perveen *et al.* 2013	Rats	Olive oil	Decreased anxiety and depression
Lee *et al.* 2018	Rats exposed to prolonged stress (model of PTSD)	Oleuropein	Decreased cognitive impairment in PTSD
Hryhorczuk *et al.* 2017	Rats	High fat diet using olive oil (*v.* palm oil or LFD)	No change in anxiety-like behaviour
Murotomi *et al.* 2015	Aged obese mice	Oleuropein supplement	Decreased anxiety-like behaviour

LFD, low-fat diet.

changes in depressive symptoms[51,53,56,61,63], duration of remission of bipolar disorder[54], symptoms of mania and depression[58], quality of life[52], attention deficit/hyperactivity disorder symptom severity[55], severity of both schizophrenic and depressive symptoms[57], tic severity[59], changes in stress[60] and changes in overall mood[62]. Eight studies reported significant improvement in mental health outcomes in both the olive oil supplementation group and the intervention group[53,55,56,58–61,63], while four studies reported significant improvements in the intervention group compared with the olive oil supplementation group[51,54,57,62], and one study reported no significant improvements in either group[52]. Of the eight studies reporting improvement, four reported significant improvement in severity of depression[53,56,61,63], one reported improvement in severity of attention deficit/hyperactivity disorder symptoms[55], one reported significant improvement in severity of mania and depression symptoms associated with bipolar disorder[58], one reported significant improvement in symptoms of Tourette's disorder[59] and one reported significant improvements in stress[60].

Lastly, four animal studies used olive oil as a comparator (Table 5). Three were designed to assess the anti-depressant or anti-anxiety effects of fish oil and reported greater benefit in the groups receiving fish oil[64–66]. The fourth study assessed the effects of a pesticide on animals with an olive oil control; a depressogenic effect of the pesticide was reported[67]. None of the studies reported benefit on anxiety or depressive-like behaviour in the olive oil group.

Discussion

This scoping review identified human and animal studies aiming to assess the mental health impact of dietary olive oil and its constituents. All four human experimental studies designed to assess the impact of olive oil on mental health symptoms demonstrated significant improvements in mental health with olive oil consumption. Ten of thirteen human studies using olive oil as a placebo reported some degree of improvement among participants receiving the olive oil control. Nine of 10 animal studies designed to assess the impact of olive oil on mental health symptoms showed significant improvements in anxiety and/or depression-like behaviour. The observational studies yielded somewhat inconsistent associations between mental health and increased consumption of olive oil or higher oleic acid levels.

Among the observational studies, the findings were more consistent among the prospective cohort studies compared to the cross-sectional studies. Among the cohort studies, five of six studies reported a protective effect of higher intake of olive oil. These prospective studies also had larger sample sizes (range: 610–12 059, mean: 6606) compared with the cross-sectional studies (range: 20–7635, mean: 1066). The heterogenous findings in the cross-sectional studies may be due to smaller sample size, uncontrolled confounding variables, reverse causation or other sources of bias that are more common in this study design. Additionally, many of these studies assessed tissue levels of oleic acid rather than olive oil intake. Given that other foods contain oleic acid, the tissue levels might not have provided an accurate indication of olive oil intake. It is noted that four of the five observational studies that reported an association between higher intake of olive oil constituents and increased psychopathology assessed oleic acid tissue levels or intake and not olive oil. Among the human and animal studies, there was a relatively high degree of consistency in the findings, despite significant heterogeneity in the populations, and outcomes assessed. The most commonly reported benefit was a reduction in depression symptoms; however, studies also reported a reduction in symptoms of anxiety, psychosis, bipolar disorder, Tourette's, attention deficit-hyperactivity disorder and stress. The doses used in the studies designed to test the effects of olive oil ranged from 15 to 47 grams per day while the doses used as comparators ranged from 280 mg to 8 grams per day; these lower doses may have contributed to the smaller benefits reported. In one study of the Mediterranean diet and cardiovascular disease, the participants in the highest tertial of olive oil intake were consuming 34·6 ± 27·4 grams per day, suggesting that doses used in the olive oil studies were more aligned with the dose obtained with the Mediterranean diet[68].

Although the mechanism of olive oil's therapeutic effects is not fully understood, the benefits are suggested to be due to its anti-inflammatory and antioxidant properties. Hydrophilic polyphenols in olive oil, namely oleuropein, demethyloleuropein and ligstroside, have been found to be protective against oxidative damage caused by redox dyshomeostasis[69,70]. Other compounds in olive oil, specifically 3,4-dihydroxyphenylglycol and hydroxytyrosol, have been found to act as inhibitors on inflammatory

Table 4. Intervention studies using olive oil as a comparator intervention

Author	Population	Study Design	Sample Size	Intervention	Control	Duration	Outcome of Interest	Results
Gertsik *et al.* 2012	Diagnosed MDD	Single-blind randomised control trial	42	Citalopram + 2 g/d *n*-3 fatty acids	Citalopram + 2 g/d olive oil	9 weeks	Depression (HAMD)	Reduction of HAMD score in both groups, The reduction in the *n*-3 groups reached statistical significance (F = 7·32, df = 1177, *P* = 0·008) The percentage of individuals achieving full remission was higher in the *n*-3 group (44 *v.* 18 %, *P* = 0·018)
Aasebø *et al.* 2019	Renal transplant recipients	Randomised controlled trial	132	2·6 g/d *n*-3 fatty acids	2·6 g/d olive oil	44 weeks	Quality of life (MCS of SF-36)	The MCS score did not change significantly in either group. There was no difference between groups (mean (SD) increase of 4 (16) in the *n*-3 group and 2 (17) in the olive oil group *P* = 0·58).
Park *et al.* 2015	Diagnosed MDD	Double-blind randomised control trial	35	1740 mg/d of *n*-3 fatty acids	Oleic acid + safflower oil (dose unspecified)	12 weeks	Depression (CES-D-K, HAMD-17, CGI-S, CGI-I)	Significant reductions from baseline in CES-D-K, HAMD-17, CGI-S, and CGI-I (*P* < 0·001) in both the *n*-3 and olive oil group. Only CGI-I was significantly reduced in the *n*-3 group compared to placebo (*P* = 0·041).
Stoll *et al.* 1999	Diagnosed bipolar disorder	Double-blind randomised control trial	30	9·6 g/d of *n*-3 fatty acids	Unspecified dose of olive oil	4 months	Duration of remission	Significantly longer period of remission in intervention group compared to placebo group (*P* = 0·002). *n*-3 group had larger improvements in CGI, GAS and HAM-D. Improvement in both groups in the YMRS, not significantly different.
Stevens *et al.* 2003	Children with ADHD-like symptoms	Double-blind randomised control trial	50	PUFAS: 480 mg/d DHA, 80 mg/d EPA, 40 mg/d AA, 96 mg/d GLA, 24 mg/d vitamin E	6·4 g/d olive oil	4 months	ADHD symptom severity (ASQ, DBD)	Both PUFA and olive oil groups had significant decreases in parent assessment ASQ-P (decrease of 28 % olive oil and 44 % in PUFA *P* = 0·25) score and improvement in DBD assessment of hyperactivity, attention, and oppositional/defiant behaviour.
Silvers *et al.* 2005	Participants being treated for a current depressive episode	Double-blind randomised control trial	77	8 g/d DHA-enriched tuna fish oil	8 g/d olive oil	12 weeks	Depression (HDRS-SF and BDI II)	Both intervention and placebo group had significant reductions in HDRS-SF (mean (SE) for olive oil group decreased from 12·4 (0·9) to 0·6 (0·6) and *n*-3: decreased from 11·5 (0·9) to 0·3 (0·8) and BDI II scores (mean (SE) for olive oil group decreased from 23·3 (3·5) to 1·5 (1·5) and *n*-3: decreased from 21·9 (3·3) to 0·3 (1·5)).

(*Continued*)

Table 4. (*Continued*)

Author	Population	Study Design	Sample Size	Intervention	Control	Duration	Outcome of Interest	Results
Pawelczyk *et al.* 2016	Diagnosed schizophrenia	Double-blind randomised control trial	71	2·2 g/d of *n*-3 fatty acids	Unspecified dose of olive oil (73·9 % MUFAs, 9·8 % PUFAs)	26 weeks	Schizophrenia symptoms (PANSS), Depression (CDSS), Functioning (GAF) and symptom severity (CGI-S)	A 50 % reduction in PANSS score was achieved by more participants in the *n*-3 group (69 *v.* 40 % $P = 0{\cdot}017$); no difference in the achieving 25 % reduction (94·4 *v.* 85·7 % $P = 0{\cdot}26$). The intervention group had significantly greater reductions in CDSS score compared to the placebo group
Gracious *et al.* 2010	Ages 6–17 diagnosed with bipolar I or II disorder	Double-blind randomised control trial	51	1000 mg/d titrated up to 12 000 mg/d flax seed oil	1000 mg/d titrated up to 12 000 mg/d olive oil	16 weeks	Symptoms of mania and depression (YMRS, CDRS-R, GAF)	Both intervention and placebo group had small significant reductions in YMRS (2·3 points, $P < 0{\cdot}05$) and CDRS-R scores (2·9 points, $P = 0{\cdot}055$), and significant increases in GAF (1·5 points, $P < 0{\cdot}05$). No difference between the two groups.
Gabbay *et al.* 2012	Ages 6–18 diagnosed with Tourette's disorder	Double-blind randomised control trial	33	500 mg/d or 1000 mg/d of *n*-3 fatty acids	280 mg/d or 560 mg/d oleic acid	20 weeks	YGTSS-Global, YGTSS-Tic, YGTSS-Impairment, CY-BOCS	Both intervention and placebo group had significant reductions in all four outcomes from baseline to endpoint. The decrease was larger in the *n*-3 group for YGTSS-Global (decrease of 14·9 +/− 12·1 *v.* 6·7 +/− 11·6), but no significant difference for the other outcomes.
Bradbury *et al.* 2017	Community members reporting chronic work stress	Double-blind randomised control trial	90	2·2 g/d EPA, 0·44 g/d DHA	3800 mg/d low-phenolic olive oil plus 200 mg/d fish oil (to aid blinding)	12 weeks	Stress (PSS-10)	Mean scores steadily decreased in both the fish oil group (from 22·93 SD 5·18 to 18·36 SD 5·39) and the olive oil group (from 21·68, SD 4·43 to 16·07 SD 6·28). No significant difference between the two groups.
Sousa and Santos. 2023	Gestational age 22–24 weeks	Double-blind randomised control trial	60	1400 mg/d DHA until childbirth	Unspecified dose of olive oil until childbirth	Gestational week 22–24 to childbirth	Depression (EPDS)	Both intervention and placebo groups had significant reductions in EPDS score compared to baseline (fish oil: 6·30 (SE 0·52) to 3·50 (0·93) and olive oil: 7·30 (0·59) to 3·75 (1·06). There was no significant difference between the two groups.
Fontani *et al.* 2005	Healthy voluntary subjects	Non-randomised control trial	49	4 g/d fish oil	4 g/d olive oil	35 d	Mood (POMS)	Significant reduction in anger, anxiety, fatigue, depression, and confusion scores on POMS in intervention group only (numerical data not provided).

(*Continued*)

Table 4. (*Continued*)

Author	Population	Study Design	Sample Size	Intervention	Control	Duration	Outcome of Interest	Results
Meyer *et al.* 2013	Diagnosed MDD	Double-blind randomised control trial	95	8 g/d tuna oil	8 g/d of olive oil	16 weeks	Depression (HDRS)	Both intervention and placebo group experienced significant reduction in HDRS scores (12·2 ± 2·1 for tuna oil and −14·4 ± 2·3 for olive oil), with no significant differences between groups.

EVOO, extra virgin olive oil; ml, milliliters; g, grams; MDD, major depression disorder; HAMD, Hamilton Depression Rating Scale; MCS, Mental Component Summary; SF-36, 36-Item Short Form Survey; CES-D-K, Center for Epidemiological Studies Depression Scale Korean version; CGI-S, Clinical Global Impression Scale; CGI-I, Clinical Global Impression Improvements; PANSS, Positive and Negative Syndrome Scale; CDSS, Calgary Depression Scale for Schizophrenia; ADHD, Attention Deficit/Hyperactivity Disorder; PBMC, peripheral blood mononuclear cells; HDRS-SF, Short Form Hamilton Depression Rating Scale; BDI II, Beck Depression Inventory II; ASQ, Abbreviated Symptom Questionnaires; DBD, Disruptive Behaviour Disorders; CES-D, Center for Epidemiological Studies Depression Scale; PSS-10, Perceived Stress Scale; YMRS, Young Mania Rating Scale; CDRS-R, Child Depression Rating Scale – Revised; GAF, Global Assessment of Functioning; YGTSS, Yale Global Tic Severity Scale; EPDS, Edinburgh Postnatal Depression Scale; POMS, Profile of Mood States psychometric scale; HDRS, Hamilton Depression Rating Scale; CY-BOCS, Children's Yale-Brown Obsessive Compulsive Scale.

Table 5. Animal studies using olive oil as a comparator intervention

Author	Animal Model	Intervention	Comparator	Results
Tung *et al.* 2019	Male rats exposed to chronic mild stress	Fish oil-rich diet	Olive oil-rich diet	Less depression behaviour in the intervention group. No significant reduction in depressive behaviour in the olive oil group.
Cutuli, Landolfo, Nobili, *et al.* 2020	Aged mice exposed to immunotoxin mu-p75-saporin	*n*-3 PUFA	Olive oil supplementation	*n*-3 supplementation prevented an increase in depression-like behaviours. This effect was not seen in the olive oil group.
Cutuli, Landolfo, Decandia *et al.* 2020	Aged mice subjected to a brain lesion meant to mimic Alzheimer's disease	*n*-3 polyunsaturated fatty acids	Olive oil supplementation	Less anxiety symptoms in the intervention group and no change in anxiety symptoms in the olive oil group.
Chen *et al.* 2014	Adolescent male rats	Chlorpyrifos (organophosphate pesticide)	Olive oil injections	Increased depressive symptoms among rats receiving Chlorpyrifos. No increase in depressive symptoms in olive oil only group.

pathways[71]. Given the known role of inflammation and oxidative stress in mental illnesses pathogenesis, these mechanisms may be responsible for a beneficial effect. Furthermore, some studies have assessed the impact of olive oil on neurotransmitter metabolism. Neurochemical studies show continual olive oil consumption decreases levels of 5-hydroxytryptamine, 5-hydroxyindoleacetic acid and dopamine in the brain and increases levels of homovalinic acid, a metabolite of dopamine[46]. Based on these findings, it is hypothesised that the anxiolytic effects are due to the reduction of 5-hydroxytryptamine synthesis and metabolism in the brain. Conversely, the anti-depressive effects of olive oil are hypothesised to be due to the increase of dopamine release and turnover[46].

In this review, our search identified many studies that used olive oil as a placebo to examine the effects of other interventions, such as *n*-3 supplements, on mental health. Ten of 13 human studies reported statistically significant favourable mental health outcomes in both the intervention group and the placebo group. None of the four animal intervention studies that used olive oil as a placebo reported benefit in the mental health outcomes in the olive oil group. As high-level evidence has suggested an anti-depressant effect of fish oil supplements[72], the human studies that reported non-inferiority may further add to the evidence of olive oil's therapeutic potential; however, given that other studies have reported conflicting or uncertain results[73], it is very challenging to draw clear conclusions from these studies. Based on these results, olive oil should be considered a poor choice of placebo in mental health research on fatty acids due to its potential therapeutic benefits; this call has been made by other researchers as well[74].

This scoping review has many strengths related to its thorough and explicit methodology. The credibility of this review is enhanced by the use of a comprehensive literature search, using multiple databases and search terms. Explicit eligibility criteria and duplicate screening minimised bias in the selection of studies for inclusion. Furthermore, this scoping review addresses a gap in the existing literature on the impact of olive oil consumption on mental health. The findings of this review may be used in the design of dietary intervention studies aimed at improving mental health outcomes, which may lead to public health recommendations regarding mental health support.

This scoping review has a few limitations. First, very few human experimental trials designed to assess the impact of olive oil compared to an inert comparator were eligible for inclusion in the analysis. When considering all of the human experimental and observational studies, significant methodological heterogeneity existed. The included studies had a wide array of study designs and methodologies, including different mental health outcomes and methods of assessing olive oil exposure. Populations also varied greatly, specifically in terms of participant characteristics, sample size and country of origin. Each of these studies used varying doses of olive oil for varying durations. Limited detail was provided about the quality, source, purity or composition of the olive oil used. Studies also varied in whether extra virgin olive oil or olive oil was

used as an intervention. There is a need for more randomised controlled trials that assess the impact of olive oil intake compared to a control intervention that is either inert or well understood in its impact on mental health, in order to fully understand the potential of this food in a mental health promoting diet.

Conclusions

Olive oil is considered an important component of the Mediterranean Diet, a diet which has been well researched for its role in promoting mental well-being. The findings of this scoping review provide early support for a role of olive oil in improving mental health; however, more research, particularly in the form of high-quality clinical trials is needed.

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