Omega-3 fatty acids for psychiatric illness

Evidence suggests they may play a role in treating mood disorders

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Epidemiologic data suggest that people who consume diets rich in omega-3 fatty acids (FAs)—long-chain polyunsaturated FAs such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)—have a decreased risk of major depressive disorder (MDD), postpartum depression, and bipolar disorder (BD).1-5 Omega-3 FA concentration may impact serotonin and dopamine transmission via effects on cell membrane fluidity.6 Therefore, decreased intake may increase the risk of several psychiatric disorders. As the average Western diet has changed over the last 2 centuries, omega-3 FA consumption has decreased.7 Omega-3 FAs cannot be synthesized by the body and must come from exogenous sources, such as fish and nuts. For a discussion of different types of dietary fats, see Box 1 (page 42).8

Should we advise our patients to increase their omega-3 FA consumption? The American Psychiatric Association (APA) and the American Heart Association (AHA) recommend omega-3 FA consumption for the general population and in some cases, supplementation for specific disorders (Box 2, page 43).9-12 New data has been published since Current Psychiatry last reviewed the evidence for using omega-3 FAs for psychiatric conditions in 2004.8 This article looks at the latest evidence on the use of omega-3 FAs to treat mood disorders, schizophrenia, dementia, and other psychiatric conditions.

Limitations of the data

Reviewing the literature on omega-3 FAs to treat psychiatric disorders is hampered by several difficulties:13

• studies may evaluate the use of EPA alone, EPA combined with DHA, or DHA alone

continued
• the doses of EPA and DHA and ratio of EPA to DHA of the supplements used in clinical trials varies greatly
• patients’ dietary consumption of omega-3 FAs is difficult to control
• DSM diagnostic criteria, as well as severity of illness, differ within studies.

In addition, studies may use omega-3 FAs as monotherapy or as adjuncts. All of these factors lead to difficulty interpreting the literature, as well as trouble in extracting data for meta-analysis.

Omega-3 FAs for mood disorders
MDD and other depressive diagnoses.
Several meta-analyses examining the use of omega-3 FAs for treating depressive disorders have had equivocal findings. Variability in results might be partially explained by differences in the severity of baseline depression among diverse study populations, diagnostic variation, differing omega-3 supplementation protocols, or other issues. In addition, publication bias also may affect results.

In a 2011 literature review and meta-analysis of omega-3 FAs as monotherapy or an adjunct to antidepressants to treat MDD, Bloch and Hannestad⑥ concluded that omega-3 FAs offer a small but nonsignificant benefit in treating MDD. This review suggested that omega-3 FAs may be more effective in patients with more severe depression. The effects of varying levels of EPA vs DHA were not examined.

In a systematic review and meta-analysis, Appleton et al⑪ concluded that omega-3 FA supplements have little beneficial effect on depressed mood in individuals who do not have a depressive illness diagnosis (eg, MDD). However, this study did not consider the differential effects of EPA vs DHA on treatment response. Patients diagnosed with a depressive illness received greater benefits from omega-3 FA supplementation, although the patients in this study were heterogeneous. Similar to Bloch and Hannestad, Appleton et al⑪ found that omega-3 FA supplementation may be most beneficial for depressed patients with more severe symptoms, but is unlikely to help those with mild-to-moderate symptoms or individuals without symptoms who aim to prevent depression.

A meta-analysis by Martins⑫ looked at EPA vs DHA to treat depressive illness and found that only supplements that were mostly or completely EPA effectively treated depressive symptoms. Martins also found that severity of illness is key for positive treatment outcomes; there was a significant relationship between higher baseline depression levels and efficacy.⑫ Martins noted that omega-3 FA therapy was more effective as a treatment than a preventive strategy, and that adding omega-3 FAs to antidepressants was more efficacious than omega-3 FAs alone.⑫

A meta-analysis of clinical trials of omega-3 FAs for depressive illness suggested EPA should be ≥60% of total EPA + DHA.⑬

BD. A recent meta-analysis of 6 randomized controlled trials (RCTs) found that adding omega-3 supplements to mood stabilizers in patients with BD was associated with a statistically significant reduction of depressive symptoms, but was not effective for treat-
The authors suggested patients with BD—especially those with comorbid cardiovascular or metabolic conditions—increase their dietary consumption of foods containing omega-3 FAs (Table, page 44) and, if necessary, take a supplement of 1 to 1.5 g/d of mixed EPA and DHA, with a higher ratio of EPA. For a box on how to read omega-3 supplement labels, see this article at CurrentPsychiatry.com.

In a small RCT of 51 children and adolescents (age 6 to 17) with symptomatic bipolar I or bipolar II disorder, supplementation with flax oil (alpha-linolenic acid, a polyunsaturated omega-3 FA that is a precursor to EPA and DHA) did not affect symptoms as measured by several rating scales.

Perinatal and postpartum depression.
Omega-3 FAs are considered a safe treatment for depressive disorders during pregnancy because they provide neurodevelopmental benefits for neonates and have few contraindications during pregnancy. RCTs of omega-3 FA monotherapy for perinatal depression have been small (≤51 patients) and produced mixed findings. A pilot study (N = 16) of patients with postpartum depression found a significant decrease in depressive symptoms with EPA treatment. More research is needed before omega-3 FA supplementation can be recommended during pregnancy.

Schizophrenia
In a Cochrane review of 8 studies of patients with schizophrenia, adjunctive treatment with omega-3 FAs led to >25% reduction in the Positive and Negative Syndrome Scale, but this improvement was not statistically significant. Omega-3 FAs did not decrease tardive dyskinesia symptoms as measured by the Abnormal Involuntary Movement Scale. The authors stated that results were inconclusive, and use of omega-3 FAs in patients with schizophrenia remains experimental. In a separate meta-analysis that included 335 patients with schizophrenia, EPA augmentation had no beneficial effect on psychotic symptoms.

In a double-blind RCT of 81 adolescents and young adults (age 13 to 25) at ultra-high risk of psychotic illness, 5% of patients who received 1.2 g/d of omega-3 FAs developed a psychotic disorder compared with 28% of patients receiving placebo. The authors concluded that supplementation with omega-3 FAs may be a safe and effective strategy for young patients with subthreshold psychotic symptoms.

Dementia
Studies evaluating the relationship between omega-3 FAs and dementia risk have revealed mixed findings. In a pilot study of 10 geriatric patients with moderately severe...
In schizophrenia, adjunctive omega-3 FAs led to >25% reduction in PANSS scores, but this was not statistically significant.

## Clinical Point

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## Foods with healthy fats: From best to worst

| Polyunsaturated fats | Omega-3 | Fish-based: oily fish, including salmon, tuna, mackerel, lake trout, herring, and sardines  
| Plant-based: tofu and other forms of soybeans; walnuts and flaxseed and their oils, and canola oil | Omega-6 | Only available in plant-based form: corn, soy, and safflower oil |
|----------------------|---------|---------------------------------------------------------------------------------------------------------------------------------|---------|---------------------------------------------------------------------------------------------------------------------------------|
| Monosaturated fats    |         | Olive and peanut oil                                                                                                                                                                      |
| Saturated fats        |         | Red meats, high-fat dairy, and partially hydrogenated oils                                                                                                                                |

**Source:** Reference 18

## Omega-3 fatty acids

dementia related to thrombotic cerebrovascular disorder, DHA supplementation led to improved Hamilton Depression Rating Scale and Mini-Mental State Examination (MMSE) scores compared with controls. In another study, administering EPA to 64 patients with Alzheimer’s disease significantly improved MMSE scores, with maximum improvement at 3 months, but this benefit dissipated after 6 months of treatment. In a study of 22 patients with various types of dementia, Suzuki et al. found that DHA supplementation improved scores on a Japanese dementia scale. These studies show promise, but more evidence is necessary before recommendations can be made.

## Other psychiatric disorders

Omega-3 FAs as monotherapy or an adjunct to psychostimulants does not seem to improve symptoms in children who meet DSM-IV-TR criteria for attention-deficit/hyperactivity disorder (ADHD). Studies of omega-3 FAs as treatment for anxiety and personality disorders are limited. To date, omega-3 FAs as adjunctive treatment in obsessive-compulsive disorder (OCD) and monotherapy in borderline personality disorder have not shown efficacy.

## Using omega-3 FAs in practice

Based on new data and several recent meta-analyses, clinical recommendations have emerged. Sarris et al. suggested patients with BD increase dietary intake of omega-3 FAs or take a supplement with 1 to 1.5 g/d of mixed EPA and DHA (with a higher ratio of EPA). In MDD, the type of omega-3 FA supplementation seems to be important; EPA seems to be the primary component for efficacy. Additionally, the more severe the depression, the more likely symptoms will respond to omega-3 FAs. Omega-3 FAs are not effective at preventing depression and evidence is equivocal for treating perinatal depression. Omega-3 FA supplementation has not shown efficacy for patients with schizophrenia, although it may prevent transition to psychosis in adolescents and young adults at ultra-high risk for a psychotic disorder. Data examining omega-3 FA supplementation in postpartum depression and dementia are limited but show promise. Omega-3 FAs appear to lack efficacy in ADHD, OCD, and borderline personality disorder.

## References

9. Mozaffarian D, Micha R, Wallace S. Effects of coronary heart disease of increasing polyunsaturated fat in


**Related Resources**


**Disclosure**

Dr. Morreale reports no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.
Because nutritional supplements vary, advise patients to look at the supplement facts on the back of a bottle of omega-3 fatty acids. The American Psychiatric Association recommends patients take a total eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA) of 1 g/d; EPA should be ≥60% of total EPA + DHA.

This image is an example of a label that would meet the appropriate criteria. Total EPA + DHA = 1,490 mg and EPA is 60% of this combined total.