

Does Fish Oil During Pregnancy Help Prevent Asthma in Kids?

The evidence on fish oil has been mixed, but this study affirms its benefits—in certain women.

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PRACTICE CHANGER

Fish oil supplementation taken by women in the third trimester of pregnancy can reduce the risk for persistent wheeze, asthma, and lower respiratory infections in their children.

STRENGTH OF RECOMMENDATION

B: Based on two double-blind randomized controlled trials (RCTs).¹

A 24-year-old G2P1 at 24 weeks' gestation presents to your clinic for a routine prenatal visit. Her older daughter has asthma, and she wants to know if there is anything she can do to reduce her second child's risk for it. What do you recommend?

Asthma is the most common chronic disease in children in resource-rich countries such as the United States.² According to the CDC, 8.4% of children were diagnosed with asthma in 2015.³

Omega-3 fatty acids, found naturally in fish oil, are thought to confer anti-inflammatory properties that offer protection against asthma. Clinical trials have shown that fish oil supplementation in pregnancy results in higher levels of omega-3 fatty acids, along with anti-inflammatory changes, in offspring.⁴ Previous epidemiologic

studies have also found that consumption of omega-3 fatty acids decreases the risk for atopy and asthma in offspring.^{5,6}

A *Cochrane review* published in 2015, however, concluded that omega-3 supplementation during pregnancy had no benefit on wheeze or asthma in offspring.⁷ Five RCTs were included in the analysis. The largest trial, by Palmer et al, which included 706 women, showed no benefit for supplementation.⁸ The second largest, by Olsen et al, which included 533 women, did show a benefit (hazard ratio [HR], 0.37; number needed to treat [NNT], 19.6).⁹

These results, however, were limited by heterogeneity in the amount of fish oil supplemented and duration of follow-up. For example, the children in the Palmer study were followed only until age 3, which is around the time that asthma can be formally diagnosed—potentially leading to underreporting.⁸ In addition, the diagnosis of asthma was based on parent report of three episodes of wheezing, use of daily asthma medication, or use of a national registry—all of which can underestimate the incidence of asthma. The reported rate of childhood asthma with IgE-sensitization (rate without sensitization was not reported) was 1.8% in both study groups—much lower than the CDC's rate of 8.4%, suggesting underdiagnosis.^{3,8} Due to these biases and other potential confounders, no firm conclusions can be drawn from the Cochrane review.

STUDY SUMMARY

Maternal fish oil supplementation reduces asthma in children

This single-center, double-blind RCT of 736 pregnant women evaluated the effect of 2.4 g/d of n-3 long-chain polyunsaturated fatty acids (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) or placebo (olive oil), starting at an estimated gestational



age of 24 to 26 weeks, on wheeze or asthma incidence in their offspring.¹

Eligible women were between 22 and 26 weeks' pregnant at the time of recruitment. Exclusion criteria included supplementation of 600 IU/d or more of vitamin D, or having any endocrine, cardiac, or renal disorders. The investigators randomized the women in a 1:1 ratio to either fish oil or placebo. Maternal EPA and DHA blood levels were tested at the time of randomization and one week after birth.

The primary outcome was persistent wheeze or asthma (after age 3, persistent wheeze was termed asthma), determined based on daily diary recordings of five episodes of troublesome lung symptoms within the past six months (each lasting for at least three consecutive days); rescue use of inhaled β_2 -agonists; and/or relapse after a three-month course of inhaled glucocorticoids. Secondary outcomes included reduced incidence of respiratory tract infections, asthma exacerbations, eczema, and allergic sensitization.

In total, 695 offspring were included in the study, with 95.5% follow-up at three years and 93.1% at five. The children had scheduled pediatric visits at 1 week; at one, three, six, 12, 18, 24, 30, and 36 months; and at 4 and 5 years. They also had acute visits for any pulmonary, allergic, or dermatologic symptoms that arose.

Results. The investigators found that the children of mothers who took fish oil had a lower risk for persistent wheeze or asthma at ages 3 to 5, compared to those who received placebo (16.9% vs 23.7%; HR, 0.69; NNT, 14.7). But this effect was significant only in the children whose mothers had baseline EPA and DHA levels in the lowest third (17.5% vs 34.1%; HR, 0.46; NNT, 5.6). Similarly, fish oil supplementation had a greater benefit in children whose mothers had consumed the least EPA and DHA before the start of the study (18.5% vs 32.4%; HR, 0.55; NNT, 7.2).

As for the secondary outcomes, only a reduction in lower respiratory infections was associated with fish oil supplementation compared with placebo (38.8% vs



45.5%; HR, 0.77; NNT, 14.9). There was no reduction in asthma exacerbations, eczema, or risk for sensitization in the fish oil group.

WHAT'S NEW?

Study adds fuel to the fire

This study strengthens the case for fish oil supplementation during pregnancy to reduce the risk for asthma in offspring, despite the recent Cochrane review that showed no benefit.^{1,7} The Palmer study used a much lower amount of omega-3s (900 mg/d fish oil vs 2,400 mg/d in the current trial).^{1,8} Olsen et al supplemented with a greater amount of omega-3s (2,700 mg/d) and did find a benefit.⁹ The NNT from the Olsen study (19.6) is consistent with that of the current investigation, suggesting that a higher dosage may be necessary to prevent the onset of asthma.

Additionally, this study followed children for a longer period than did the Palmer study, which may have led to more accurate diagnoses of asthma.^{1,8} Lastly, the diagnosis of asthma in the Palmer study was based on parent survey data and use of daily asthma medicine rather than on daily diary cards, which are often more accurate.

Consider fish consumption. Both this study and the Olsen trial were performed in Denmark.^{1,9} While Denmark and the United States have had a relatively similar level of fish consumption since the 1990s, women in Denmark may eat a higher proportion of oily fish than women in the United States, given the more common inclusion of mackerel and herring in their diet.¹⁰ Thus, the effect of supplementation may be more pronounced in women in the US.

CAVEATS

Ideal dose? Which women to treat?

The FDA currently recommends 8 to 12 oz of fish per week for pregnant women, but there are no guidelines on the ideal amount



of fish oil to be consumed.¹¹ The Palmer study, using 900 mg/d of fish oil, did not show a benefit, whereas there did appear to be a benefit in this study (2,400 mg/d) and the Olsen study (2,700 mg/d).^{1,8,9} Further research is needed to determine the optimal dosage.

The decreased risk for persistent wheeze or asthma was seen only in the children of women whose EPA and DHA blood levels were in the lowest third of the study population. Thus, only women whose blood levels are low to begin with will likely benefit from this intervention. Currently, EPA and DHA levels are not routinely checked, but there may be some benefit to doing so.

One proxy for blood levels is maternal intake of fish at baseline. The investigators found that there was an association between dietary intake of fish and blood levels of EPA and DHA ($r, 0.32$).¹ Therefore, additional screening questions to gauge fish consumption would be useful to identify women most likely to benefit from supplementation.

CHALLENGES TO IMPLEMENTATION

Multiple pills, additional cost

Since omega-3 fatty acids are relatively safe and the NNT in the general population is low, it may be worth supplementing all pregnant women, even without a commercially available blood test for EPA or DHA. Nevertheless, some women may find it challenging to take up to four additional pills per day for 13 or more weeks. Also, there is an associated cost with these supplements, although it is low. **CR**

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