

Essential fatty acids, asthma and allergies in children

A summary of epidemiological evidence

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IEM Symposium during FENS 2011
Madrid, October 27 2011

Content

- Motivation to study fat intake and asthma/allergies
- Fats & allergies: potential mechanisms
- Observational studies
Interventional studies
Fish oil to treat asthma
- The potential role of FADS genes
- Summary & key messages

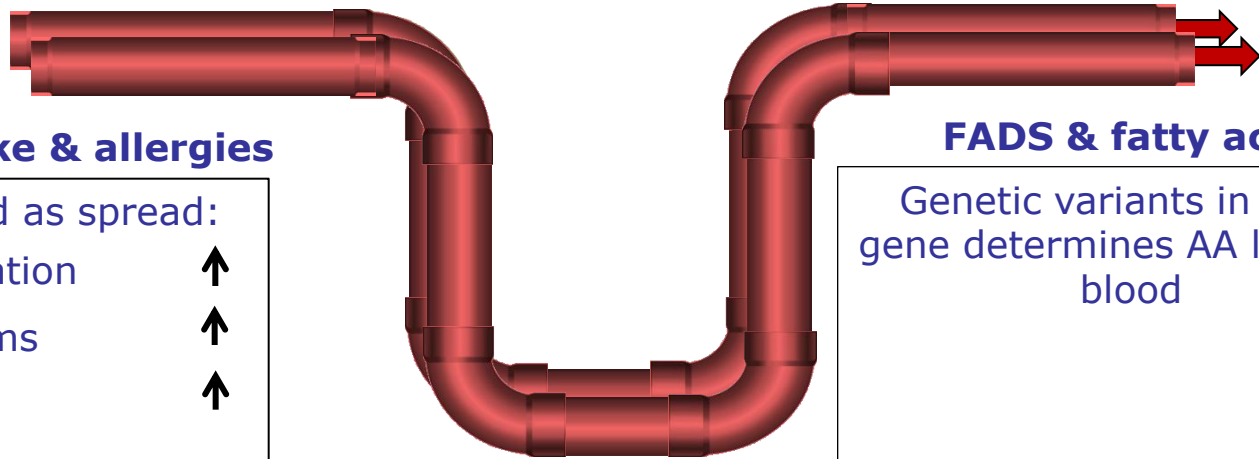
Our Motivation

- **Von Mutius et al. 1998:** 2334 children, 9-11 years, Leipzig, repeated examinations in 1991 and 1996, increased prevalence of hay fever and allergic sensitization
Margarine intake → hay fever ↑
- **Heinrich et al. 2001: ecological study adults 20 – 44 years**
MUFA → atopic sensitization ↑
PUFA → atopic sensitization ↑
- **Bolte et al. 2001:** 2348 children, 5-14 years
margarine used as spread → allergic sensitisation (boys) ↑
→ rhinitis symptoms (boys) ↑
- **Dunder et al. 2001:** 308 children, 3-18 years
margarine consumption → atopic diseases ↑
- **Farchi et al. 2003:** 4104 children, 6-7 years
bread with margarine → wheeze ↑
- **Bolte et al. 2005:** 7127 adults, 18-79 years
margarine consumption → asthma ↑

Fatty Acids in Butter and Margarine

Fatty acids g / 100g	Butter	Margarine
Saturated fatty acids	54.8	29.9
Monounsaturated fatty acids	22.8	29.7
C18:1 trans fatty acids	2.8	2.8
Polyunsaturated fatty acids	2.6	20.5
Linoleic acid	1.2	17.6
Linolenic acid	0.4	2.6
Arachidonic acid	0.1	-

The Diet-Allergy Pipeline



Margarine intake & allergies

Margarine used as spread:
Allergic sensitization ↑
Rhinitis symptoms ↑
Asthma ↑

Bolte et al 2006
Sausenthaler et al 2001, 2006
Bolte et al 2000 ARJCCM

FADS & fatty acid

Genetic variants in FADS
gene determines AA levels in
blood

Schäffer et al HMG 2006
Rzehak et al 2009
Rzehak et al Plos one 2010

Intake of FA & allergies

Intake of MUFA, palmetoleic
acid and oleic acid
→ allergic rhinitis ↑

Trak-Fellermeier et al ERJ 2004

Fatty acids & allergies

Oleic acid in blood
→ allergic sensitization ↑

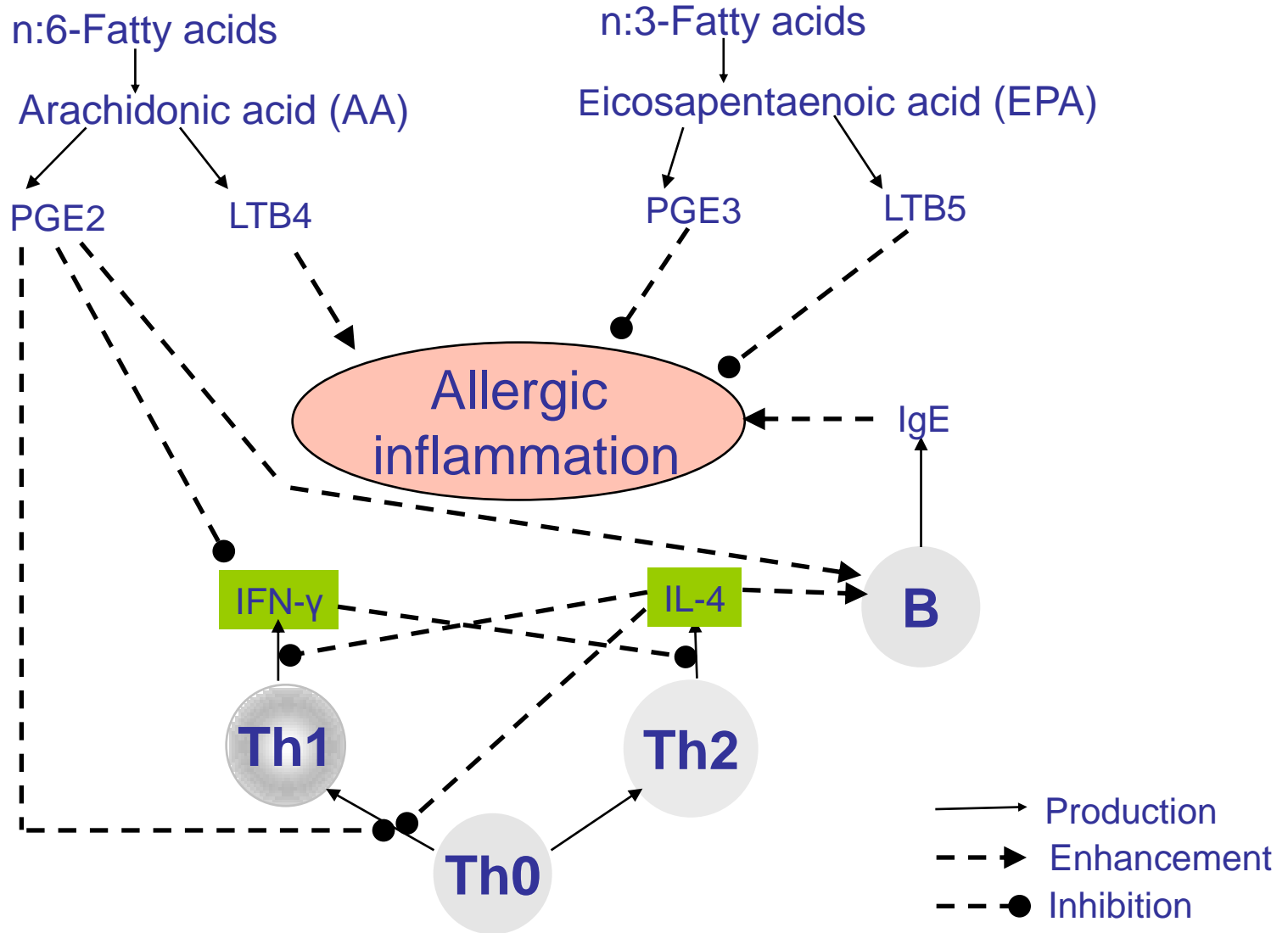
Kompauer et al BJN 2005

FADS x fat intake x allergies

Fat intake and asthma
is modified by FADS
gene variants

Standl et al CEA 2011

Fatty acids and allergy



Atopy Risk in Infants and Children in Relation to Early Exposure to Fish, Oily Fish, or Long-Chain Omega-3 Fatty Acids: A Systematic Review

Lefkothea-Stella Kremmyda · Maria Vlachava · Paul S. Noakes · Norma D. Diaper · Elizabeth A. Miles · Philip C. Calder

- Hypothesis: Fish and fish oil are sources of LC-n-3 PUFA; these fatty acids oppose the action of n-6 PUFA. Thus, fish oil might protect against atopy
- Fish oil supplementation during pregnancy and lactation leads to higher n-3 PUFA status in infants and children to immunological changes in CB (clinical relevance and persistence is not clear)
- Epidemiological studies

5 Studies on fish intake during pregnancy and atopic outcomes in offsprings: consistent protective associations

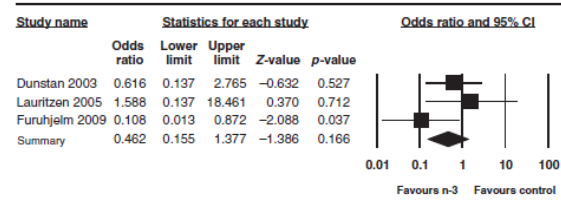
1 Study on fish intake during lactation: no effects

14 studies on fish intake during infancy and childhood on atopic outcomes: 9 positive

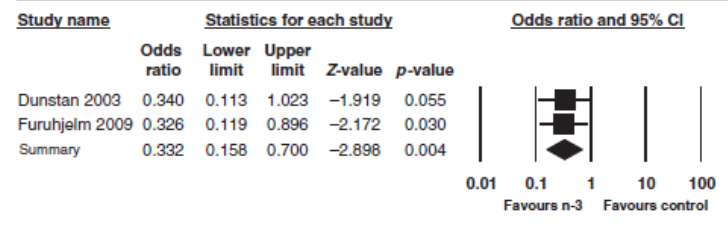
The effect of perinatal omega-3 fatty acid supplementation on inflammatory markers and allergic diseases: a systematic review*

CM Klemens,^a DR Berman,^b EL Mozurkewich^b

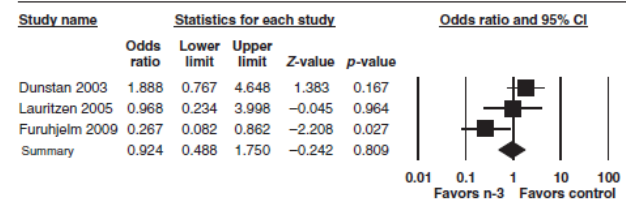
- RCT's with n-3 PUFA supplementation during pregnancy and/ or lactation
- 5 RCT's:
Dunstan et al 2003: 83/98 Fish oil vs. Olive oil
Lauritzen et al 2005: 72/147 Fish oil vs. Olive oil
Krauss-Etschmann et al 2008 141/157 Fish oil vs. ?
Olsen et al 2008 399/402 marine n-3 PUFA vs. Olive oil
Furuhjelm et al 2009 117/145 EPA + DHA vs. Soy oil
- Miles et al AJCN 2011 RCT with salmon increase DHA and EPA in CB
- Conclusion of authors: n-3 PUFA supplementation during pregnancy decreases childhood asthma and responses to SPT



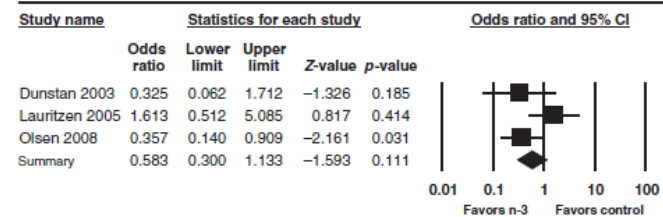
Food allergy



SPT+



Eczema



Asthma

More studies...

and more confusion

- The Ryukyus Child Health study
23,388 schoolchildren (6-15 yrs.) in Okinawa
ISAAC & Dietary history
- Consumption of n-3 and n-6 PUFA was positive associated with eczema
- AA intake inversely related to eczema and rhinoconjunctivitis
- The KOALA Birth Cohort
1275 children with follow up to 6-7 yrs. in NL
ISAAC & fatty acids in PL of maternal blood samples
- Neither n-3 PUFA nor n-6 PUFA in PL were associated with eczema and asthma
- Increasing AA in PL were associated with decreasing risk of eczema during first 7 months of life

Miyake et al. *BMC Public Health* 2011, 11:358
<http://www.biomedcentral.com/1471-2458/11/358>



RESEARCH ARTICLE

Open Access

Polyunsaturated fatty acid intake and prevalence of eczema and rhinoconjunctivitis in Japanese children: The Ryukyus Child Health Study

Yoshihiro Miyake^{1*}, Keiko Tanaka¹, Satoshi Sasaki² and Masashi Arakawa³

doi: 10.1111/j.1365-2222.2010.03672.x

Clinical & Experimental Allergy 41, 407–416

ORIGINAL ARTICLE Epidemiology of Allergic Disease

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Maternal fatty acid status in pregnancy and childhood atopic manifestations: KOALA Birth Cohort Study

M. L. Notenboom¹, M. Mommers¹, E. H. J. M. Jansen², J. Penders^{1,3} and C. Thijs¹

Fatty acids for treatment of asthma

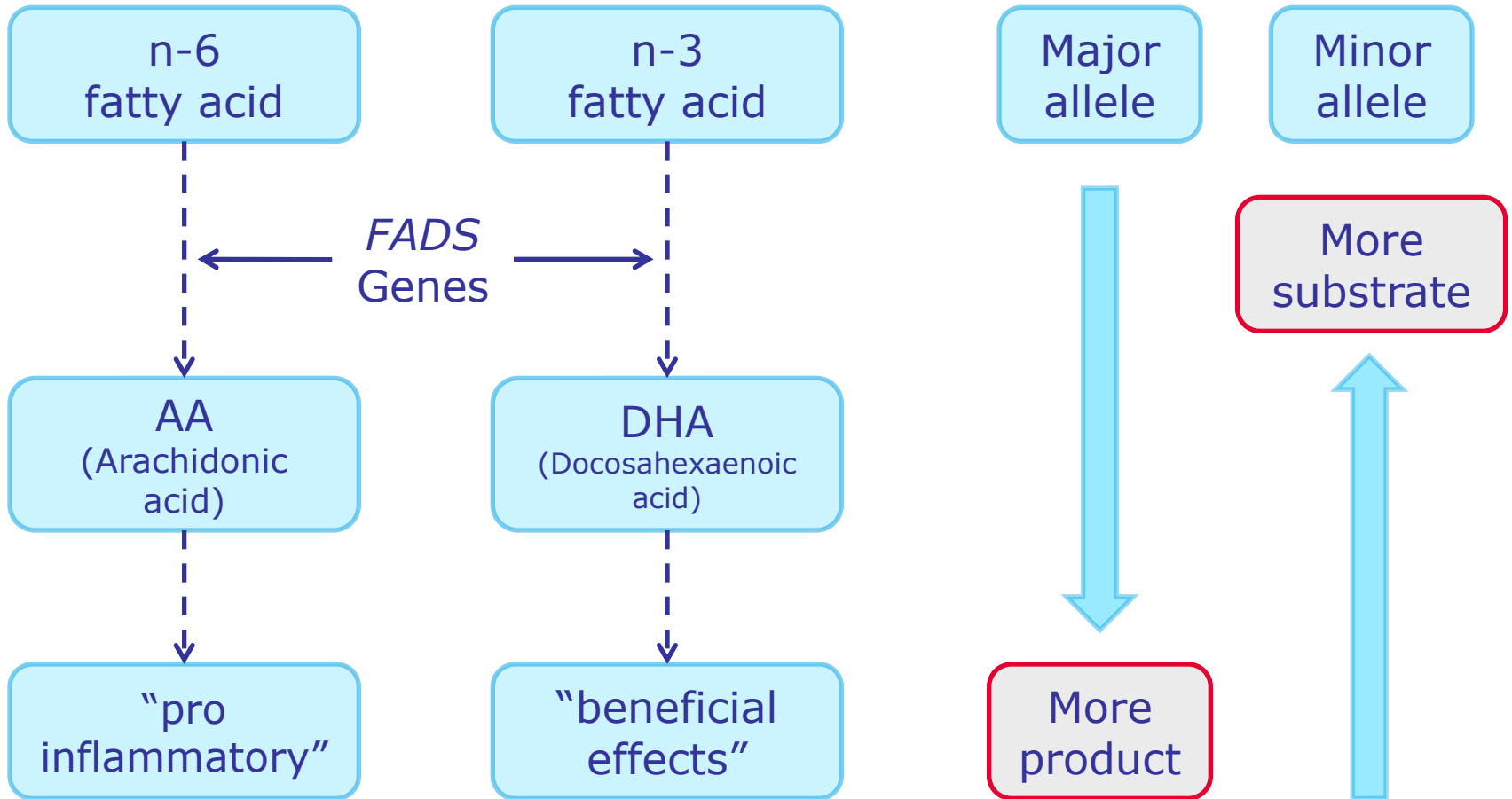
- Cochrane review (Thien et al 2010)

fish oil supplementation for at least 4 weeks
5 trials, 2 in children
- Conclusion: Fish oil supplementation cannot be recommended as a treatment method for asthma
- ESPGHAN Committee on Nutrition (ESPGHAN 2011)
- Conclusion: Shared the view by Cochrane review

What can genes tell us?

- Several candidate gene approaches and also genomwide scans had consistently shown: fatty acids composition in blood is under genetic control (reviews by Koletzko et al 2011, Lattka et al 2011)
- Proof of principle, if there is an effect modifying effect of fatty acid intake and atopic outcomes.

Fatty acid metabolism

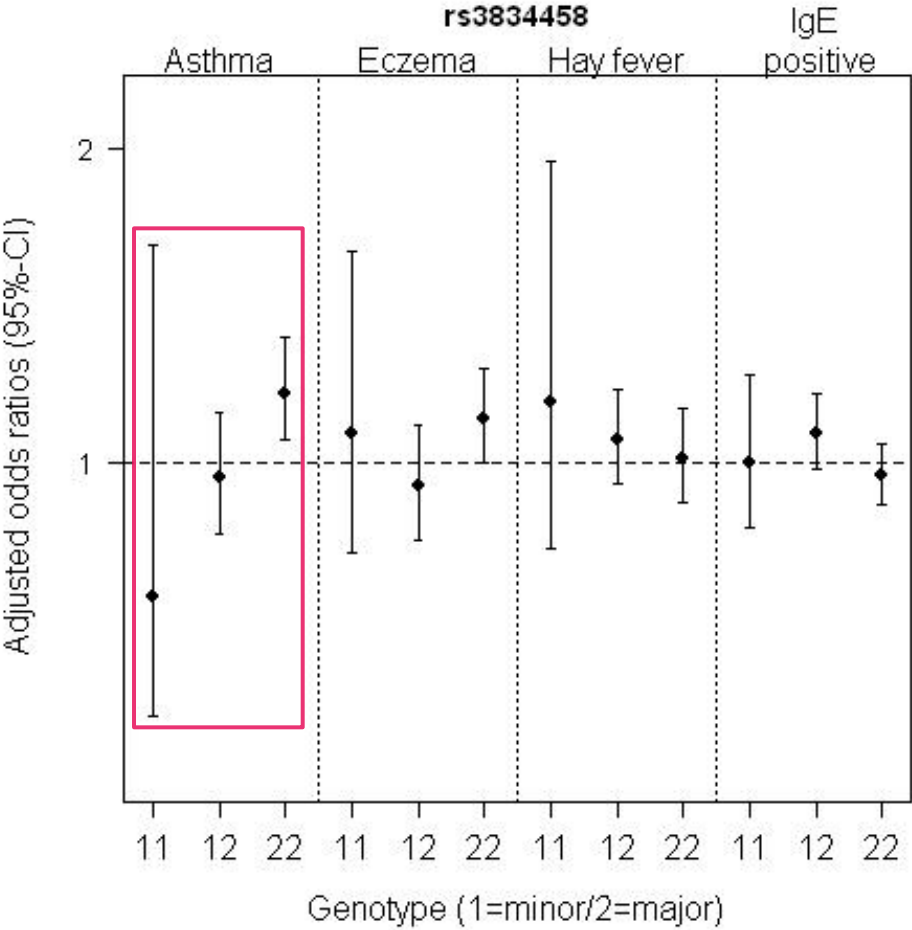


Association between *FADS1* *FADS2* Gene Cluster, Fatty Acid Intake and Atopy

- N=2000 children, 9 to 12 years of age from the GINIplus and LISAplus studies
- Fatty acid intake derived from FFQ
 - Total n-3/total n-6 ratio
 - Daily margarine intake in gram
- Outcome variables:
 - Doctor diagnosis of asthma, eczema, hay fever at age 6, 7, 8 or 9 years
 - Positive RAST screening test results for inhalant and food allergens

Standl et al. CEA 2011

Association between Margarine Intake and Atopy stratified by genotype (rs3834458)



Standl et al. CEA 2011

Association between *FADS1 FADS2* Gene Cluster, Fatty Acid Intake and Atopy

- Margarine intake is associated with an increased risk for asthma in homozygous major allele carriers (after adjustment for multiple testing)
- The association between dietary intake of fatty acids and allergic diseases might be modulated by *FADS* gene variants in children.

Standl et al. CEA 2011

Key Messages on Essential Fatty Acids and Allergies to the Audience

Fish oil, n-3 fatty acids and onset of allergies

- Observational studies: inconsistent results, although the majority of the studies (nine of 14) showed a protective effect (Kremmyda et al. 2011).
- Randomized controlled trials: Larger randomized trials are needed to confirm the protective effect before any clinical recommendations can be made (Klemens et al. 2011).

Fish oil, n-3 fatty acids and symptoms in asthmatics

- Cochrane review (Thien et al. 2010): Five studies examined the effect of fish oil supplementation in asthmatics. Overall, this review concluded that fish oil supplementation cannot be recommended as a method of treating asthma.
- “there is something going on here of great importance” (Olsen SF commentary BJOG, S. 924 f). However, neither the results from observational nor interventional trials are consistent.

No systematic review published so far has concluded that the data is sufficient to derive specific fatty acid intake recommendations for the prevention or treatment of allergies.

Key Messages to the General Public

- There is a biologically plausible mechanism for a potential causal relationship between increased n-3 fatty acids intake and beneficial effects on immune parameters, including atopic manifestations.
Recent genetic study findings support the notion of a causal effect of fatty acid intake and asthma.
- Neither the results from observational nor interventional trials are consistent.
- No systematic review published so far has concluded that the data is sufficient to derive specific fatty acid intake recommendations for the prevention or treatment of allergies.