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The Role of Omega-3 Polyunsaturated Fatty Acids in Prevention and Treatment of Mental Health Disorders - a review

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ABSTRACT

Omega-3 polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been extensively studied because of their therapeutic potential in mental health disorders. The objective of this review is to provide a synopsis of the current evidence from clinical trials and meta-analyses on the efficacy of omega-3 PUFAs supplementation in depressive disorder, bipolar disorder(BD), anxiety disorders, schizophrenia, and attention deficit hyperactivity disorder (ADHD). The neurobiological mechanisms through which omega-3 PUFAs may provide their benefits are anti-inflammatory actions, modulation of neurotransmitter systems, enhancement of neuroplasticity, and regulation of membrane fluidity. In depressive disorders, several meta-analyses have demonstrated that EPA-dominant formulations can significantly alleviate depressive symptoms, particularly in individuals with a clinical diagnosis and severe depression. In bipolar disorder, the data are more limited and mixed, but some evidence supports the use of EPA-rich supplementation as an adjunct to mood stabilizers in reducing depressive episodes. In anxiety disorders, although results remain heterogeneous, recent meta-analyses suggest that EPA-rich omega-3 supplements, at doses around 2 g/day, may help reduce anxiety symptoms. Findings in schizophrenia are modest but suggest that early supplementation or use in high-risk individuals may offer benefits, particularly for negative symptoms. In ADHD, several trials indicate that omega-3 PUFAs may improve attention and behavior, with enhanced effects in those with low baseline omega-3 levels. In summary, omega-3 PUFAs supplementation shows promising results in the treatment of various mental health disorders, especially as an adjunctive treatment. However, the heterogeneity of study designs, study populations and dosages of supplements emphasize the necessity for more standardized, high-quality research.

Keywords: omega-3 polyunsaturated fatty acids, mental health disorders, depression, anxiety, adjunctive treatment

1. INTRODUCTION

Mental disorders are a growing global health concern. One of the most prevalent is depression, which affects more than 280 million people worldwide, according to the World Health Organization (WHO). Despite advances in pharmacological and psychotherapeutic interventions, a significant number of individuals with depression and other mental health disorders do not achieve complete remission or experience adverse side effects from current treatments. Therefore, one of the fields that gathered high interest is nutritional psychiatry, which explores the role of dietary factors in the development, progression, and treatment of psychiatric disorders. Among the most studied nutrients in this area are omega-3 PUFAs.

The Role of Omega-3 PUFAs in Brain Structure and Function

The omega-3 PUFAs most relevant to brain health are EPA and DHA. Crucially, humans cannot synthesize them de novo and therefore rely on dietary intake, particularly from fatty fish and supplements (Bazinet and Layé, 2014). DHA accounts for approximately 40% of the total polyunsaturated fatty acids in the brain and is particularly concentrated in the gray matter, where it is incorporated into membrane phospholipids such as phosphatidylethanolamine (PE) and phosphatidylserine (PS). DHA ensures optimal membrane fluidity and the functional integrity of synaptic proteins and receptors, which are critical for effective neuronal signaling (Salem et al., 2001; Innis, 2007). Synaptic dysfunction and impaired neuronal signaling have been observed across a wide range of mood and cognitive disorders, contributing to their pathophysiology (Patrick and Ames, 2015). Additionally, DHA reduces oxidative stress, supports synaptic plasticity, and promotes neurotrophic signalling. The DHA derivative, neuroprotection D1, has been proven to protect from neuronal damage and enhance neuron survival (Dighriri et al., 2022).

EPA is also essential for proper brain function. It modulates inflammation and supports vascular function in the central nervous system (CNS) (Liao et al., 2019). Unlike DHA, which is structurally integrated into neural membranes, EPA acts dynamically by influencing inflammatory signalling pathways and producing specialized pro-resolving lipid mediators. Chronic low-grade inflammation is a recognized component of the pathophysiology of depression. EPA has shown anti-inflammatory effects by inhibiting the production of inflammatory cytokines including IL-1β, IL-6 and TNF-α. In addition, EPA enhances the biosynthesis of resolvins and protectins that restore central nervous system homeostasis (Dyall, 2015).

2. REVIEW METHOD

We conducted this literature review by searching for relevant papers in the digital databases PubMed, Google Scholar, and the Cochrane Library. The search included studies published between January 2005 and January 2025, with the priority given to articles published after 2015. Search terms included combinations of the following: “omega-3 polyunsaturated fatty acids,” “eicosapentaenoic acid,” “docosahexaenoic acid,” “brain function,” “depression,” “mental health,” “bipolar disorder,” “anxiety,” “schizophrenia,” and “attention deficit hyperactivity disorder.” We selected only English-language and human studies. We screened all articles by title and abstract, followed by a full-text review of the most significant studies. Inclusion criteria covered randomized controlled trials (RCTs), systematic reviews, and meta-analyses. We excluded studies that combined omega-3 supplementation with other nutrients without isolating omega-3 independent effect (Reason 1). In total, 27 articles met all the criteria. Figure 1 presents the diagram of study selection process.

3. RESULTS AND DISCUSSION

Depressive Disorders

Recent meta-analyses have investigated the effectiveness of omega-3 PUFAs supplementation in reducing depressive symptoms. A 2023 systematic review and meta-analysis involving 10 RCTs with 1426 participants discovered that EPA-rich supplementation (consisting of ≥60% of total EPA+DHA) at dosages ranging from 1 to 2 g/day significantly mitigated depression severity. Higher dosages (≥2 g/day) have not shown significant therapeutic effects. The research identified considerable heterogeneity among trials and possible publication bias, underscoring the necessity for more rigorous research in this domain (Liao et al., 2023).

Another meta-analysis comprising 26 studies with 2160 participants indicated an overall positive effect of omega-3 PUFAs on depressive symptoms. Specifically, formulations containing pure EPA (100%) or those with a primary composition of EPA (≥60% EPA) exhibited noteworthy clinical advantages, especially at dosages ≤1 g/day. In contrast, DHA-pure and DHA-major formulations failed to show comparable efficacy (Guu et al., 2019).

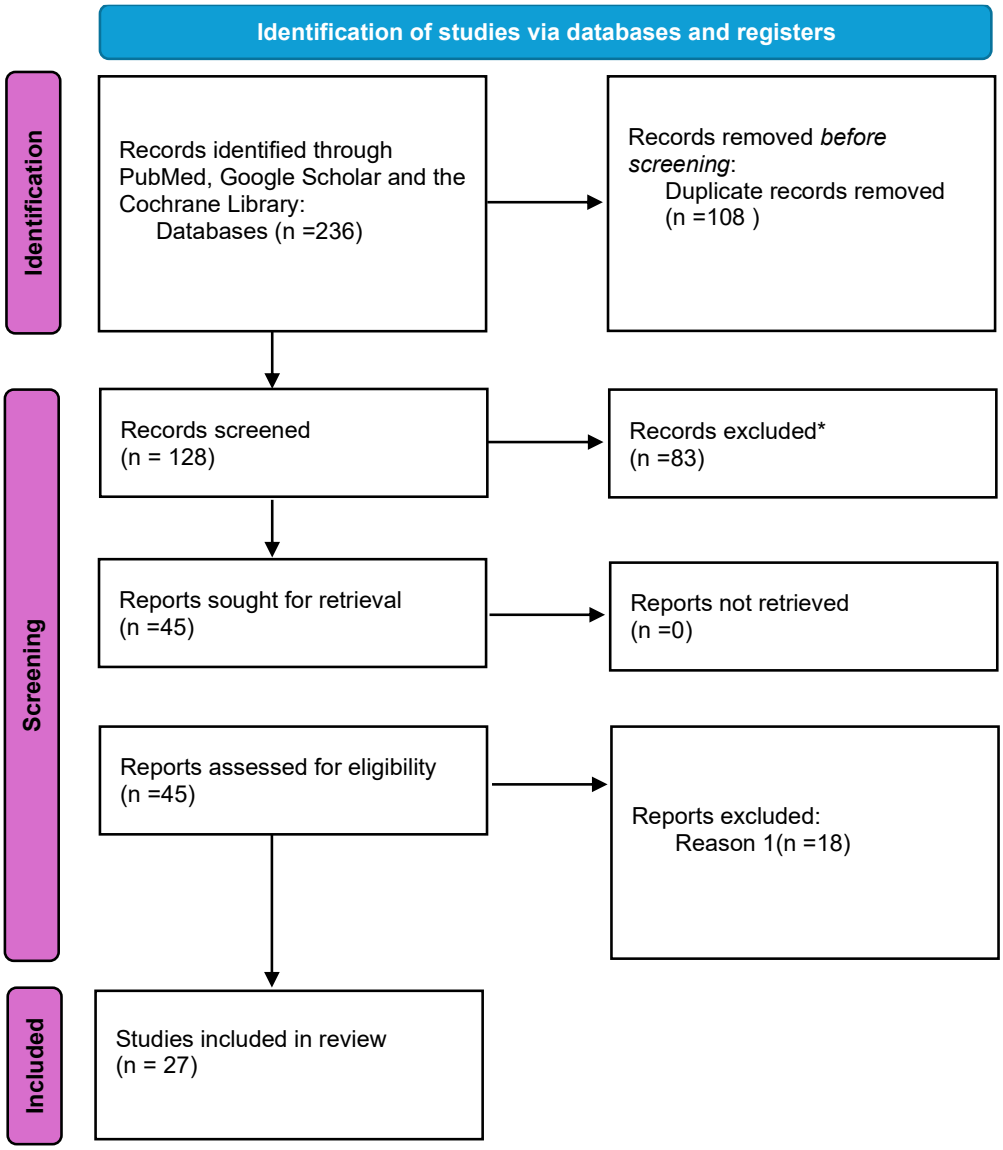

Figure 1 PRISMA Flow Diagram of study selection

Findings from a 2016 meta-analysis suggested that higher amounts of EPA (>1 g/day) were associated with reduction of depressive symptoms, particularly in individuals with high inflammation markers, those with comorbid cardiovascular diseases, cases of late-onset depression, and pediatric populations. These effects have been linked to increased levels of anti-inflammatory and pro-resolving lipid mediators derived from omega-3 PUFAs (Köhler et al., 2016).

On the other hand, a Cochrane systematic review updated in 2021, which incorporated 35 trials, determined that while there may be a small-to-modest positive effect of omega-3 PUFAs compared to placebo, the evidence was of low to very low certainty. The review emphasized the need for higher-quality studies to determine the true efficacy of omega-3 supplementation in the treatment of major depressive disorder (MDD) (Appleton et al., 2021).

Bipolar Disorder (BD)

Several meta-analyses and clinical trials have investigated the role of omega-3 PUFAs in the treatment of bipolar disorder (BD), particularly concerning depressive symptoms.

A meta-analysis by Sarris et al. (2012) evaluated the adjunctive use of omega-3 PUFAs in BD treatment. The findings indicated a significant improvement in depressive symptoms with omega-3 supplementation, while no substantial effect has been on manic

symptoms. This outcome suggests that omega-3 PUFAs may be more effective in addressing the depressive phase of BD (Sarris et al., 2012).

Another systematic review and meta-analysis by Kishi et al. (2021) focused on double-blinded, randomized, placebo-controlled trials assessing omega-3 fatty acids for residual depressive symptoms in adult BD patients. The analysis has shown a significant decrease in depressive symptoms, which emphasises the role of omega-3 PUFAs in managing bipolar depression (Kishi et al., 2021).

Li et al., (2023) have investigated the role of omega-3 PUFAs in preventing relapse in patients with stable BD over six months. Results showed reduction in the recurrence and also severity of depressive episodes, suggesting its potential effectiveness in maintenance treatment of BD.

Nevertheless, not all studies have demonstrated positive results. A 52-week randomized controlled trial by McPhilemy et al., (2021) evaluated the adjunctive use of 1 g EPA plus 1 g DHA daily in BD patients. The study reported no significant differences between the omega-3 and placebo groups in terms of mood episode relapses, hospital admissions, or medication adjustments. However, a minor reduction in hypomania scores has been observed in the omega-3 group.

Anxiety Disorders

A comprehensive dose-response meta-analysis by Bafkar et al., (2024) evaluated the efficacy of omega-3 supplementation on anxiety symptoms across 23 RCTs involving 2189 participants. The analysis found that each 1-gram per day increase in omega-3 intake was associated with a moderate decrease in anxiety symptoms. The biggest improvement was noted while supplementing doses of 2 grams daily. Lower doses showed a lot less significant effect. Moreover, no adverse events were observed, indicating safety profile of the supplementation.

Another meta-analysis by Su et al., (2018) included 19 clinical trials with 1203 participants receiving omega-3 PUFA treatment and 1037 participants in control groups. The study reported a significant association between omega-3 supplementation and reduced symptoms of anxiety. Subgroup analyses indicated that higher dosages (at least 2 g/day) were more effective, and the anxiolytic effects were more pronounced in individuals with specific clinical diagnoses than those without.

A more recent systematic review and meta-analysis by Kelaiditis et al., (2023) focused on the effects of long-chain omega-3 PUFAs on anxiety and depression. While the primary emphasis was on depressive symptoms, the review included studies that assessed anxiety outcomes. The findings suggested that EPA-enriched interventions, particularly those with EPA constituting ≥60% of the total EPA+DHA content and doses between 1 and 2 grams per day, were associated with significant reductions in depression severity, with promising but less conclusive anxiolytic effects.

Schizophrenia

A meta-analysis by Chen et al., (2015) evaluated the efficacy of omega-3 supplementation across different stages of schizophrenia. The analysis included ten randomized, double-blinded, placebo-controlled trials and found that omega-3 supplementation reduced psychotic symptom severity and lowered conversion rates to first-episode psychosis in individuals at ultra-high risk (UHR). In first-episode schizophrenia patients, omega-3 supplementation decreased nonpsychotic symptoms, required lower antipsychotic medication dosages, and improved early treatment response rates. However, in chronic schizophrenia, the results were mixed, with some patients experiencing significant benefits while others did not.

A randomized controlled trial by Saxena and Kumar, (2022) assessed the efficacy of omega-3 fatty acid supplementation as an adjunctive treatment in schizophrenia. The study involved 40 participants and found a significant reduction in the Positive and Negative Syndrome Scale (PANSS) scores in the omega-3 group compared to the placebo group after three months, suggesting an improvement in symptom severity.

Another study by Fusar-Poli et al., (2021) conducted a network meta-analysis of 21 studies involving 1983 participants at clinically high risk for psychosis. The analysis found that omega-3 PUFAs had a lower probability of transition to psychosis compared with the control group at 6 months, 12 months, and even after 24 months, suggesting a preventive effect in high-risk individuals.

However, not all research has shown favorable outcomes. A RCT conducted by Amminger et al., (2015) revealed that omega-3 supplementation did not notably decrease the transition to psychosis in individuals at ultra-high risk over 12 months. The researchers proposed that the duration of omega-3 supplementation may be an important factor influencing its effectiveness.

Attention Deficit Hyperactivity Disorder (ADHD)

A meta-analysis by Chang et al., (2018) assessed the effectiveness of omega-3 supplementation in children and adolescents diagnosed with ADHD. The analysis comprised seven randomized controlled trials (RCTs) featuring a total of 534 participants. It revealed that omega-3 supplementation significantly improved ADHD clinical symptom scores and cognitive measures related to attention. Additionally, it has been discovered that children and adolescents with ADHD exhibited lower levels of DHA, EPA, and overall omega-3 PUFAs when compared to the control group.

Another meta-analysis by Bloch and Qawasmi (2011) encompassed ten RCTs involving 699 children, demonstrating that omega-3 fatty acid supplementation had a small yet significant effect on ameliorating ADHD symptoms. Importantly, higher doses of EPA within the supplements have been linked with enhanced efficacy in addressing ADHD symptoms.

A randomized, double-blind, placebo-controlled trial by Widenhorn-Müller et al., (2014) investigated the impacts of omega-3 supplementation on behavior and cognition in children aged 6-12 years diagnosed with ADHD. Participants were administered a daily dosage of 600 mg EPA and 120 mg DHA over 16 weeks. The research indicated that supplementation led to elevated EPA and DHA concentrations in erythrocyte membranes and enhanced working memory function. However, no significant impacts were found on additional cognitive measures or behaviour as rated by parents and teachers.

In a study conducted by Bos et al., (2015), 40 boys aged 8-14 years with ADHD were given daily supplementation of 650 mg EPA and 650 mg DHA for 16 weeks. The research reported advancements in parent-rated attention for both children with ADHD and those typically developing. Nevertheless, no considerable effects have been noted on cognitive control or fMRI assessments of brain activity.

A 12-week, double-blinded, placebo-controlled trial by Chang et al., (2019) investigated the effects of high-dose EPA (1,2 g/day) on cognitive function in youth aged 6-18 years with ADHD. The study determined that EPA supplementation improved focused attention and vigilance, especially among participants with low baseline EPA levels. However, in individuals with high baseline EPA levels, EPA supplementation was correlated with less improvement or even a deterioration in specific ADHD and emotional symptoms. The key findings of this review are summarized in Table 1.

Table 1 Key findings of omega-3 supplementation in selected mental health disorders

Mental Health Disorder	Effects of Omega-3 Supplementation
Depression	Reduction of depressive symptoms by EPA-rich formulations (≥60%).
Bipolar Disorder	Effective as an adjunctive treatment for depressive episodes, minimal impact on manic symptoms.
Anxiety Disorders	Reduction of anxiety symptoms at higher doses (2 g/day).
Schizophrenia	Potential benefits in early-stage or high-risk patients, mixed results in chronic cases.
ADHD	Improvement in attention and cognitive functions, particularly in patients with low baseline omega-3 levels.

4. CONCLUSION

Omega-3 polyunsaturated fatty acids play a crucial role in regulating processes relevant to psychiatric disorders, including inflammation, neurotransmission, and synaptic plasticity. Accumulating evidence suggests that especially EPA-rich omega-3 formulations at doses between 1 and 2 grams per day may offer modest yet clinically meaningful benefits in reducing symptoms of major depressive disorder, anxiety, and possibly bipolar depression. While findings in schizophrenia and ADHD are more variable, some studies report improvements in negative symptoms, attention, and cognitive performance, particularly in individuals with low baseline omega-3 levels or early-stage illness. Despite these promising outcomes, inconsistencies in study design, sample characteristics, and EPA: DHA composition limit generalizability. Therefore, omega-3 PUFAs may be considered a safe and potentially effective adjunctive treatment for several mental health conditions. Still, high-quality, large-scale trials are needed to clarify their efficacy, optimal dosing, and clinical indications.

Author's Contributions

Maria Mroczka- Conceptualization, review, editing, investigation and methodology
Kinga Świtała - Methodology, investigation, visualization, supervision
Patrycja Pysz - Conceptualization, visualization, resources
Roksana Hrapkowicz- Review, data curation, investigation
Agnieszka Czernecka- Resources, writing- rough preparation, data curation
Kinga Erazmus- Visualization, data curation, investigation
Justyna Kuciel - Review, visualization, formal analysis
Dominik Tomczak- Supervision, writing- rough preparation, data curation
Karolina Jałocha - Review and editing, formal analysis, supervision
Marek Borecki- Resources, writing- rough preparation, formal analysis
Project administration- Maria Mroczka

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Informed consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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