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Systematic review and meta-analysis investigating a role for n3 polyunsaturated fatty acids in major depressive disorder

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Various lines of evidence suggest a potential role for n3 polyunsaturated fatty acids (n3PUFAs) in depressive conditions. The evidence, however, is far from conclusive, and reviews and meta-analyses clearly demonstrate heterogeneity between studies[(e.g. 1,2)]. Investigations of heterogeneity show differential effects of n3PUFAs dependent on severity of depressive symptoms, suggesting a possible benefit in studies of individuals with more severe depressive symptomology[(1)]. This work aimed to investigate the impact of n3PUFAs on depressive symptomology in adults with major depressive disorder (MDD).

A systematic review of the literature was undertaken by searching The Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Registers, CINAHL and International Trial Registries over all years to May 2014, for: randomized controlled trials; that provided n3PUFAs as an intervention; used a comparator; measured depressive symptomology, and were conducted in adults with MDD. Primary outcomes were depressive symptomology (continuous data collected using a standard rating scale) and adverse events. Secondary outcomes were depression remission and response, quality of life and failure to complete studies. Quality of the evidence was also assessed. Data from all included trials were combined, by comparator, in meta-analyses.

Twenty-one studies involving 1153 participants investigating the impact of n3PUFAs compared to placebo, and one study involving 40 participants investigating the impact of n3PUFAs compared to antidepressant treatment, were identified. For the placebo comparison, the mean depressive symptomology in n3PUFA groups was 0·36 (95%CI: 0·12, 0·59) SDs lower than placebo following treatment. This effect is small-modest, and unlikely to be clinically significant. In assessments of adverse events, no differences were found between intervention and placebo groups (OR = 1·10, 95%CI: 0·82, 1·48; 15 studies, 942 participants). For the antidepressant comparison, no differences between conditions in depressive symptomology were found (MD (HDRS) = −0·08 (95%CI: −0·70, 0·54), and adverse events could not be analysed. The evidence on which these results are based, however, is very limited. Few studies and few participants contributed to all analyses, and the majority of studies were small and likely to be at high risk of bias. The analyses were also strongly influenced by two large trials, although these were judged to be largely at low risk of bias. Substantial heterogeneity between studies was found. Publication bias was suggested by asymmetry in the funnel plot. Sensitivity analyses suggested that the above result was likely to be influenced by the positive results of the many small studies at high risk of bias.

The evidence investigating the effect of n3PUFAs on depressive symptomology in MDD is limited, heterogeneous and likely to be biased. A small-modest beneficial effect compared to placebo was found but this effect is unlikely to be clinically meaningful. The findings from our sensitivity analyses and from large well-conducted trials also suggest that any true effect is likely to be smaller. Rates of adverse events were similar between n3PUFA and placebo groups, and the reported benefits of n3PUFAs appear comparable to those of antidepressants. Further well designed large trials are needed.

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2. Lin P-Y, Su K-P. (2007) A meta-analytic review of double-blind, placebo-controlled trials of anti-depressant efficacy of omega-3 fatty acids. *J Clin Psychiatry* **68**, 1056–61.