

PLoS One. 2013; 8(11): e80048.

PMCID: PMC3827145

Published online 2013 Nov 12. doi: [10.1371/journal.pone.0080048](https://doi.org/10.1371/journal.pone.0080048)

PMID: [24265794](https://pubmed.ncbi.nlm.nih.gov/24265794/)

# Fish and Fish Oil Intake in Relation to Risk of Asthma: A Systematic Review and Meta-Analysis

[Huan Yang](#),<sup>1, 2, 3, 4</sup> [Pengcheng Xun](#),<sup>2, 3, 4</sup> and [Ka He](#)<sup>2, 3, 4, \*</sup>

Lynette Kay Rogers, Editor

<sup>1</sup> Institute of Toxicology, Third Military Medical University, Chongqing, China,

<sup>2</sup> Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States of America,

<sup>3</sup> Department of Nutrition, Gillings School of Global Public Health and School of Medicine, University of North Carolina at Chapel Hill, North Carolina, United States of America,

<sup>4</sup> Department of Epidemiology and Biostatistics, School of Public Health, Indiana University, Bloomington, Indiana, United States of America,

The Ohio State University, United States of America,

\* E-mail: [kahe@indiana.edu](mailto:kahe@indiana.edu).

**Competing Interests:** The authors have declared that no competing interests exist.

Conceived and designed the experiments: KH. Analyzed the data: PX. Contributed reagents/materials/analysis tools: HY PX KH. Wrote the paper: HY PX KH.

Received 2013 Apr 9; Accepted 2013 Sep 30.

[Copyright](#) © 2013 Yang et al

This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are properly credited.

## Abstract

Although laboratory studies suggest that long-chain n-3 polyunsaturated fatty acids (LCn3PUFAs) may reduce risk of asthma, epidemiological data remain controversial and inconclusive. We quantitatively reviewed the epidemiological studies published through December 2012 in PubMed and EMBASE by using a fixed-effects or random-effects model. Eleven studies, comprised of 99,093 individuals (3,226 cases), were included in the final dataset. Of them, 7 studies examined associations between intake of fish or LCn3PUFA and risk of asthma: 4 studies in children (996 cases from 12,481 children) and 3 in adults (1,311 cases from 82,553 individuals). Two studies (69 cases from 276 infants) investigated LCn3PUFA levels in mothers' milk, and two studies assessed maternal fish consumption (786 cases from 2,832 individuals) during lactation and/or plasma LCn3PUFA levels during pregnancy (64 cases from 951 infants) in relation to offspring's asthma. The pooled relative risk of child asthma were 0.76 (95% CI, 0.61–0.94) for fish consumption and 0.71 (95% CI, 0.52–0.96) for LCn3PUFA intake. No statistically significant association was found in studies among adults. Epidemiological data to date indicate that fish or LCn3PUFA intake may be beneficial to prevent asthma in children. Further studies are needed to establish causal inference and to elucidate the potential mechanisms.

## Introduction

Asthma, a chronic inflammation of the airways that results in narrowing of the bronchial tubes [1], has increased dramatically over the past three decades all around the world, in both adults and children [2]–[4]. According to the data from US center of disease control (CDC), the prevalence of asthma increased from 7.3% to 8.4% in the US over the first 10 years of this century [5], and it affected 235 million people worldwide in 2011 with an increasing prevalence [6]. This situation leads to a considerable economic burden in both direct and indirect medical costs. It has been suggested that there may be an additional 100 million people who may suffer from asthma by 2025 [6]. Therefore, identifying potential protective or risk factors of asthma is of great public health significance.

Since the laboratory studies suggest that asthma is an inflammatory process, it has been hypothesized that high intake of long-chain n-3 polyunsaturated fatty acids (LCn3PUFAs) may be beneficial to preventing asthma. In the past decades, a number of epidemiological studies have examined the association between the intake of fish or LCn3PUFAs and the risk of asthma [7]–[15]. However, the findings from these studies were inconsistent. Two cohort studies that recruited 3,595 and 3,086 participants, respectively, found that people who ate fish more than once per week had their risk of asthma lowered significantly by 6% to 45% as compared with non-consumers [15], [16]. Another cohort study reported a 16% risk reduction in fish consumers compared with non-consumers, though it was statistically non-significant [17]. One case-control study found a non-significant risk reduction comparing the highest fish consumption group with the lowest [18], while one cross-sectional study found fish consumption was positively associated with the risk of asthma when comparing participants who consumed fish 1–2 servings/week with those who consumed 1–2 servings/month [19]. A few randomized clinical trials (RCTs) have been published. One trial reported beneficial effect of fish oil supplementation on asthma [27].

To provide an integrated review and a reliable quantitative assessment of the association between the intake of fish and LCn3PUFAs and the risk of asthma, we conducted a systematic review and meta-analysis of prospective cohort studies as well as RCTs with the existing data.

## Methods

### Study Selection

The meta-analysis was performed based on the checklist of the Meta-analysis of Observational Studies in Epidemiology [20]. All prospective cohort studies published in English-language journals from 1966 to December 2012, which reported the association between fish or fish oil intake/biomarker and incidence of asthma, were identified by searching PubMed using MESH words “((((("Fish Oils" [Mesh]) OR "Fishes" [Mesh]) OR "Fatty Acids, Omega-3" [Mesh]) OR "Seafood" [Mesh]) AND "Asthma" [Mesh])) OR (((((n-3 fatty acids) OR fish) OR fish oil) OR sea foods) AND asthma)” or using free words “(((n-3 fatty acids) OR fish) OR fish oil) OR sea foods) AND asthma” and by searching EMBASE using Emtree words “omega 3 fatty acid'/exp OR 'fish'/exp OR 'fish oil'/exp OR 'sea food'/exp AND asthma'/exp” or using free words “'n-3 fatty acids' OR 'fish' OR fish oils' OR 'sea foods' AND 'asthma.’” Additional information was retrieved through Google and a hand search of the references from relevant articles.

Two of our authors (HY and PX) independently reviewed all relevant papers and identified eligible studies. Discrepancies were resolved by group discussion. A study would be included if it was a prospective cohort design, and the relative risks (RRs) and corresponding 95% confidence intervals (CIs) of asthma relating to fish and/or LCn3PUFA intake/biomarker were presented or such information could be recalculated.

As shown in [Figure 1](#), of 1,333 non-duplicated abstracts from PubMed and EMBASE, we excluded 1,320 publications because they were non-original studies (e.g., reviews, editorials or letters to editor); were not epidemiological studies; were neither a prospective cohort nor a RCT; were not carried out in a general population; did not report RR for the association between fish or LCn3PUFA intake/biomarker and risk of asthma; did not assess fish or fish consumption properly; did not use the lowest exposure category as the reference; or were not in English. In addition, two articles were

identified by reviewing the reference lists. Thus, 15 studies [3], [4], [14]–[17], [21]–[29], including 11 prospective cohorts and 4 RCTs, that reported results on fish or LCn3PUFA intake and risk of asthma were included in this systematic review. Seven studies [4], [21], [22], [24], [26], [27], [29] including 3 prospective cohorts and 4 RCTs were excluded from the meta-analysis due to the insufficient information for pooling the results.

[Open in a separate window](#)

### [Figure 1](#)

Process of study selection.

## Data extraction

The dataset includes the first author's name, year of publication, study population, country of origin, study design, number of participants, average age at baseline, proportion of males, duration of follow-up, methods for diet measurement, categories of fish or LCn3PUFA intake, case identification methods, number of events, and adjusted covariates, as well as RRs and 95% CIs of asthma risk in the corresponding categories. RRs transformed to their natural logarithms ( $\ln$ ), and the 95% CIs were used to compute the corresponding standard errors (SEs).

## Statistical Analysis

RR was used as a loose term for measuring the association of interest across all primary studies. Hazard ratio and risk ratio were both considered as RR. [30] Because the incidence of asthma in the reference group ( $P_0$ ) is relatively low, the odds ratio (OR) is also used to approximate RR. We transformed OR to RR by combining the information of  $P_0$  in a sensitivity analysis.

We estimated the pooled RRs and 95% CIs of asthma, comparing the highest to the lowest fish or LCn3PUFA intake using a fixed-effects or random-effects model according to the heterogeneity among studies within each group. In addition, Cochran's test was used to test for heterogeneity among studies, and  $I^2$  was computed to determine the degree of inconsistency across studies. Publication bias was assessed by visualizing the funnel plot and determined by the Egger asymmetry test or Begg's test as appropriate. Sensitivity analysis was conducted to investigate the influence of a single study on the overall estimate.

$P \leq 0.05$  was considered statistically significant for all tests. All analyses were performed using STATA statistical software (Version 11.0, STATA Corp, College Station, TX).

## Results

### Study characteristics

The characteristics of the 11 included independent cohorts are shown in [Table 1](#). Four of them [4], [15]–[17] examined fish consumption and risk of asthma including 12,481 children and 996 cases identified during 1 to 6 years of follow-up; three of them were included in the meta-analysis. Two studies [23], [28] reported the association between the LCn3PUFA levels in mothers' expressed breast milk (EBM) during the breast-feeding period and risk of asthma in 276 infants. Sixty nine cases were diagnosed during a mean follow-up of 5.3 years. The other two studies [26], [29] related risk of asthma in offspring either to maternal fish intake (786 cases/2,832 individuals) or to maternal plasma LCn3PUFA levels (64 cases/951 individuals) during pregnancy with a mean follow-up of 6 and 7 years, respectively. In addition, 3 studies [14], [25], [31] examined fish and/or LCn3PUFA intake and risk of asthma in 82,533 adults including 1,311 incident cases identified during a mean follow-up of 9.9 years.

## Table 1

### Characteristics of included prospective studies.

[Open in a separate window](#)

Abbreviations: FFQ, Food Frequency Questionnaire; NA, Not Available; BAMSE, Barn/Children, Allergy/Asthma, Milieu, Stockholm, Epidemiologic; PIAMA, Prevention and Incidence of Asthma and Mite Allergy; EBM, Expressed Breast Milk; MACS, Melbourne Atopy Cohort Study; KOALA, Child, Parent and Health: Lifestyle and Genetic Constitution; NHS, Nurses' Health Study; BMI, Body Mass Index; EPIC, European Prospective Investigation into Cancer and Nutrition; CARDIA, Coronary Artery Risk Development in Young Adults.

We also included randomized controlled trials (RCTs) [21], [22], [24], [27] in this systematic review. A total of 1, 063 participants with 607 participants in the fish oil treatment group were involved in ([Table 2](#)).

## Table 2

### Characteristics of included randomized controlled trials (RCTs).

[Open in a separate window](#)

Abbreviations: NA, Not Available; PUFA, Polyunsaturated fatty acids.

## Infants' fish consumption and risk of asthma in childhood

Meta-analysis suggested that fish consumption in infants was inversely associated with the incidence of asthma in their childhood. The pooled RR of asthma was 0.76 (95% CI, 0.61–0.94), comparing the highest to the lowest category of fish consumption ([Figure 2](#)). No substantial heterogeneity was observed across studies ( $I^2=11.5\%$ ,  $P=0.32$ ).

[Open in a separate window](#)

### [Figure 2](#)

#### Multivariable adjusted relative risk and 95% confidence interval of risk of asthma.

The pooled estimates were obtained using a fixed-effects or random-effects model depending on the heterogeneity test. The dots indicate the adjusted RRs by comparing highest vs. lowest of the exposure of interest. The size of the shade square is proportional to the percent weight of each study. The horizontal lines represent 95% CIs. The diamond data markers indicate the pooled RRs. Abbreviations: CI, confidence interval; EBM, Expressed Breast Milk; LCn3PUFA: long-chain n-3 polyunsaturated fatty acid; RR, relative risk.

LCn3PUFA levels in maternal EBM were found to be inversely associated with the incidence of asthma in offspring. The combined RR was 0.71 (95% CI, 0.52–0.96), comparing the highest to the lowest group of LCn3PUFA levels ([Figure 2](#)). No significant heterogeneity was observed across studies ( $I^2=0.0\%$ ,  $P=0.36$ ).

### Maternal fish consumption and risk of asthma in offspring

Because the exposures in these two studies were not the same, the results cannot be pooled. In Willers's study [[29](#)], the maternal fish consumption frequency during pregnancy was not related to asthma development in offspring, the OR of asthma was 1.01 (95% CI, 0.85–1.20) comparing individuals who consumed fish  $\geq 1$ /week with those ate fish  $< 1$ /week. Consistently, Notenboom *et al.* [[26](#)] reported that maternal plasma LCn3PUFA concentration was not related to the risk of asthma in offspring.

### Fish consumption and risk of asthma in adults

Comparing those in the highest group of fish consumption with those in the lowest group, no significant association was found between fish and asthma. The pooled RR of incidence of asthma was 0.90 (95% CI: 0.69–1.18). Significant heterogeneity among studies was not found ( $I^2=0.0\%$ ,  $P=0.89$ ). Similar results were observed for LCn3PUFA intake (RR: 0.70, 95% CI, 0.46–1.05;  $I^2=78.5\%$ ,  $P=0.01$ ).

### Sensitivity analysis

Omitting 1 study each time and recalculating the pooled RRs for the remainder of the studies show that none of the individual studies substantially influenced the results. Considering the information of incidence of asthma in the reference group when transforming the ORs into RRs, the results were not materially changed.

### Fish oil supplementation and asthma in children

Only one study [[27](#)] found maternal LCn3PUFA supplementation to be beneficial for offspring's asthma risk, however, results from other trials were inconsistent. To date, findings from clinic trials do not support that LCn3PUFA supplementation is beneficial in terms of asthma prevention in childhood ([Table 2](#)).

## Discussion

---

By pooling data from published prospective cohort studies on the association of fish consumption or LCn3PUFA intake/biomarker and risk of asthma, we found that intake of fish or LCn3PUFAs was significantly inversely related to the risk of asthma in children based on the available literature. This inverse association was attenuated in adults.

Laboratory studies suggested that LCn3PUFAs might have the ability to inhibit the production of prostaglandin E<sub>2</sub> (derived from arachidonic acid), suppress T-helper 2 (Th2) cell's response to allergens [[32](#)], and consequently modulate the intensity and duration of inflammatory responses [[33](#)], [[34](#)]. Thus, it was hypothesized that the increased intake of LCn3PUFAs can reduce the risk of atopic diseases such as asthma [[32](#)]. In the present meta-analysis, we found that the potential beneficial effect of fish or LCn3PUFA intake was more pronounced in children. The mechanism for the difference between children and adults is unclear. It might be explained by the suggestion that children are more sensitive to LCn3PUFAs. Studies suggest that chronic inflammation may affect the immune system [[1](#)]. It may be particularly true in children because a child's immune system is under development [[35](#)]. Presumably, LCn3PUFAs are important in the stage of immune system development. In other words, children may be more sensitive to LCn3PUFA intake than adults. Nevertheless, further studies are needed.

Findings from other types of epidemiological studies on fish or LCn3PUFA and asthma are not so consistent. Two cross-sectional studies [36], [37] found an inverse association: one observed a 46% risk reduction in doctor-diagnosed asthma in children with per unit increment of fish consumption [36]; and the other one reported that the risk of asthma reduced by 68% comparing those in the highest with those in the lowest tertile of fish consumption [37]. However, another cross-sectional study found a positive association of fish consumption with the risk of asthma [19]. In addition, one case-control study found a non-significant risk reduction comparing the highest fish consumption group with the lowest [18]. Moreover, a meta-analysis summarized 9 randomized controlled trials (RCTs) and found that LCn3PUFA supplementation was not associated with improved asthma symptoms [38], both in children and adults. Another meta-analysis on RCTs [39] also reported a non-significant inverse association between fish oil supplementation and asthma risk in children. The null findings were in concordance with our results in adults. Of note, all included RCTs in that meta-analysis [38] had relatively small sample sizes (from 12 to 45) and short follow-up periods (from 8 weeks to 12 months). Also, in RCTs, fish oil supplementation was used, which may reflect a different health impact from consuming whole fish – a package of nutrients [40]. Thus, our meta-analysis of cohort studies, coupled with the other meta-analysis of RCTs, provided important evidence for future research and primary prevention of asthma.

Since our meta-analysis is based on observational studies, the inherent limitations of primary studies may have affected our findings. For example, the possibility of residual confounding cannot be ruled out. In addition, although we identified 11 cohort studies on this topic, these studies had to be divided into 3 subgroups because of the various exposure measurements. Nevertheless, our results should not be substantially biased given the potential biological mechanisms and the consistence with findings from RCTs.

In conclusion, our pooled analysis suggests that intake of fish or LCn3PUFAs in expectant mothers or infants is inversely associated with asthma development, particularly, in childhood. This meta-analysis adds evidence to the literature that fish, as a general healthy food, should be recommended to pregnant women and infants, though certain types of fish with high level of contaminants need to be avoided.

## Supporting Information

Checklist S1

PRISMA 2009 Checklist.

(DOC)

[Click here for additional data file.](#) (65K, doc)

## Funding Statement

This study was partially supported by a grant from National Institutes of Health (R21NS056445) <http://www.nih.gov/>. No additional external funding received for this study. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

## References

1. Orihara K, Dil N, Anaparti V, Moqbel R (2010) What's new in asthma pathophysiology and immunopathology? *Expert Rev Respir Med* 4: 605–629. [[PubMed](#)] [[Google Scholar](#)]
2. Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, et al. (2006) Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 368: 733–743. [[PubMed](#)] [[Google Scholar](#)]

3. Li J, Xun P, Zamora D, Sood A, Liu K, et al. (2013) Intakes of long-chain omega-3 (n-3) PUFAs and fish in relation to incidence of asthma among American young adults: the CARDIA study. *Am J Clin Nutr* 97: 173–178. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
4. Willers SM, Wijga AH, Brunekreef B, Scholtens S, Postma DS, et al. (2011) Childhood diet and asthma and atopy at 8 years of age: the PIAMA birth cohort study. *Eur Respir J* 37: 1060–1067. [[PubMed](#)] [[Google Scholar](#)]
5. Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, et al... (2012) Trends in asthma prevalence, health care use, and mortality in the United States, 2001–2010.. In: Statistics NCfH, editor. Hyattsville, MD: DHHS.
6. Masoli M, Fabian D, Holt S, Beasley R, Global Initiative for Asthma P (2004) The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 59: 469–478. [[PubMed](#)] [[Google Scholar](#)]
7. Robison R, Kumar R (2010) The effect of prenatal and postnatal dietary exposures on childhood development of atopic disease. *Curr Opin Allergy Clin Immunol* 10: 139–144. [[PubMed](#)] [[Google Scholar](#)]
8. Allan K, Devereux G (2011) Diet and asthma: nutrition implications from prevention to treatment. *J Am Diet Assoc* 111: 258–268. [[PubMed](#)] [[Google Scholar](#)]
9. Nurmatov U, Devereux G, Sheikh A (2011) Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. *J Allergy Clin Immunol* 127: 724–733 e721–730. [[PubMed](#)]
10. Calder PC (2012) Omega-3 polyunsaturated fatty acids and inflammatory processes: Nutrition or pharmacology? *Br J Clin Pharmacol*. [[PMC free article](#)] [[PubMed](#)]
11. Chipps BE, Zeiger RS, Borish L, Wenzel SE, Yegin A, et al... (2012) Key findings and clinical implications from The Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) study. *J Allergy Clin Immunol* 130: 332–342 e310. [[PMC free article](#)] [[PubMed](#)]
12. Lumia M, Luukkainen P, Kaila M, Tapanainen H, Takkinen HM, et al. (2012) Maternal dietary fat and fatty acid intake during lactation and the risk of asthma in the offspring. *Acta Paediatr* 101: e337–343. [[PubMed](#)] [[Google Scholar](#)]
13. Nwaru BI, Takkinen HM, Niemela O, Kaila M, Erkkola M, et al... (2012) Timing of infant feeding in relation to childhood asthma and allergic diseases. *J Allergy Clin Immunol*. [[PubMed](#)]
14. Troisi RJ, Willett WC, Weiss ST, Trichopoulos D, Rosner B, et al. (1995) A prospective study of diet and adult-onset asthma. *Am J Respir Crit Care Med* 151: 1401–1408. [[PubMed](#)] [[Google Scholar](#)]
15. Kull I, Bergstrom A, Lilja G, Pershagen G, Wickman M (2006) Fish consumption during the first year of life and development of allergic diseases during childhood. *Allergy* 61: 1009–1015. [[PubMed](#)] [[Google Scholar](#)]
16. Oien T, Storro O, Johnsen R (2010) Do early intake of fish and fish oil protect against eczema and doctor-diagnosed asthma at 2 years of age? A cohort study. *J Epidemiol Community Health* 64: 124–129. [[PubMed](#)] [[Google Scholar](#)]
17. Nafstad P, Nystad W, Magnus P, Jaakkola JJ (2003) Asthma and allergic rhinitis at 4 years of age in relation to fish consumption in infancy. *J Asthma* 40: 343–348. [[PubMed](#)] [[Google Scholar](#)]
18. Kunitsugu I, Okuda M, Murakami N, Hashimoto M, Yamanishi R, et al... (2011) Self-reported seafood intake and atopy in Japanese school-aged children. *Pediatr Int*. [[PubMed](#)]
19. Takemura Y, Sakurai Y, Honjo S, Tokimatsu A, Gibo M, et al. (2002) The relationship between fish intake and the prevalence of asthma: the Tokorozawa childhood asthma and pollinosis study. *Prev Med* 34: 221–225. [[PubMed](#)] [[Google Scholar](#)]

20. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, et al. (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 283: 2008–2012. [[PubMed](#)] [[Google Scholar](#)]
21. Dunstan JA, Mori TA, Barden A, Beilin LJ, Taylor AL, et al. (2003) Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: a randomized, controlled trial. *J Allergy Clin Immunol* 112: 1178–1184. [[PubMed](#)] [[Google Scholar](#)]
22. Lauritzen L, Kjaer TM, Fruekilde MB, Michaelsen KF, Frokiaer H (2005) Fish oil supplementation of lactating mothers affects cytokine production in 2 1/2-year-old children. *Lipids* 40: 669–676. [[PubMed](#)] [[Google Scholar](#)]
23. Lowe AJ, Thien FC, Stoney RM, Bennett CM, Hosking CS, et al. (2008) Associations between fatty acids in colostrum and breast milk and risk of allergic disease. *Clin Exp Allergy* 38: 1745–1751. [[PubMed](#)] [[Google Scholar](#)]
24. Marks GB, Mahrshahi S, Kemp AS, Tovey ER, Webb K, et al. (2006) Prevention of asthma during the first 5 years of life: a randomized controlled trial. *J Allergy Clin Immunol* 118: 53–61. [[PubMed](#)] [[Google Scholar](#)]
25. Nagel G, Linseisen J (2005) Dietary intake of fatty acids, antioxidants and selected food groups and asthma in adults'. *Eur J Clin Nutr* 59: 8–15. [[PubMed](#)] [[Google Scholar](#)]
26. Notenboom ML, Mommers M, Jansen EH, Penders J, Thijs C (2011) Maternal fatty acid status in pregnancy and childhood atopic manifestations: KOALA Birth Cohort Study. *Clin Exp Allergy* 41: 407–416. [[PubMed](#)] [[Google Scholar](#)]
27. Olsen SF, Osterdal ML, Salvig JD, Mortensen LM, Rytter D, et al. (2008) Fish oil intake compared with olive oil intake in late pregnancy and asthma in the offspring: 16 y of registry-based follow-up from a randomized controlled trial. *Am J Clin Nutr* 88: 167–175. [[PubMed](#)] [[Google Scholar](#)]
28. Wijga AH, van Houwelingen AC, Kerkhof M, Tabak C, de Jongste JC, et al. (2006) Breast milk fatty acids and allergic disease in preschool children: the Prevention and Incidence of Asthma and Mite Allergy birth cohort study. *J Allergy Clin Immunol* 117: 440–447. [[PubMed](#)] [[Google Scholar](#)]
29. Willers SM, Wijga AH, Brunekreef B, Kerkhof M, Gerritsen J, et al. (2008) Maternal food consumption during pregnancy and the longitudinal development of childhood asthma. *Am J Respir Crit Care Med* 178: 124–131. [[PubMed](#)] [[Google Scholar](#)]
30. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA (2011) Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. *BMJ* 342: d671. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
31. Wu Y, Li J, Wu J, Morgan P, Xu X, et al. (2012) Discovery of potent and selective matrix metalloprotease 12 inhibitors for the potential treatment of chronic obstructive pulmonary disease (COPD). *Bioorg Med Chem Lett* 22: 138–143. [[PubMed](#)] [[Google Scholar](#)]
32. Calder PC (2006) n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases. *Am J Clin Nutr* 83: 1505S–1519S. [[PubMed](#)] [[Google Scholar](#)]
33. Calder PC (2010) Omega-3 fatty acids and inflammatory processes. *Nutrients* 2: 355–374. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
34. Kiefte-de Jong JC, de Vries JH, Franco OH, Jaddoe VW, Hofman A, et al. (2012) Fish Consumption in Infancy and Asthma-like Symptoms at Preschool Age. *Pediatrics* 130: 1060–1068. [[PubMed](#)] [[Google Scholar](#)]
35. Barker DJ (2012) Human growth and chronic disease: a memorial to Jim Tanner. *Ann Hum Biol* 39: 335–341. [[PubMed](#)] [[Google Scholar](#)]

36. Kim JL, Elfman L, Mi Y, Johansson M, Smedje G, et al. (2005) Current asthma and respiratory symptoms among pupils in relation to dietary factors and allergens in the school environment. *Indoor Air* 15: 170–182. [[PubMed](#)] [[Google Scholar](#)]
37. Tabak C, Wijga AH, de Meer G, Janssen NA, Brunekreef B, et al. (2006) Diet and asthma in Dutch school children (ISAAC-2). *Thorax* 61: 1048–1053. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
38. Woods RK, Thien FC, Abramson MJ (2002) Dietary marine fatty acids (fish oil) for asthma in adults and children. *Cochrane Database Syst Rev*: CD001283. [[PubMed](#)]
39. Anandan C, Nurmatov U, Sheikh A (2009) Omega 3 and 6 oils for primary prevention of allergic disease: systematic review and meta-analysis. *Allergy* 64: 840–848. [[PubMed](#)] [[Google Scholar](#)]
40. He K (2009) Fish, long-chain omega-3 polyunsaturated fatty acids and prevention of cardiovascular disease—eat fish or take fish oil supplement? *Prog Cardiovasc Dis* 52: 95–114. [[PubMed](#)] [[Google Scholar](#)]

---

Articles from PLoS ONE are provided here courtesy of **Public Library of Science**