

Supplementary Materials

Early-life high-dose omega-3 polyunsaturated fatty acid supplementation reduces risk of childhood asthma/wheezing: A meta-analysis of randomized controlled trials

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Supplementary Table 1. Characteristics of included randomized controlled trials (RCTs) evaluating prenatal or early-life omega-3 PUFA supplementation for the prevention of childhood asthma and wheeze

Study	Setting and participants	Groups	Intervention and timing	Follow-up (age; completed/enrolled, n; rate, %)	Outcomes
Dunstan et al., 2003 ¹	N=98 atopic pregnant women were recruited between January 1999 and September 2001 in Western Australia, 83 complete the trial.	Fish oil group (n = 40) Placebo group (n = 43)	Fish oil group: fish oil capsules 4×1 g/d (3,700 mg/d Omega-3 PUFA;1,000 mg/d EPA; 2,100 mg/d DHA). Placebo group: olive oil capsule 4×1 g /d. From 20 weeks GA to delivery.	1 year; 83/98; 84.7%	Asthma; Recurrent wheeze
Toelle et al., 2010 ²	N=616 pregnant women at the risk of giving birth to a child with asthma were recruited through the antenatal clinics of 6 hospitals between September 1997 and December 1999, in Sydney, 450 complete the trial.	Fish oil group (n = 230) Placebo group (n = 220)	Fish oil group: tuna fish oil (500 mg/d) plus canola-based oils and spreads (151 mg/d EPA,34 mg/d DHA). Placebo group: sunola oil (500 mg/d) supplements plus oils and spreads low in Omega-3 PUFA. From 6 months to 5 years.	8 years; 450/616; 73.1%	Asthma; Wheeze
Furuhjelm et al., 2011 ³	N=145 pregnant women, at risk of having an allergic infant, were recruited through antenatal care clinics in 2003–2005, in Sweden, 119 complete the trial.	Fish oil group (n = 54) Placebo group (n = 65)	Fish oil group: nine fish oil capsules a day (2,700 mg/d Omega-3 PUFA;1,600 mg/d EPA; 1,100 mg/d DHA). Placebo group: nine soybean oil capsules per day. From 25 weeks GA to 3.5 months of breast feeding.	2 years; 119/145; 82.1%	Asthma
Imhoff-Kunsch et al., 2011 ⁴	N=1,094 pregnant women were recruited between February 2005 and February 2007, in Mexico, 834 complete the trial.	Fish oil group (n = 420) Placebo group (n = 414)	Fish oil group: two DHA capsules (400 mg DHA) a day (400 mg/d Omega-3 PUFA;0 mg/d EPA; 400 mg/d DHA). Placebo group: two capsules (a mixture of corn and soy oil) a day. From 18~22 weeks GA to delivery.	0.5 year; 834/1,094; 76.2%	Wheeze
D'Vaz et al., 2012 ⁵	N=420 healthy term infants of allergic women, allergic (otherwise healthy), nonsmoking women with restricted fish intake were recruited at 36 weeks of pregnancy, in Australia, 241 complete the trial.	Fish oil group (n = 115) Placebo group (n = 126)	Fish oil group: fish oil capsules 650 mg /d (390 mg/d Omega-3 PUFA;110 mg/d EPA; 280 mg/d DHA). Placebo group: olive oil capsules 650 mg/d. From delivery to 6 months of breast feeding.	1 year; 241/420; 57.4%	Parent reported recurrent wheeze
Noakes et al., 2012 ⁶	N=123 pregnant women in the area of Princess Anne Hospital (Southampton, United Kingdom) were enrolled in the study, 83 complete the trial.	Fish oil group (n = 46) Placebo group (n = 37)	Fish oil group: 2 portions per week of farmed salmon (495 mg/d Omega-3 PUFA; 165 mg/d EPA; 330 mg/d DHA). Placebo group: continue their habitual diet. From 20 weeks GA to delivery.	0.5 year; 83/123; 67.5%	Wheeze

RCT: randomized controlled trial; Omega-3 PUFA: omega-3 polyunsaturated fatty acid; GA: gestational age; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid

Supplementary Table 1. Characteristics of included randomized controlled trials (RCTs) evaluating prenatal or early-life omega-3 PUFA supplementation for the prevention of childhood asthma and wheeze (cont.)

Study	Setting and participants	Groups	Intervention and timing	Follow-up (age; completed/enrolled, n; rate, %)	Outcomes
Berman et al., 2016 ⁷	N = 118 women, both with and without history of allergic disease, were recruited in the United States, 84 complete the trial.	Fish oil group (n = 31) Placebo group (n = 26)	Fish oil group1: EPA-rich fish oil (1,334 mg/d Omega-3 PUFA;1,060 mg/d EPA; 274 mg/d DHA). Fish oil group2: DHA-rich fish oil (1,080 mg/d Omega-3 PUFA;180 mg/d EPA; 900 mg/d DHA). Placebo group: soy oil. From 12-20 weeks GA to delivery.	3 years; 84/118; 71.2%.	Asthma or wheeze
Hansen et al., 2017 ⁸	N = 533 Danish pregnant women with singleton pregnancies were recruited through antenatal care clinics in 1990, in Denmark, 402 complete the trial.	Fish oil group (n = 266) Placebo group 1 (n = 136); Placebo group 2 (n = 131)	Fish oil group: fish oil capsules 4×1 g/d (2,700 mg/d Omega-3 PUFA;1,570 mg/d EPA; 1,130 mg/d DHA). Placebo group 1: olive oil capsules 4×1 g/d. Placebo group 2: no oil capsules 4×1 g/d. From 30 weeks GA to delivery.	24 years; 402/533; 75.4%.	Clinically diagnosed asthma
Best et al., 2018 ⁹	N = 706 children, born to mothers who participated in the (DOMInO) RCT, with a family history of allergic disease, were recruited in South Australia, 566 complete the trial.	Fish oil group (n = 290) Placebo group (n = 276)	Fish oil group: fish oil capsules (900 mg/d Omega-3 PUFA;100 mg/d EPA; 800 mg/d DHA). Placebo group: vegetable oil capsules. From 21 weeks GA to delivery.	6 years; 566/706; 80.2%.	Wheeze symptoms with sensitization
Gunaratne et al., 2019 ¹⁰	N = 657 women with Infants born at < 33 weeks gestation were enrolled from the neonatal units of 5 participating centers, between 2005 and 2008, in Australia, 569 complete the trial.	Fish oil group (n = 278) Placebo group (n = 291)	Fish oil group: DHA-rich fish oil capsules 6×0.5g/d (1,095 mg/d Omega-3 PUFA;195 mg/d EPA; 900 mg/d DHA). Placebo group: soy oil capsules 6×0.5g/d. From delivery to 2 months of breast feeding.	7 years; 569/657; 86.6%.	Parent-reported Asthma ever; Parent-reported wheeze
Bisgaard et al., 2023 ¹¹	N = 736 pregnant women completed the Copenhagen Prospective Studies on Asthma in Childhood2010 (COPSAC2010) pregnancy, in Denmark, were recruited, 435 complete the trial.	Fish oil group (n = 219) Placebo group (n = 216)	Fish oil group: fish oil capsules 4 × 1 g/d (2,400 mg/d Omega-3 PUFA;1,320 mg/d EPA; 880 mg/d DHA). Placebo group: olive oil capsules 4 × 1 g/d. From 24 weeks GA to delivery.	6 years; 435/736; 59.1%.	Asthma

RCT: randomized controlled trial; Omega-3 PUFA: omega-3 polyunsaturated fatty acid; GA: gestational age; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid

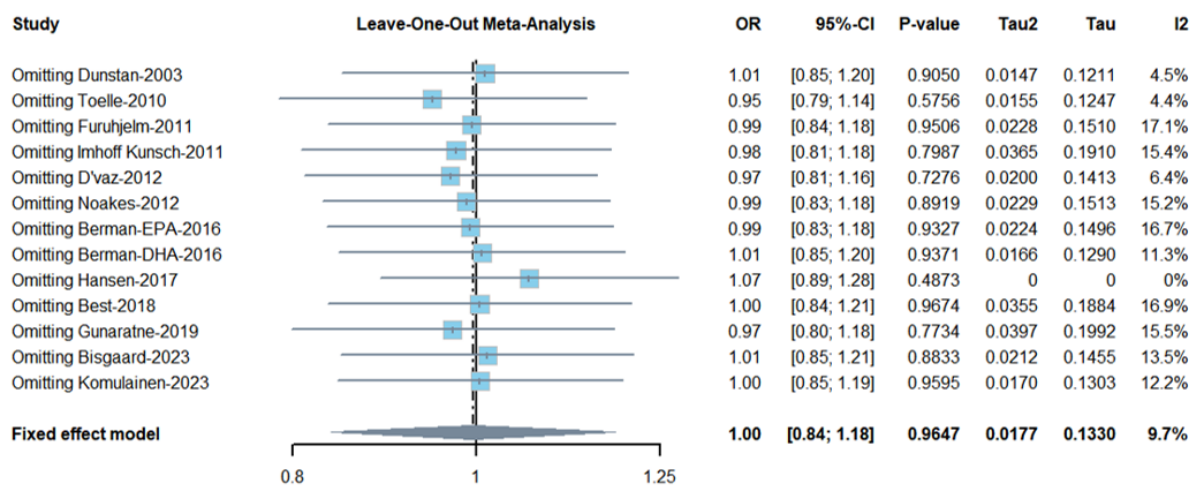
Supplementary Table 1. Characteristics of included randomized controlled trials (RCTs) evaluating prenatal or early-life omega-3 PUFA supplementation for the prevention of childhood asthma and wheeze (cont.)

Study	Setting and participants	Groups	Intervention and timing	Follow-up (age; completed/enrolled, n; rate, %)	Outcomes
Komulainen et al., 2023 ¹²	N = 439 pregnant women with absence of chronic diseases (allergic diseases allowed) were recruited between 2013 and 2017, in University of Turku and Turku University Hospital, in Finland, 264 complete the trial.	Fish oil group (n = 135) Placebo group (n = 129)	Fish oil group: two Fish oil capsules a day (2,400 mg/d Omega-3 PUFA; 220 mg/d EPA; 1,900 mg/d DHA). Placebo group: placebo capsules mainly providing medium-chain fatty acids. From early pregnancy (12-16 weeks GA) to 6 months of breast feeding.	2 years; 264/439; 60.1%.	Regular asthma medication; Parent reported recurrent wheezing

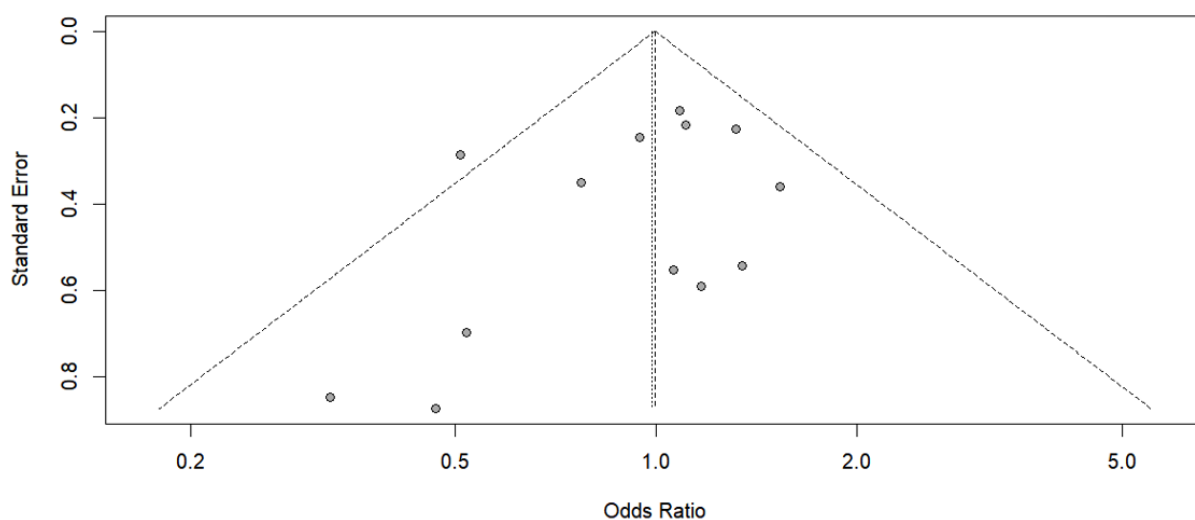
RCT: randomized controlled trial; Omega-3 PUFA: omega-3 polyunsaturated fatty acid; GA: gestational age; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid.

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Supplementary Figure 1. Sensitivity analysis for the meta-analysis



Supplementary Figure 2. Funnel plots for the publication bias of the meta-analysis