Omega-3 fatty acids as treatments for mental illness: which disorder and which fatty acid?

Ross B M, Seguin J, Sieswerda L E

CRD summary
This review evaluated the effectiveness of omega-3 polyunsaturated fatty acid (PUFA) as a treatment for mental illness. The authors concluded that omega-3 PUFA is not recommended in any form, although some evidence favours its use with mood disorders. The limited search strategy, together with shortcomings in the review process, means that the extent to which the authors’ conclusions are reliable is unclear.

Authors' objectives
To evaluate the effectiveness of omega-3 polyunsaturated fatty acid (PUFA) as a treatment for mental illness.

Searching
PubMed and PsycINFO were searched to identify relevant studies for inclusion in the review; the search terms were reported.

Study selection
Placebo-controlled trials of omega-3 PUFA (including n-3 alpha-linoleic, eicosapentaenoic and docosahexaenoic acids; ALA, EPA and DHA, respectively) measuring psychopathology outcomes in patients with psychiatric disorders were eligible for inclusion. The included studies comprised men and women (mean age 9 to 53 years) receiving a variety of fatty-acid formulations and doses, including DHA- or EPA-rich fish oils, as well as a semi-purified (96%) ethyl-EPA ester. The majority of participants were in receipt of other medications. The outcomes were assessed (over 6 weeks to 4 months) using a variety of measures for a range of psychiatric disorders, categorised by general disease class: attention-deficit hyperactivity disorder (ADHD) and related disorders; schizophrenia; anxiety, personality, major depressive and bipolar disorders; and post-partum depression.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Trial quality was assessed using the Jadad scale in terms of blinding, randomisation and withdrawals. The highest achievable score was 5.

The authors did not state how the validity assessment was performed.

Data extraction
Data were extracted or calculated for the change-from-baseline scores and mean differences between study groups. For ADHD and depression outcomes, the standardised mean differences (SMDs) in change-from-baseline scores were extracted for comparable trials and 95% confidence intervals (CIs) reported.

The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
For the depression trials, a random-effects meta analysis was conducted using inverse-variance weighting. Studies were also combined in a narrative. Meta-regression analysis was used to explore heterogeneity.

Results of the review
Twenty-three trials (1,702 participants) were included in the review.

The included trials varied in quality, with 10 achieving a score of 5 (range: 2 to 5). Statistical significance was discussed in the results, but p-values were not available for all outcomes.

ADHD and related disorders (6 trials).
Two double-blind trials reported statistically significant findings resulting from mixed omega-3 and omega-6 (including EPA and DHA) supplementation. The first, involving 29 children with learning difficulties (but not clinically diagnosed ADHD), reported improvements in psychosomatic symptoms and inattention. However, only a modest difference was noted between placebo and treatment groups (-4.6 change from baseline score). The second trial, involving 117 children with Developmental Coordination Disorder, reported statistically significant improvements in reading and spelling age, and on opposition, cognitive problems, hyperactivity, anxiety, perfectionism, social problems, impulsivity and inattention. The magnitude of difference between placebo and treatment groups was small (range: -3.8 to + 6.2 change from baseline scores). Substantial clinical heterogeneity was noted amongst all trials in this group.

Anxiety disorders (2 trials).

One double-blind trial compared omega-3 (EPA and DHA) supplementation with a vegetable oil placebo in 24 men affected by substance abuse (but without clinically diagnosed anxiety disorder). The findings were statistically significant for improvements in tension and anxiety in favour of the treatment group (-2.9 change from baseline score).

Schizophrenia (5 trials).

Two double-blind trials (involving 71 medicated and unmedicated schizophrenic participants) of omega-3 (EPA and DHA) compared with a corn oil placebo reported statistically significant improvements in the Positive and Negative Syndrome Scale (range: -4.1 to -3.6 change from baseline score). Two further trials (155 medicated participants) compared various doses of ethyl ester EPA with a liquid paraffin placebo and found statistically significant improvements in symptom scores, although one trial reported improvements in both study groups.

Mood disorders and depression (10 trials).

The meta-analysis of 9 trials (involving 575 participants) investigating major depressive disorder and bipolar disorder showed that omega-3 fatty acid supplementation is significantly more effective than placebo in treating depression (SMD 0.91, 95% CI: 0.41, 1.42, p<0.001). A high level of heterogeneity was reported (I²=75%). Individual trial results for major depressive disorder, bipolar disorder and post-partum depression were reported in the paper.

A preliminary interpretation of the meta-regression analysis suggested that supplementation with EPA may be more beneficial than DHA in treating mood disorders (p=0.009).

Authors' conclusions
Omega-3 PUFA cannot be recommended either as a mono- or adjunctive-therapy in any mental illness. The strongest evidence appears to be in favour of its use in the treatment of mood disorders.

CRD commentary
The review addressed a broad question that was supported by sufficiently focused inclusion criteria. The limitation to two electronic databases in the search strategy, along with no apparent attempt to seek unpublished material, means that relevant studies might have been missed and publication bias cannot be ruled out. In addition, there was no information on how the review process was carried out and whether attempts were made to minimise errors and bias at the study selection, quality assessment and data extraction stages. An appropriate validity assessment tool was used to evaluate the trials, and the results of this were used to highlight the findings. Given the substantial heterogeneity identified amongst the included studies, the value of the meta-analysis conducted on the mood disorder and depression trials may be limited. The authors' conclusions largely reflect the evidence presented, but several methodological limitations (including heterogeneity and small sample sizes) were acknowledged. This, together with some substantial shortcomings in the review process, means that the reliability of the authors' conclusions is unclear.

Implications of the review for practice and research
Practice: The authors stated that 1 to 2 g per day of omega-3 PUFA is indicated as an effective treatment for mood disorders. There appear to be no serious side-effects associated with this treatment.

Research: The authors stated that further research into the differential effects of various formulations of omega-3 PUFA supplementation is justified, especially in relation to attentional, anxiety and mood disorders.
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.