The effect of maternal omega-3 (n–3) LCPUFA supplementation during pregnancy on early childhood cognitive and visual development: a systematic review and meta-analysis of randomized controlled trials

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CRD summary
This review concluded that there was no conclusive evidence to support or refute omega-3 long chain polyunsaturated fatty acid supplementation in pregnancy as a way of improving cognitive or visual development in offspring. These conclusions reflect the limitations of the evidence base and appear reliable.

Authors’ objectives
To assess the impact of maternal omega-3 long chain polyunsaturated fatty acid (LC-PUFA) supplementation in pregnancy on neurologic and visual development in offspring.

Searching
Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE, MEDLINE, PsycINFO and CINAHL were searched to August 2012 without language restrictions. Search terms were reported. Reference lists of included articles and review articles were handsearched.

Study selection
Eligible studies were randomised controlled trials (RCTs) that reported the effects of oral omega-3 LC-PUFA supplementation during pregnancy or pregnancy and lactation on the neurologic (IQ and motor development) or visual development (visual acuity) of the offspring. Trials were included where the intervention contained other nutrients so long as the only difference between the intervention and control groups was the presence/absence of omega-3 LC-PUFAs. The primary outcome was Developmental Standard Score (in infants, toddlers and preschool children) or IQ (in children), measured with a standardised psychometric test where the mean is 100 and the standard deviation is 15. Secondary outcomes were defined in the review.

Most studies were performed in high-income countries (one was in the UK) within antenatal clinics or hospitals. Two studies only included pregnant women with allergic disease. More than half of the studies performed the interventions from pregnancy (varying from 14 and 28 weeks gestation) to birth. The form and dosage of omega-3 LC-PUFA supplementation varied across the studies as did the tools used to measure. Most control groups reportedly received vegetable oil containing no omega-3 LC-PUFA. Standardised scales were used to assess cognition, language development or motor development. Length of follow-up varied for each outcome within individual studies; across the studies maximum follow-up for any outcome ranged from five days to seven years.

Two reviewers independently assessed the studies for inclusion; any disagreements were resolved by a third reviewer.

Assessment of study quality
Trial quality was assessed independently by three reviewers using the Cochrane Risk of Bias tool.

Data extraction
Post-intervention means and standard deviations for the outcomes were extracted to enable calculation of mean differences and 95% confidence intervals. Study authors were contacted for further information where necessary. Two reviewers independently extracted the data.

Methods of synthesis
Mean differences and 95% confidence intervals were pooled using a fixed-effect model, or a random-effects model where substantial statistical heterogeneity was indicated. Statistical heterogeneity was assessed using the I² statistic (I² more than 50% indicated substantial heterogeneity). Pre-planned separate meta-analyses were conducted for studies that administered the intervention during pregnancy and lactation or during pregnancy only (with each of these meta-analyses performed separately for different age groups of the offspring at assessment). Each meta-analysis included
subgroup analyses based on the instruments used to measure the outcome.

**Results of the review**
Twenty-three publications reporting on 11 RCTs were included in the review (5,272 participants, range 48 to 2,399 per trial). One trial was at a low risk of bias for all of the quality domains assessed; results for the other trials were variable.

In the subgroup of preschool children aged two to five years, scores of cognition were statistically significantly higher among those whose mothers had taken DHA (a specific omega-3 LC-PUFA) during pregnancy and lactation compared with those who had not (WMD 3.92, 95% CI 0.77 to 7.08; two RCTs; I²=0%). Among the other studies conducted during pregnancy and lactation, no other statistically significant differences between groups were found in relation to cognitive development of infants aged under 12 months (one RCT), toddlers aged 12 to 24 months (two RCTs) or school-age children aged five to 12 years (two RCTs). Among studies conducted during pregnancy only, no statistically significant differences between groups were found in relation to cognitive development of toddlers (one RCT), preschool children (one RCT) and school-age children (one RCT).

Among studies conducted during pregnancy and lactation, there were no statistically significant differences between groups in relation to motor development of infants (one RCT), toddlers (two RCT) or preschool children (one RCT). Similarly, no significant differences in motor development were observed between groups in studies conducted during pregnancy only (one RCT).

In studies performed during pregnancy only, no statistically significant differences were observed between groups in relation to language development of toddlers (one RCT) and preschool children (one RCT). Six of the eight visual outcome assessments reported by studies (five RCTs) demonstrated no significant differences between the treatment and control groups.

Further details of the results were reported in the review.

**Authors’ conclusions**
There was no conclusive evidence to support or refute omega-3 LC-PUFA supplementation in pregnancy as a way of improving cognitive or visual development in offspring.

**CRD commentary**
The review question and inclusion criteria were clearly defined. Various major databases were accessed (one of which contained unpublished data) and no date or language restrictions were applied, which reduced the risk that relevant studies were missed. Efforts were made to minimise reviewer error and bias throughout the review process. Suitable quality assessment criteria were employed and results across the trials were variable.

The methods of synthesis seemed appropriate and the authors stated that strong inferences from the studies could not be made due to their methodological weaknesses. Limitations of the studies included small sample sizes, high attrition rates and lack of intention-to-treat analyses.

The authors’ conclusions reflect the limitations of the evidence base and appear reliable.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for future practice.

**Research:** The authors stated that large high-quality RCTs with specialised assessments for various ages were needed to assess the effect of omega-3 LC-PUFA supplementation during pregnancy further and its clinical significance. Further clarification of the effect of omega-3 LC-PUFA supplementation on visual development in offspring was suggested.

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