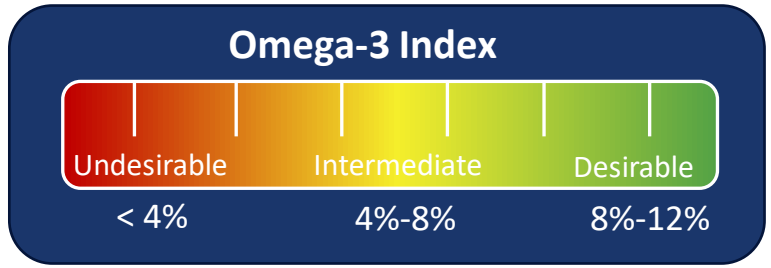
Effect of Omega-3 Long Chain Polyunsaturated Fatty Acids (n-3 LCPUFA) Supplementation on Cognition in Children and Adolescents: A Systematic Literature Review with a Focus on n-3 LCPUFA Blood Values and Dose of DHA and EPA

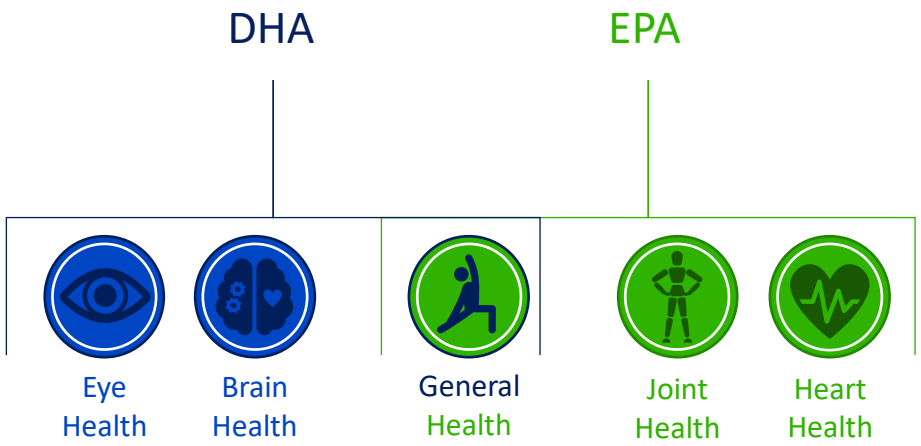
van der Wurff ISM, Meyer BJ, de Groot RHM. Effect of Omega-3 Long Chain Polyunsaturated Fatty Acids (n-3 LCPUFA) Supplementation on Cognition in Children and Adolescents: A Systematic Literature Review with a Focus on n-3 LCPUFA Blood Values and Dose of DHA and EPA. Nutrients. 2020 Oct 12;12(10):3115. doi: 10.3390/nu12103115. PMID: 33053843; PMCID: PMC7599612.

Juice Plus+
Science Institute
Advancing plant-based nutrition

BACKGROUND

- Long-chain fatty acids (LCPUFA) are key components of the brain and therefore heavily involved in several brain processes.
- Various studies have examined the effect of omega-3 LCPUFA, like DHA and EPA on cognition, cognitive function, depression and other psychological disorders.
- The O3I (omega-3 Index) is EPA+DHA expressed as a weight % of total fatty acids (FAs) in erythrocytes.
- Results from studies show that an O3I of 8% or more is protective against fatal coronary heart disease.
- It has been suggested that such a protective range could also exist for mental health disease





Juice Plus+ Science Institute
Advancing plant-based nutrition

AIM

The aim of this review was to investigate:

What Omega-3 Index level is necessary to achieve, in order to improve cognition

Whether a minimum daily dose of DHA/EPA plays a role in the effect of n-3 LCPUFA supplementation on cognition in children and adolescents (4-25 years)

Juice Plus+
Science Institute
Advancing plant-based nutrition

METHODS

Systematic Literature Review

- Web of Science and PubMed were searched (up to 3rd July 2019)
- Search terms:
  - 'LCPUFA', 'EPA', 'DHA', 'Omega-3', in combination with 'cogniti*, and 'child*, 'adolescen*', 'toddler'
- No date restrictions

Since the included studies did not measure O3I directly but many of them reported fatty acid data, recalculation of the O3I was conducted with help of the recently published "O3I equivalence formulae*".

Studies included if:

- Average age of participants: between 4-25 years old
- Supplementation with DHA and/or EPA
- Included at least one measurement of cognition
- Randomized placebo-controlled trial
- Cross over study with a wash out period of at least 4 months
- Minimum of 10 participants per treatment arm
- Published in English

Juice Plus+ Science Institute
Advancing plant-based nutrition

*Stark KD, Aristizabal Henao JJ, Metherel AH, Pilote L. Translating plasma and whole blood fatty acid compositional data into the sum of eicosapentaenoic and docosahexaenoic acid in erythrocytes. Prostaglandins Leukot Essent Fatty Acids. 2016 Jan;104:1-10. doi: 10.1016/j.plefa.2015.11.002. Epub 2015 Nov 28. PMID: 26802936.

MAIN RESULTS

This review included 33 placebo controlled randomized trials

- **Cohort**
  - 21 of 33 trials focused on typically developing children and adolescents
  - 12 of 33 trials focused on children and adolescents with a disorder/disease*
- **Age**
  - 24 trials included children (< 12 years)
  - 8 trials included late adolescents (20-25 years)
  - 1 trial included early/mid adolescents (12-20 years)
- **Studies Duration**
  - 4 to 52 weeks

*11 studies on attention deficit hyperactivity disorder (ADHD); 1 study on phenylketonuria (PKU).

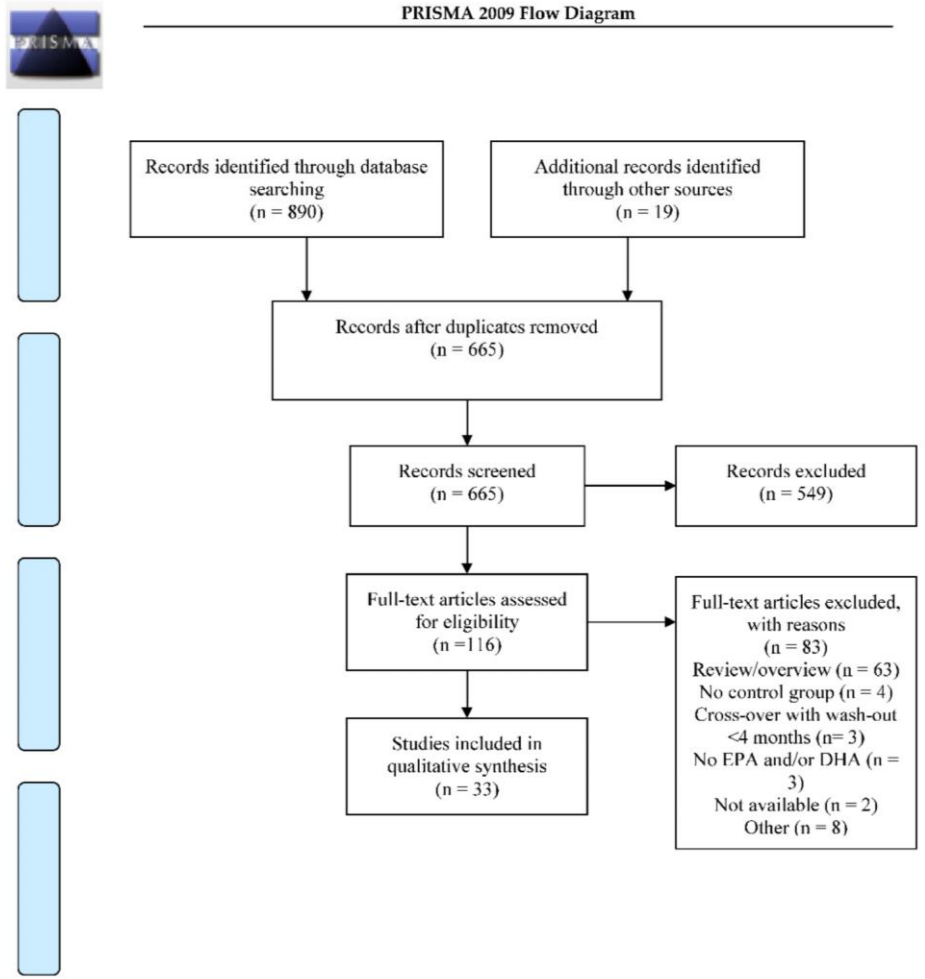


Figure 1. Flow-chart of the search strategy, adapted from [26]. EPA = eicosapentaenoic acid, DHA = docosahexaenoic acid.

MAIN RESULTS –OMEGA-3 INDEX EQUIVALENCE

20 of 33 included trials reported blood fatty acid values →
Recalculation of O3I was possible for 9 out of these 20 studies

- Increase of the O3I in the active groups varied between 0.87 % and 4.75 %
- 4 of 9 studies showed positive significant effect of supplementation on at least one cognitive measure (baseline levels of O3I in these 4 studies ranging from 3.31 % to 4.13 %)
  - In 3 of these 4 studies the post supplementation O3I increased to over 6%
  - The remaining study has shown a small increase (0.87 %) in O3I from 3.31 % at baseline to 4.21 % post intervention in the active group
- 2 studies had an O3I-equivalence > 6% post supplementation and no positive effect on cognition

Juice Plus+ Science Institute
Advancing plant-based nutrition

MAIN RESULTS – SUPPLEMENTATION DOSE

Supplementation dose varied across the included trials:
from 16.5 mg to 3600 mg DHA/day and from 0 mg to 1740 mg EPA/day

- Typically developing children/adolescents:
  - Of 15 studies supplementing with ≥ 450 mg DHA + EPA /day, 8 (53%) showed a positive effect on cognition
  - 2 of 8 studies with a supplementation < 450mg DHA+EPA /day, showed a significant effect on cognition (one in favor of the placebo group)
  - Overall, there is evidence that dosages above 450 mg DHA + EPA /day led to improved cognition in typically developing children and adolescents
- Children/adolescents with a disease/disorder
  - 6 out of 12 studies showed a positive effect of DHA+EPA supplementation on cognition
  - Authors were not able to show a clear cut-off daily dose of DHA+EPA above which a positive effect on cognition could be shown

Juice Plus+ Science Institute
Advancing plant-based nutrition

CONCLUSION

"An increase in the O3I > 6% and daily supplementation of ≥ 450 mg DHA + EPA makes it more likely to show positive effects of supplementation on cognition in children and adolescents. However, more research is needed where the O3I is measured, to be able to determine a more precise O3I target range for the positive effects on cognitive functioning."

Juice Plus+
Science Institute
Advancing plant-based nutrition

Article avalable at: https://pubmed.ncbi.nlm.nih.gov/33053843/