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## **Meta-analysis of the effects of eicosapentaenoic acid (EPA) in clinical trials in depression.**

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**+ Author information**

### **Abstract**

**OBJECTIVE:** Randomized trials of omega-3 polyunsaturated fatty acid (PUFA) treatment for depression have differed in outcome. Recent meta-analyses ascribe discrepancies to differential effects of eicosapentaenoic acid (EPA) versus docosahexaenoic acid (DHA) and to diagnostic heterogeneity. This meta-analysis tests the hypothesis that EPA is the effective component in PUFA treatment of major depressive episodes.

**DATA SOURCES:** PubMed/MeSH was searched for studies published in English from 1960 through June 2010 using the terms fish oils (MeSH) AND (depressive disorder [MeSH] OR bipolar depression) AND randomized controlled trial (publication type). The search was supplemented by manual bibliography review and examination of relevant review articles.

**STUDY SELECTION:** The search yielded 15 trials involving 916 participants. Studies were included if they had a prospective, randomized, double-blinded, placebo-controlled study design; if depressive episode was the primary complaint (with or without comorbid medical conditions); if omega-3 PUFA supplements were administered; and if appropriate outcome measures were used to assess depressed mood.

**DATA EXTRACTION:** Extracted data included study design, sample sizes,

doses and percentages of EPA and DHA, mean ages, baseline and endpoint depression ratings and standard deviations for PUFA and placebo groups, and P values. The clinical outcome of interest was the standardized mean difference in the change from baseline to endpoint scores on a depression rating scale in subjects taking PUFA supplements versus subjects taking placebo.

**DATA SYNTHESIS:** In a mixed-effect model, percentage of EPA in the supplements was the fixed-effect predictor, dichotomized into 2 groups: EPA < 60% or EPA  $\geq$  60% of the total EPA + DHA. Secondary analyses explored the relevance of treatment duration, age, and EPA dose.

**RESULTS:** Supplements with EPA  $\geq$  60% showed benefit on standardized mean depression scores (effect size = 0.532; 95% CI, 0.277-0.733; t = 4.195; P < .001) versus supplements with EPA < 60% (effect size = -0.026; 95% CI, -0.200 to 0.148; t = -0.316; P = .756), with negligible contribution of random effects or heteroscedasticity and with no effects of treatment duration or age. Supplements with EPA < 60% were ineffective. Exploratory analyses supported a nonlinear model, with improvement determined by the dose of EPA in excess of DHA, within the range of 200 to 2,200 mg/d of EPA.

**CONCLUSIONS:** Supplements containing EPA  $\geq$  60% of total EPA + DHA, in a dose range of 200 to 2,200 mg/d of EPA in excess of DHA, were effective against primary depression. Translational studies are needed to determine the mechanisms of EPA's therapeutic benefit.

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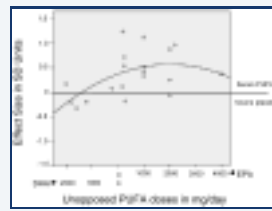
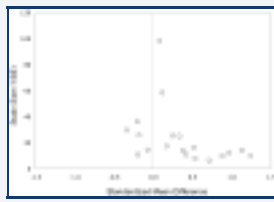
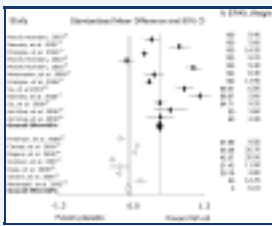
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