Effect of n–3 long-chain polyunsaturated fatty acid supplementation of women with low-risk pregnancies on pregnancy outcomes and growth measures at birth: a meta-analysis of randomized controlled trials

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ABSTRACT

Background: It is hypothesized that the intake of long-chain polyunsaturated fatty acids (LC-PUFAs) throughout pregnancy is important to maternal health and fetal and infant development.

Objective: The objective was to evaluate systematically the effect of LC-PUFA supplementation of pregnant women’s diets on pregnancy outcomes and growth measures at birth.

Design: We searched MEDLINE, EMBASE, CINAHL, and the Cochrane Library through August 2005 and also searched the references in reviewed articles for randomized controlled trials (RCTs) comparing LC-PUFA supplementation with placebo or no supplementation.

Results: Of 6 included RCTs, only 1 was judged to be at low risk of bias. Supplementation with n–3 LC-PUFAs in these 6 RCTs (1278 infants) was associated with a significantly greater length of pregnancy [weighted mean difference (WMD): 1.57 d; 95% CI: 0.35, 2.78 d; findings stable on sensitivity analysis] than in control subjects. We found no evidence that supplementation influenced the percentage of preterm deliveries, the rate of low-birth-weight infants, or the rate of preeclampsia or eclampsia. We found no significant difference in the 6 RCTs (1278 infants) in birth weight (WMD: 54 g; 95% CI: −3.1, 111 g) and no significant difference in 5 RCTs (1262 infants) in birth length (WMD: 0.23 cm; 95% CI: −0.04, 0.5 cm), but, in 4 RCTs (729 infants), there was a significant increase in head circumference (WMD: 0.26 cm; 95% CI: 0.02, 0.49 cm; significance lost on sensitivity analysis).

Conclusions: n–3 LC-PUFA supplementation during pregnancy may enhance pregnancy duration and head circumference, but the mean effect size is small. The implications of these findings for later growth and development remain to be elucidated. Am J Clin Nutr 2006;83:1337–44.

KEY WORDS Nutrition, feeding, development, long-chain polyunsaturated fatty acids, supplementation, pregnancy

INTRODUCTION

Two long-chain polyunsaturated fatty acids (LC-PUFAs)—docosahexaenoic acid (DHA, 22:6n–3) and arachidonic acid (AA, 20:4n–6)—are important to fetal and infant growth and development. In the cerebral cortex and retina, DHA constitutes a large percentage of the phospholipid fatty acids ([FAs] 1, 2); AA, which is also essential for normal growth and development (3), is the precursor of eicosanoids (4, 5). These FAs, which are essential components of membrane phospholipids, are deposited in relatively large amounts in the central nervous system during brain growth. Deposition is especially high during the last trimester of pregnancy and first months of life (6, 7), when an insufficient amount can lead to adverse effects or irreversible damage (8, 9).

DHA and AA are members of the n–3 and n–6 families of FAs, respectively. Because humans do not possess desaturase enzymes that are capable of inserting either the n–3 or the n–6 double bonds, both can be derived only from the diet and thus are regarded as essential. DHA may be obtained directly from dietary fish oils or from the precursor α-linolenic acid (18:3n–3); the usual precursor of AA is dietary linoleic acid (18:2n–6) from plant sources. When fish oil is provided in the diet, eicosapentaenoic acid (EPA, 20:5n–3) will be supplied, as well as DHA.

Both n–3 and n–6 FAs required for the fetus are supplied to the fetus during pregnancy by preferential placental transfer (5, 10, 11, 12). Although both precursor essential FAs and preformed LC-PUFAs can be transported, there is a preferential transfer of the latter form (5). The fetus and newborn infant depend, therefore, on a maternal supply of DHA and AA. It has been proposed that an additional supply of LC-PUFAs, particularly DHA, during pregnancy or lactation or both would improve an infant’s later cognitive and visual development (13, 14). It has also been suggested that a greater intake of LC-PUFAs, particularly that of DHA and EPA obtained from fish and fish oils, may have a beneficial effect on pregnancy outcomes (15).

Several studies, many of them observational, have assessed the effect of LC-PUFA supplementation of the diet of pregnant women on pregnancy outcomes. Most studies undertaken had the aim of improving pregnancy outcomes—ie, preventing preeclampsia, prolonging gestation, preventing preterm birth, and...
improving fetal growth (15, 16). The rationale for the supplementation was to modify the balance of production of prostaglandins involved in the initiation of labor, and thus these studies exclusively used n-3 LC-PUFAs, precursors of the 3 and 5 series eicosanoids (15, 16). However, no firm dietary recommendations can be based on the available evidence (17).

In this study, we sought to explore the potential beneficial effects of supplementation of pregnant women with LC-PUFAs on pregnancy outcomes and fetal growth by conducting a systematic review and meta-analysis of randomized controlled trials (RCTs).

MATERIALS AND METHODS

Criteria for inclusion of studies

Studies included in this review had to be RCTs or quasi-RCTs comparing LC-PUFA supplementation with placebo or no supplementation in healthy pregnant women. After an initial assessment of the included trials, we decided to focus our attention on pregnancy outcomes and growth measures at birth. In addition, we extracted any data related to adverse events. Trials in women with high-risk pregnancies were not included. A high-risk pregnancy was defined as one in which a condition places the mother, the developing fetus, or both at higher-than-normal risk for complications during or after the pregnancy and birth (eg, a preterm delivery during an earlier pregnancy, intrauterine growth retardation, pregnancy-induced hypertension, or multiparity). Trials in which precursor essential FAs (α-linolenic and linoleic acids) were used in the intervention group were not included, because intake of the precursors is far less effective with respect to LC-PUFA deposition in fetal brain. Trials with only biochemical outcomes were not included.

Search strategy to identify studies

The search strategy included the use of a validated filter for identifying RCTs (18), which was combined with a topic-specific strategy using PubMed’s MeSH terms—eg, FA or omega or n-6 or n-3 or eicosapentaenoic acid or EPA or docosahexaenoic acid or DHA or arachidonic acid or LC-PUFA or long-chain FA or essential FA or fish oil. The full search strategy is available from the authors on request.

We performed a computerized literature search of MEDLINE (from 1966 to August 2005), EMBASE (from 1980 to August 2005), the Cumulative Index to Nursing and Allied Health (CINALH) (from 1982 to August 2005), and the Cochrane Library (issue 2, 2005). We supplemented this search by examining published reviews and position papers. Additional sources were references in reviewed articles. We imposed no limit with respect to the language of publication, but certain publication types (ie, letters to the editor, abstracts, and proceedings from scientific meetings) were excluded.

Methods of the review

Trial selection

One of us (AH) initially screened the title, abstract, and key words of every report identified by the search strategy; this reviewer then retrieved the full text for potentially relevant trials and for reports whose relevance was not clear. Two of us (HS and AH) independently applied the inclusion criteria to each potentially relevant trial to ascertain its eligibility. If differences in opinion existed, they were resolved by discussion.

Quality assessment of trials

Two of us (AH and HS) independently, but without being blinded to the authors or journal, assessed the quality of the studies that met the inclusion criteria. We assessed the use of the following strategies associated with good-quality studies: generation of allocation sequences and allocation concealment; blinding of investigators, participants, outcome assessors, and data analysts (yes, no, or not reported); intention-to-treat analysis (yes or no); and comprehensive follow-up. The generation of allocation sequences was considered adequate if the resulting sequences were unpredictable (eg, computer-generated random numbers) and inadequate if the resulting sequences were predictable (eg, according to case record number). Allocation concealment was considered adequate when the randomization method used did not allow the investigator or the participant to identify or influence the intervention group before enrollment of eligible participants in the study. The quality of the allocation concealment was considered unclear when randomization was used but no information about the method was available and considered inadequate when inappropriate methods of randomization were used.

Methods for blinding were considered double-blind (neither patients nor care providers or assessors knew which treatment was given), single-blind (either patients or care providers or assessors were aware of treatment), and open (all parties were aware of treatment). With respect to an intention-to-treat analysis, a positive finding on the reviewers’ part meant that the authors had specifically reported undertaking this type of analysis or that our own study confirmed this finding or both. Conversely, a negative finding meant that authors did not report the use of intention-to-treat analysis, that we could not confirm its use on study assessment, or both. To evaluate the completeness of patient follow-up, we ascertained the percentage of participants excluded or lost to follow-up. Completeness of follow-up was considered to be adequate if ≥80% of participants were included in the final analysis and assumed to be adequate when there was no mention of losses to follow-up. We defined the categories of risk of bias by the number of criteria judged inadequate in each study: low risk of bias (≤1 inadequate criterion), medium risk of bias (≤3 inadequate criteria), and high risk of bias (> 3 inadequate criteria).

Data extraction

Two of us (AH and HS) independently performed data extraction by using standard data-extraction forms. When important data were not reported or were unclear, as in the case of studies by Smuts et al (19, 20), we contacted the corresponding authors of the primary studies for clarification. Discrepancies between reviewers were resolved by discussion. For dichotomous outcomes, we extracted the total number of participants and the number of participants who experienced the event. For continuous outcomes, we extracted the total number of participants and the means and SDs. In one RCT (21), participants were randomly assigned to 3 groups: an intervention group that received fish oil, a control group that received olive oil, and another control group that received no oil supplementation. Because the objective of...
our review was to compare supplementation with placebo or no supplementation, we combined both control arms into a single control group according to the method of Hogg and Craig (22). We compared the extracted data to identify errors. One reviewer (HS) entered the data into REVIEW MANAGER for WINDOWS software (REVMAN version 4.2; The Cochrane Collaboration, Oxford, United Kingdom) for analysis.

### Statistical analysis

We used the REVMAN software for all statistical analyses. The weighted mean difference (WMD) between the treatment and control groups was selected to represent the difference in continuous outcomes with 95% CIs. The dichotomous outcomes for individual studies and pooled statistics are reported as the risk ratio (RR) between the experimental and control groups (with 95% CI). To pool the data, we used either a fixed effect or random effects model approach, according to the heterogeneity in outcomes across studies; this was analyzed by using Cochrane’s Q statistic with $\alpha = 0.05$ for statistical significance and by using the statistic $I^2$, which is derived from Q and which describes the proportion of total variation that is due to heterogeneity beyond chance. Sensitivity analyses assessed the robustness of results after removal of studies that were judged to have a high risk of bias. To test for publication bias, we used a test for asymmetry of funnel plot proposed by Egger et al (23). This test detects funnel plot asymmetry by ascertaining whether the intercept deviates significantly from zero in a regression of the normalized statistic $Q$ against precision (reciprocal of the variance of the estimate, as ascertainment with the use of STATSDIRECT software (version 2.3.8; StatsDirect Ltd, Sale, United Kingdom).

### Description of studies

We initially identified 21 articles. The characteristics of the included trials are summarized in **Table 1**. Six RCTs (14, 19, 20, 21, 24, 25), with 1278 participants, met our defined inclusion criteria. All were fully peer-reviewed publications. When studies
TABLE 2
Characteristics of the excluded studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design, purpose, or reason(s) for exclusion</th>
</tr>
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<tbody>
<tr>
<td>Boris et al (27)</td>
<td>Reported the same population as in another study; reported only biochemical data</td>
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<tr>
<td>Borod et al (28)</td>
<td>Abstract of subsequently published randomized controlled trials</td>
</tr>
<tr>
<td>Colombo et al (26)</td>
<td>Reported the same population as in another study; did not report any of our defined outcomes</td>
</tr>
<tr>
<td>de Groot et al (29)</td>
<td>Supplementation with α-linolenic acid</td>
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<tr>
<td>de Groot et al (30)</td>
<td>Supplementation with α-linolenic acid</td>
</tr>
<tr>
<td>Hagen et al (31)</td>
<td>Reported the same population as in another study; did not report clinical outcomes</td>
</tr>
<tr>
<td>Helland et al (32)</td>
<td>Reported the same population as in another study; did not report any of our defined outcomes</td>
</tr>
<tr>
<td>van Houwelingen et al (33)</td>
<td>Reported the same population as in another study; reported only biochemical data</td>
</tr>
<tr>
<td>Malcolm et al (47)</td>
<td>Did not report any of our defined outcomes</td>
</tr>
<tr>
<td>Montgomery et al (34)</td>
<td>Reported only biochemical data</td>
</tr>
<tr>
<td>Olsen et al (35)</td>
<td>Reported the same population as in another study</td>
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<tr>
<td>Otto et al (36)</td>
<td>Reported only biochemical data</td>
</tr>
<tr>
<td>Salving et al (37)</td>
<td>Reported the same population as in another study; did not report any of our defined outcomes</td>
</tr>
<tr>
<td>Sorensen et al (38)</td>
<td>Reported the same population as in another study; reported only biochemical data</td>
</tr>
<tr>
<td>Sorensen et al (39)</td>
<td>Did not report any of our defined outcomes</td>
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had groups assigned both randomly and nonrandomly, the nonrandomized arm was not considered further in this review. Investigators in one trial (14) reported supplementation during pregnancy and lactation, but we included in this review only that data related to supplementation during pregnancy. Investigators in other trials reported supplementation with either DHA alone (18, 19) or in combination with eicosapentaeonic acid (EPA; 14, 21, 24, 25) in healthy pregnant women. The duration and the sources and amounts of n-3 LC-PUFA, DHA, and EPA supplied varied between trials. The highest doses—1183 mg DHA and 803 mg EPA/d and 920 mg DHA and 1280 mg EPA/d—were used in the studies by Helland et al (14) and Olsen et al (21), respectively. In the remaining studies, the dose of DHA was ~150–200 mg/d. On the basis of the dose of supplementation, studies could be divided into 2 groups: a group with higher—~1000 mg/d—(14, 21) and a group with lower—~200 mg/d—(19, 20, 24, 25) DHA intake. The trials differed in the starting time of intervention, beginning as early as week 15 of gestation (24) or as late as week 30 of gestation (21). Trials with all LC-PUFA (n-3 and n-6) supplementation were considered for this review. However, none of the trials used n-6 supplementation in the intervention group. Thus, the remainder of this review applies only to n-3 LC-PUFA supplementation.

The characteristics of the excluded trials, including the reasons for exclusion, are summarized in Table 2. In brief, trials were excluded because they were not RCTs, the population was the same as reported in another study, or only biochemical data were reported. They also were excluded if there was no report of any of our defined outcomes, if they were abstracts of subsequently published randomized controlled trials, or if they were duplicate publications.

The quality of methods of the included studies

The results of the quality assessment of the methods of included studies are shown in Table 1. We assessed the risk of bias as low in only one trial (21). Only 2 trials (21, 25) used an adequate method to conceal allocation. The method used in the remaining 4 trials (14, 19, 20, 24) was unclear. Five trials (14, 19, 20, 21, 24) were described as “double-blinded”, and 1 trial (25) was open. An adequate description of the intention-to-treat analysis was provided in only one RCT (21). Withdrawals and dropouts were described adequately in all studies. Three trials (20, 21, 25) included an adequate proportion (i.e., ≥80%) of participants in the final analysis, and 3 trials (14, 19, 24) included an inadequate proportion.

RESULTS

Duration of pregnancy

n-3 Supplementation was associated, as compared with no supplementation in control subjects, with significantly greater duration of pregnancy (WMD = 1.57 d; 95% CI: 0.35, 2.78 d) in 1278 participants of 6 RCTs (14, 19, 20, 21, 24, 25; Figure 1). There was no heterogeneity (chi-square = 5.61, P = 0.35, I² = 10.8%), and significance was stable on sensitivity analysis (WMD: 1.59 d; 95% CI: 0.31, 2.87 d).

Other pregnancy outcomes

We found no significant difference between supplemented and nonsupplemented subjects in the percentage of preterm deliveries (ie, < 37 wk gestation; RR = 0.67; 95% CI: 0.41, 1.10) of 861 infants from 3 RCTs (19, 20, 21) or in the rate of low birth weight (ie, < 2500 g; RR = 0.66; 95% CI: 0.34, 0.26) in 328 infants from 2 RCTs (19, 20). There was no significant difference between supplemented and nonsupplemented subjects in the rate of preeclampsia or eclampsia (RR = 0.73; 95% CI: 0.22, 2.37) in

![FIGURE 1](https://academic.oup.com/ajcn/article-abstract/83/6/1337/4633041)

**FIGURE 1.** Weighted mean difference (WMD) and 95% CI of the duration of pregnancy in women supplemented with n-3 long-chain polyunsaturated fatty acid as compared with women who received no supplementation or placebo. Values for individual trials and pooled data (fixed-effect model) are shown.
328 women from 2 RCTs (19, 20) or in the rate of cesarean delivery (RR: 1.17 (95% CI: 0.79, 1.74) in those women and in 669 women from 3 RCTs (14, 19, 20). In addition, there was no significant difference between supplemented and nonsupplemented subjects in the rate of gestational diabetes (RR: 0.73; 95% CI: 0.22, 2.37) in 328 women from 2 RCTs (19, 20). In 4 RCTs (14, 19, 20, 25) involving 685 participants, no significant difference between supplemented and nonsupplemented subjects was found in the placental weight (WMD: 10.9 g; 95% CI: 10.4, 32.2). For all studied outcomes, there was no significant heterogeneity between the studies, and findings were stable on sensitivity analyses.

Growth measures in newborn infants

In the 6 RCTs (1278 infants), we found no significant difference in birth weight between supplemented and nonsupplemented control subjects (pooled WMD: 54 g; 95% CI: −3.1, 111 g; Figure 2). There was no heterogeneity (chi-square = 7.69, P = 0.17, I² = 35%), and this finding was stable on sensitivity analysis (WMD: 59 g; 95% CI: −0.2, 119 g).

Five RCTs involving 1262 infants showed no significant difference between supplemented and nonsupplemented subjects in the length at birth (pooled WMD: 0.23 cm; 95% CI: −0.04, 0.5 cm; Figure 3). There was no heterogeneity (chi-square = 5.67, P = 0.23, I² = 29.4%), and again, this finding was stable on sensitivity analysis (WMD: 0.26 cm; 95% CI: −0.02, 0.5 cm).

Supplementation was associated in 4 RCTs (729 infants) with significantly greater head circumference of the infants in the supplemented group, as compared with those of the nonsupplemented control group (pooled WMD: 0.26 cm; 95% CI: 0.02, 0.49 cm; Figure 4). There was no heterogeneity (chi-square = 4.60, P = 0.20, I² = 34.8%). The significantly greater head circumference of the infants in the supplemented group was lost in sensitivity analysis (WMD: 0.26 cm; 95% CI: −0.02, 0.53 cm).

Publication bias

We found no evidence of publication bias in any of the comparisons of the 6 included trials.

Adverse events

A narrative synthesis of the data on adverse events was undertaken. Of the 6 trials included in the review, adverse effects were reported in only 3 (14, 20, 21). Helland et al (14) reported similar rates of withdrawal because of patients who felt discomfort while taking the supplement (43.1% in the cod liver oil group and 38.7% corn oil group). These investigators reported supplementation during both pregnancy and lactation; separate data on the incidence of adverse effects with supplementation during pregnancy were not reported. Olsen et al (21) showed that the proportion of women who reported belching and unpleasant taste attributed to the oil capsules was significantly (P < 0.001) greater in the fish-oil group than in the control groups (70% compared with 20% and 42% compared with 7.4%, respectively). There was a trend regarding blood loss at delivery, which was greatest in the fish-oil group and lowest in the olive-oil group (P = 0.1, analysis of variance); the difference between the fish-oil and olive-oil groups was significant (P = 0.04). There were no significant differences between groups in other possible side effects of the fish oil, such as prolongation of labor or the need for a surgical delivery. In a study in which DHA was consumed from eggs, Smuts et al (20) reported that the proportion of mothers who experienced ≥1 adverse event was significantly (P < 0.01) higher in the regular egg group than in the supplemented group (38% and 25%, respectively). Serious adverse events occurred in the high-DHA egg group no more often than was expected for the

![FIGURE 2](https://academic.oup.com/ajcn/article-abstract/83/6/1337/4633041/FIGURE_2.png)

**FIGURE 2.** Weighted mean difference (WMD) and 95% CI of the birth weight (in g) of infants born to women who during pregnancy were supplemented with n-3 long-chain polyunsaturated fatty acid as compared with the infants born to women who received no supplementation or placebo. Values for individual trials and pooled data (fixed-effect model) are shown.

![FIGURE 3](https://academic.oup.com/ajcn/article-abstract/83/6/1337/4633041/FIGURE_3.png)

**FIGURE 3.** Weighted mean difference (WMD) and 95% CI of the birth length (in cm) of infants born to women who during pregnancy were supplemented with n-3 long-chain polyunsaturated fatty acid as compared with the infants born to women who received no supplementation or placebo. Values for individual trials and pooled data (fixed-effect model) are shown.
population, and the 2 groups had the same number of total serious adverse events. Consequently, serious adverse events were not clearly linked to DHA supplementation. Neonates born to supplemented and unsupplemented women did not differ significantly in rates of adverse events or serious adverse events.

**DISCUSSION**

The results of this analysis indicate that n-3 LC-PUFA supplementation during pregnancy may increase the duration of pregnancy by an average of 1.6 d. Furthermore, n-3 LC-PUFA supplementation during pregnancy was associated with a trend toward greater growth measures at birth; however, this difference was significant only for head circumference, which was an average of 0.26 cm greater in the supplemented group, but significance was lost on sensitivity analysis.

These findings are based on the pooled results of included trials. However, only one trial (21) was of high quality with respect to fulfilling all criteria for method quality. In that RCT, supplementation with fish oil was associated with a significantly greater duration of pregnancy (WMD: 2.77 d; 95% CI: 0.8, 5 d) and significantly greater birth weight (WMD: 97 g; 95% CI: 8, 186 g) than were seen in the control subjects. A difference of this magnitude in birth weight appears to be of little of clinical importance for most healthy babies; however, such a shift in the birth-weight distribution of a population may affect the proportion of infants born with a low birth weight, which is associated with greater risks with respect to long-term child health (40, 41).

In the 2 RCTs that involved infants with a birth weight <2500 g, there was only a nonsignificant trend toward a reduction in the proportion of low-birth-weight infants with supplementation. Therefore, the question as to whether n-3 LC-PUFA supplementation can affect birth weight deserves further attention in future studies with larger numbers of subjects. n-3 LC-PUFA supplementation during pregnancy had no clear effect on other pregnancy outcomes—including rates of gestational diabetes, preeclampsia or eclampsia, and cesarean delivery—or on placental weight. Whereas no benefit existed for these pregnancy outcomes, neither was there an indication of any safety concerns with respect to the use of n-3 LC-PUFA supplementation to enhance the n-3 PUFA supply to fetal tissues or for other reasons. To minimize bias, we chose to include only RCTs in our review (42).

However, it is noteworthy that some observational studies, mainly in populations with high consumption of seafood, have suggested that greater marine n-3 LC-PUFA intake during pregnancy promotes longer gestation and higher birth weight (15, 43, 44); other studies did not confirm these findings (45).

The conclusions from our review apply only to women whose pregnancies are not high-risk pregnancies. Available results from RCTs involving women at high risk of preterm birth indicate that fish-oil supplementation during pregnancy has a small effect of prolonging gestation; no such effect was observed in women with twin pregnancies (46). There appears to be no benefit of fish-oil supplementation in increasing birth weight or preventing preeclampsia in women with high-risk pregnancies (46). A full-scale systematic review is needed to ascertain the effect of supplementation in that patient population.

This review focused on the effect of LC-PUFA supplementation during pregnancy on pregnancy outcomes and infant growth measures. Available studies suggest no beneficial or harmful effects on infants’ visual function (47) or cognitive development (26) as a result of LC-PUFA supplementation during pregnancy. However, one cannot exclude the possibility that longer supplementation is needed. Results from one RCT showed that the children of women who supplemented their diet with DHA during both pregnancy and lactation scored higher on standardized intelligence and achievement tests (Kaufman Assessment Battery for Children) at 4 y of age than did the children of women who supplemented their diets with FAs that did not contain DHA (26). Because these conclusions are based on limited available evidence, further studies are needed to examine this issue.

**Limitations**

We acknowledge several limitations to this review. The sample sizes in some trials, as well as the number of trials for some comparisons (eg, low-birth-weight infants and preeclampsia or eclampsia), were very small. The pooled sample sizes were also small, and, thus, there was little statistical power; consequently, we cannot exclude chance as an explanation for the results of many comparisons. Marked variability among study populations, baseline n-3 LC-PUFA status, and the interventions tested may have decreased the sensitivity for detecting possible effects. The quality of the methods and the quality of reporting results varied and sometimes were poor. As discussed earlier, potential limitations include unclear or inadequate allocation concealment, no intention-to-treat analysis, and no blinding. The findings are, therefore, likely to be affected to various degrees by selection, attrition, or performance biases (or all). In our meta-analysis, the statistical tests of the homogeneity (total consistency) of the results were nonsignificant. However, it is important to stress that the power of the statistical methods that investigate heterogeneity is limited, particularly for meta-analyses based on a small number of studies, as in this case. Consequently, the results of our meta-analysis, particularly those regarding pregnancy outcomes, should be viewed with caution. Similarly, given the small number of studies, statistical conclusions about the publication bias may be flawed.
Conclusions

Some evidence exists that maternal LC-PUFA supplementation is associated with a small increment in the duration of pregnancy; however, the implications of this finding for later growth and development are not clear. Further studies that have larger sample sizes and that take confounding factors into account are needed to examine the effects of such supplementation on growth measures and the rates of low birth weight.

BK conceptualized this review, and all authors helped write the protocol. AH identified articles for inclusion in the review. HS and AH extracted the data and also assessed study quality. HS assumed the main responsibility for the analysis and for writing of the review, although all authors contributed to (and agreed on) the final version. None of the authors had any personal or financial conflict of interest.

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