WHAT IS THE RELATIONSHIP BETWEEN OMEGA-3 FATTY ACID SUPPLEMENTS CONSUMED DURING PREGNANCY AND LACTATION AND DEVELOPMENTAL MILESTONES, INCLUDING NEUROCOGNITIVE DEVELOPMENT?: SYSTEMATIC REVIEW PROTOCOL

This document describes the protocol for a systematic review to answer the following question: What is the relationship between omega-3 fatty acids from supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?

The 2020 Dietary Guidelines Advisory Committee, Pregnancy and Lactation Subcommittee, answered this question by conducting a systematic review with support from the USDA’s Nutrition Evidence Systematic Review (NESR).

NESR methodology for answering a systematic review question involves:
- searching for and selecting articles,
- extracting data and assessing the risk of bias of results from each included article,
- synthesizing the evidence,
- developing a conclusion statement,
- grading the evidence underlying the conclusion statement, and
- recommending future research.

More information about NESR’s systematic review methodology is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews.

This protocol is up-to-date as of: 4/20/2020.

This document reflects the protocol as it was implemented. It now includes the electronic databases and search terms, and literature search and screening results, including a list of included articles, and a list of excluded articles with the rationale for exclusion.

This document includes details about the methodology as it will be applied to the systematic review:

- Analytic framework .................................................................2
- Literature search and screening plan ........................................3
- Inclusion and exclusion criteria .................................................3
- Electronic databases and search terms ....................................5
- Literature search and screening results ..................................10
- Included articles .......................................................................11
- Excluded articles .....................................................................14
**ANALYTIC FRAMEWORK**

The analytic framework (Figure 1) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The inclusion and exclusion criteria that follow provide additional information about how parts of the analytic framework were defined and operationalized for the review.

**Figure 1: Analytic framework**

<table>
<thead>
<tr>
<th>Intervention/exposure</th>
<th>Comparator</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to, including intake of <strong>Omega-3 fatty acids</strong> from:</td>
<td>Different level of exposure to, including intake of <strong>Omega-3 fatty acids</strong> from:</td>
<td>Developmental domains, examined via milestone achievement and/or scales/indices, including:</td>
</tr>
<tr>
<td>• Dietary supplements (including multiple-nutrient supplements)</td>
<td>• Dietary supplements (including multiple-nutrient supplements)</td>
<td>• Cognitive.</td>
</tr>
<tr>
<td><strong>Population:</strong> Women before and during pregnancy and/or during lactation, healthy and/or at risk for chronic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Key Confounders:</strong> Age, Race/ethnicity, Socioeconomic status, Fish and other seafood consumption, Anthropometry (pre-pregnancy BMI and gestational weight gain (during pregnancy) or Obesity status (before pregnancy and lactation)), Smoking, Parity, Child sex, Gestational age, Human milk feeding practices (intensity, duration). <strong>Other factors to be considered:</strong> Maternal substance use (alcohol, drug use), Family history/diagnosis of neurocognitive disorders, complementary feeding.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Key definitions**

- **Dietary Supplement** - a product (other than tobacco) that is intended to supplement the diet; contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and other substances) or their constituents; is intended to be taken by mouth as a pill, capsule, tablet, or liquid; and is labeled on the front panel as being a dietary supplement (ODS, Dietary Supplement Health and Education Act, 1994).
- **“Before pregnancy”** - includes up to 6 months before pregnancy.

**Legend**

- The relationship of interest in the systematic review
- Factors that may impact the relationship of interest in the systematic review
Question: What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?

### Inclusion and exclusion criteria
This table provides the inclusion and exclusion criteria for the systematic review. The inclusion and exclusion criteria are a set of characteristics used to determine which articles identified in the literature search were included in or excluded from the systematic review.

#### Table 1. Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
</table>
| Study design | • Randomized controlled trials  
• Non-randomized controlled trials including quasi-experimental and controlled before-and-after studies  
• Prospective cohort studies  
• Retrospective cohort studies  
• Nested case-control studies | • Uncontrolled trials  
• Case-control studies  
• Uncontrolled before-and-after studies  
• Cross-sectional studies  
• Narrative reviews  
• Systematic reviews  
• Meta-analyses |
| Intervention/exposure | • Exposure to, including intake of, Omega-3 fatty acids from:  
  o Dietary supplements (including multiple-nutrient supplements) | • Exposure to multiple-micronutrient supplements in which nutrients other than the nutrient of interest vary |
| Comparator | • Different levels of exposure to, including intake of, Omega-3 fatty acids from:  
  o Dietary supplements (including multiple-nutrient supplements) | • No comparator  
• Exposure to multiple-micronutrient supplements in which nutrients other than the nutrient of interest vary |
| Outcome: Developmental milestones, including neurocognitive health | • Developmental domains, examined via milestone achievement and/or scales/indices, including:  
  o Cognitive,  
  o Language/communication,  
  o Movement/physical,  
  o Social-emotional  
• Academic performance  
• Attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD)  
• Anxiety  
• Depression  
• Autism spectrum disorder (ASD) | • N/A |
<table>
<thead>
<tr>
<th>Category</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date of publication</strong></td>
<td>• January 1980 – February 2020</td>
<td>• Articles published prior to January 1980 or after February 2020</td>
</tr>
<tr>
<td><strong>Publication status</strong></td>
<td>• Articles that have been peer-reviewed</td>
<td>• Articles that have not been peer-reviewed and are not published in peer-reviewed journals, including unpublished data, manuscripts, reports, abstracts, and conference proceedings</td>
</tr>
<tr>
<td><strong>Language of publication</strong></td>
<td>• Articles published in English</td>
<td>• Articles published in languages other than English</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>• Studies conducted in countries ranked as high or very high human development</td>
<td>• Studies conducted in countries ranked as medium or lower human development</td>
</tr>
<tr>
<td><strong>Study participants</strong></td>
<td>• Human participants</td>
<td>• Non-human participants (e.g., animal or in-vitro models)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Studies that exclusively enroll women who became pregnant using Assisted Reproductive Technologies</td>
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<tr>
<td></td>
<td></td>
<td>• Studies that exclusively enroll women with multiple gestation pregnancies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Studies that enroll both singleton and multiple pregnancies and do not account for singleton and multiple gestation in the design or analyses and only present aggregate findings</td>
</tr>
<tr>
<td><strong>Life stage of study participants - intervention or exposure</strong></td>
<td>• Women up to 6 months before pregnancy</td>
<td>• N/A</td>
</tr>
<tr>
<td></td>
<td>• Women during pregnancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Women during lactation</td>
<td></td>
</tr>
<tr>
<td><strong>Life stage of study participants - outcomes</strong></td>
<td>• Infants and toddlers (birth – 24 months)</td>
<td>• Adults (19 – 64 years)</td>
</tr>
<tr>
<td></td>
<td>• Children and adolescents (2 – 18 years)</td>
<td>• Older adults (65 years and older)</td>
</tr>
<tr>
<td><strong>Health status of study participants</strong></td>
<td>• Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity</td>
<td>• Studies that exclusively enroll participants diagnosed with a disease, or hospitalized with an illness or injury. (For this criterion,</td>
</tr>
</tbody>
</table>

Question: What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?
<table>
<thead>
<tr>
<th>Category</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Studies that enroll <strong>some</strong> participants diagnosed with a disease or with the health outcome of interest:</td>
<td>studies that exclusively enroll participants with obesity will not be excluded.)</td>
</tr>
<tr>
<td></td>
<td>o Gestational diabetes</td>
<td>• Studies that <strong>exclusively</strong> enroll participants with the outcome of interest (gestational diabetes, hypertensive disorders of pregnancy) (i.e., studies that aim to treat participants who have already been diagnosed with the outcome of interest)</td>
</tr>
<tr>
<td></td>
<td>o Hypertensive disorders of pregnancy</td>
<td>• Studies that <strong>exclusively</strong> enroll infants born preterm (gestational age &lt;37 weeks and 0/7 days gestational age) infants with low birth weight (&lt;2500g), and/or infants born small for gestational age</td>
</tr>
<tr>
<td></td>
<td>o Neurocognitive disorders (ADD, ADHD, anxiety, depression, or ASD)</td>
<td>• Studies that <strong>exclusively</strong> enroll participants with the outcome of interest (gestational diabetes, hypertensive disorders of pregnancy) (i.e., studies that aim to treat participants who have already been diagnosed with the outcome of interest)</td>
</tr>
<tr>
<td></td>
<td>o Studies that enroll some participants who are deficient in omega-3 fatty acids</td>
<td>• Studies that exclusively enroll infants born preterm (gestational age &lt;37 weeks and 0/7 days gestational age) infants with low birth weight (&lt;2500g), and/or infants born small for gestational age</td>
</tr>
<tr>
<td></td>
<td>• Studies that enroll <strong>some</strong> mothers with infants who are born preterm (&lt;37 weeks and 0/7 days gestational age)</td>
<td>• Studies that <strong>exclusively</strong> enroll participants with the outcome of interest (gestational diabetes, hypertensive disorders of pregnancy) (i.e., studies that aim to treat participants who have already been diagnosed with the outcome of interest)</td>
</tr>
<tr>
<td></td>
<td>• Studies that <strong>exclusively</strong> enroll or <strong>enroll some</strong> mothers diagnosed with the outcome of interest that is to be examined in the infant/child (developmental milestones, including neurocognitive development)</td>
<td>• Studies that <strong>exclusively</strong> enroll participants with the outcome of interest (gestational diabetes, hypertensive disorders of pregnancy) (i.e., studies that aim to treat participants who have already been diagnosed with the outcome of interest)</td>
</tr>
</tbody>
</table>

\[1\] In order to determine the inclusion exclusion criteria for country, the Human Development classification was used. This classification is based on the Human Development Index (HDI) ranking from the year the study intervention occurred or data were collected (UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: http://hdr.undp.org/en/data). If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1980, and then from 1990 to present. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. If a study was conducted in 2018 or 2019, the most current HDI classification was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank was used instead (The World Bank. World Bank country and lending groups. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-country-and-lending-groups)
Electronic databases and search terms

**PubMed (U.S. National Library of Medicine)**

- **Date(s) Searched:** Feb 5, 2020
- **Search Strategy:**

**Omega-3**


**Pregnancy and Lactation**


**Neurocognitive**


**NOT**("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])))


**Question:** What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?

Filters: Publication date from 1980/01/01 to 2020/02/05; English

**Embase (Elsevier)**
- Date(s) Searched: Feb 5, 2020
- Search Strategy:

**Omega-3**
'omega 3 fatty acid'/exp OR 'linolenic acid*':ab,ti OR 'omega-3':ab,ti OR 'n-3 fatty acid*':ab,ti OR pufa*:ab,ti OR 'alpha-linolenic acid*':ab,ti OR 'eicosapentaenoic acid*':ab,ti OR 'docosahexaenoic acid*':ab,ti OR monounsatur*:ti,ab OR mono-unsat*:ti,ab OR polyunsat*:ti,ab OR 'fish oils'/exp OR fish oil*':ti,ab OR 'plant oils'/exp OR 'plant oil*':ti,ab OR 'vegetable oil*':ti,ab OR 'n-3 oil*':ti,ab OR 'n3 oil*':ti,ab OR 'n3 fatty acid*':ab,ti

**Pregnancy and Lactation**
pregnancy:ab,ti OR 'pre pregnancy':ab,ti OR prenatal:ab,ti OR 'pre natal':ab,ti OR maternal:ab,ti OR mother:ab,ti OR mothers:ab,ti OR 'pre conception':ab,ti OR preconception:ab,ti OR 'peri conception':ab,ti OR preconception:ab,ti OR peri partum:ab,ti OR 'peri partum':ab,ti OR gestation*:ab,ti OR natal:ab,ti OR antenatal:ab,ti OR 'ante natal':ab,ti OR post partum:ab,ti OR postpartum:ab,ti OR 'peri partum':ab,ti OR 'peri natal':ab,ti OR puerperium:ab,ti OR postpartal:ab,ti OR postpartal:ab,ti OR postnatal:ab,ti OR 'post delivery':ab,ti OR 'after birth':ab,ti OR 'pregnancy'/exp OR 'pregnancy complication'/exp OR 'prenatal exposure'/exp OR 'maternal exposure'/exp OR 'pregnant woman'/exp OR 'mother'/mj OR 'puerperium'/exp OR 'maternal nutrition'/exp OR Lact*:ab,ti OR breastfeeding:ab,ti OR breast-feeding:ab,ti OR 'breast feed*':ab,ti OR breastfeeding:ab,ti OR 'breast fed':ab,ti OR breastfeeding:ab,ti OR 'human milk':ab,ti OR 'nursing women':ab,ti OR 'lactation'/exp OR 'breast feeding'/exp OR 'breast milk'/exp

**Neurocognitive**
'mental disease'/exp OR 'cognition'/exp OR 'cognitive defect'/exp OR 'depression'/exp OR 'psychomotor performance'/de OR 'executive function'/de OR 'attention deficit disorder'/de OR 'autism'/exp OR 'child development'/de OR 'developmental disorder'/exp OR 'psychomotor disorder'/de OR 'problem solving'/de OR 'academic performance'/exp OR 'mental disorder*':ab,ti OR cognition:ab,ti OR cognitive:ab,ti OR metacognition:ab,ti OR neurocognitive:ab,ti OR neurodevelop*:ab,ti OR neurological:ab,ti OR depression:ab,ti OR anxiety:ab,ti OR 'executive function*':ab,ti OR 'attention deficit disorder*':ab,ti OR adhd:ab,ti OR 'developmental disorder*':ab,ti OR autism:ab,ti OR asperger:ab,ti OR 'language processing':ab,ti OR 'language delay':ab,ti OR 'developmental delay':ab,ti OR 'developmental disability*':ab,ti OR 'motor skill*':ab,ti OR 'developmental domain*':ab,ti OR 'academic performance*':ab,ti OR 'academic achievement*':ab,ti OR 'academic failure':ab,ti OR 'academic success*':ab,ti

**Question:** What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?

CINAHL (Ebscohost)
- Date(s) Searched: Feb 5, 2020
- Search Strategy:

Omega-3
"omega-3" OR "omega 3" OR "N-3 fat*" OR PUFA* OR "alpha-linolenic acid*" OR "eicosapentaenoic acid" OR "docosahexaenoic acid" OR "linolenic acid" OR "fish oils" OR fish oil* OR (MH "plant oils") OR "plant oil*" OR "vegetable oil*" OR "n-3 oil*" OR "n3 oil*" OR "n3 fat*" OR (MH "Docosahexaenoic Acids") OR (MH "Eicosapentaenoic Acid")

Pregnancy and Lactation
postpartum OR post-partum OR MH "Postpartum Period" OR postpartal OR post-partal OR postnatal OR post-natal OR "post deliver*" OR "after birth" OR MH "pregnancy" OR MH "pregnancy complications" OR MH "Prenatal Exposure Delayed Effects" OR MH "Maternal Exposure" OR MH "pregnant women" OR "pregnan*" OR "pre-pregnancy" OR prepregnancy OR prenatal OR antenatal OR maternal OR mother OR mothers OR perinatal OR peri-natal OR periconception OR periconception OR MH "Peripartum Period" OR peripartum OR peri-partum OR "Mother Nutritional Physiological Phenomena" OR MH "Breast Feeding" OR breastfeeding OR breast-feeding OR MH "Milk, Human" OR "human milk" OR MH Lactation OR lactation OR lactating OR breastfeeding OR "breast feed*" OR breast-feed* OR breastfed OR breast-fed OR breastfeed* OR "nursing women" OR "nursing mother*"

Neurocognitive
(MH "Mental Disorders+") OR “mental disorder*” OR (MH "Cognition+") OR cognition OR cognitive OR metacognition OR neurocognitive OR neurodevelop* OR neurological OR “cognitive dysfunction" OR “depressive disorders OR (MH "Depression") OR depression OR (MH "Anxiety") OR anxiety OR (MH "Psychomotor Performance") OR motor skill* OR (MH "Executive Function") OR executive function* OR (MH "Attention Deficit Hyperactivity Disorder") OR attention deficit disorder* OR ADHD OR (MH "Child Behavior Disorders") OR (MH "Child Development") OR "child develop*" OR developmental disorder* OR (MH "Autistic Disorder") OR autism OR Asperger OR “language processing" OR language delay* OR (MH "Developmental Disabilities") OR developmental delay* OR developmental disabilit* OR (MH "Motor Skills Disorders") OR motor skill* OR (MH "Problem Solving") OR "problem solve*" OR developmental domain* OR (MH "academic performance") OR “academic performance" OR “academic achievement” OR “academic failure" OR academic success* NOT (MH "Literature Review" OR MH "Meta-Analysis" OR MH "Systematic Review" OR MH "News" OR MH "Retracted Publication" OR MH "Retraction of Publication")

Question: What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?
Filters - Published Date: 1980-2020, English Language; Human

COCHRANE (John S. Wiley & Sons)

- Date(s) Searched: Feb 5, 2020
- Search Strategy:

Omega-3
"linolenic acid**" OR "omega 3" OR "omega-3" OR "N3 fatty acid**" OR "n-3 fat**" OR pufa* OR "alpha-linolenic acid**" OR "eicosapentaenoic acid**" OR "docosahexaenoic acid**" OR [mh "Fatty Acids, Unsaturated"] OR ((fat OR fatty OR fats) NEAR/5 (unsatur* OR monounsatur* OR mono-unsatur* OR polyunsatur* OR poly-unsatur* OR "linolenic acid**") OR [mh "fish oils"] OR fish oil* OR [mh "plant oils"] OR "plant oil**" OR "vegetable oil**" OR "n-3 oil**" OR "n3 oil**" OR "n3 fat**"

Pregnancy and Lactation
[mh "Pregnancy"] OR [mh "Pregnancy Complications"] OR [mh "Prenatal Exposure Delayed Effects"] OR [mh "Maternal Exposure"] OR [mh "Pregnant Women"] OR [mh "Mothers"] OR [mh "Peripartum Period"] OR [mh "Maternal Nutritional Physiological Phenomena"] OR [mh "Postpartum Period"] OR pregnancy OR pre-pregnancy OR prenatal OR pre-natal OR maternal OR mother* OR postpartum OR perinatal OR peri-natal OR pre-conception OR preconception OR peri-conception OR periconception OR peripartum OR peri-partum OR gestat* OR natal OR antenatal OR ante-natal OR puerperium OR postpartum OR post-partum OR perinatal OR prenatal OR puerperium OR postpartal OR postnatal OR "post delivery" OR "after birth" OR [mh Lactation] OR [mh "Breast Feeding"] OR [mh "Milk, Human"] OR lact* OR breastfeeding OR breast-feeding OR breast feed* OR breast-feed* OR breastfed OR breast-fed OR breastfeed OR "human milk" OR "nursing women"

Neurocognitive
[mh "Mental Disorders"] OR [mh "Cognition"] OR [mh "Cognitive Dysfunction"] OR [mh "Depressive Disorder"] OR [mh "Depression"] OR [mh "Psychomotor Performance"] OR [mh "Executive Function"] OR [mh "Attention Deficit and Disruptive Behavior Disorders"] OR [mh "Child Behavior Disorders"] OR "behavior disorder***" OR "behaviour disorder***" OR "behavioral disorder***" OR "behavioural disorder***" OR "developmental disorder***" OR [mh "Child Development"] OR [mh "Autism Spectrum Disorder"] OR [mh "Developmental Disabilities"] OR [mh "Motor Skills Disorders"] OR [mh "Problem Solving"] OR "mental disorder***" OR cognition OR cognitive OR metacognition OR neurocognitive OR neurodevelop* OR depression OR anxiety OR "motor skill***" OR "executive function***" OR "attention deficit disorder***" OR ADHD OR "developmental disorder***" OR autism OR autistic OR Asperger* OR "language processing" OR "language delay" OR "child develop***" OR "developmental delay" OR "developmental disabilit***" OR "motor skill***" OR "developmental domain***" OR "academic performance" OR [mh "academic performance"] OR "academic achievement" OR "academic failure" OR "academic success***"

Filters – Date limited from 1980 to 2020, Trials
LITERATURE SEARCH AND SCREENING RESULTS

The flow chart (Figure 2) below illustrates the literature search and screening results for articles examining the systematic review question. The results of the electronic database searches, after removal of duplicates, were screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles met the inclusion criteria. Refer to Table 2 for the rationale for exclusion for each excluded full-text article. A manual search was done to find articles that were not identified when searching the electronic databases; all manually identified articles are also screened to determine whether they meet criteria for inclusion.

Figure 2: Flow chart of literature search and screening results

![Flow chart of literature search and screening results]

Question: What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?
Included articles


16. Huang Y, Iosif AM, Hansen RL, Schmidt RJ. Maternal polyunsaturated fatty acids and risk for
autism spectrum disorder in the MARBLES high-risk study. Autism 2020;1362361319877792
17. Innis SM, Friesen RW. Essential n-3 fatty acids in pregnant women and early visual acuity
intake on neuropsychological status and visual acuity at five years of age of breast-fed term
19. Jensen CL, Voigt RG, Prager TC, et al. Effects of maternal docosahexaenoic acid intake on
visual function and neurodevelopment in breastfed term infants. Am J Clin Nutr
docosahexaenoic acid supplementation on infant outcomes in African American women living
in low-income environments: A randomized, controlled trial. Psychoneuroendocrinology
on maternal depression and neurodevelopment of young children: a randomized controlled
randomized trial of prenatal DHA supplementation. JAMA 2014;311(17):1802-4 doi:
10.1001/jama.2014.2194.
docosahexaenoic acid supplementation during pregnancy and visual evoked potential
development in term infants: a double blind, prospective, randomised trial. Arch Dis Child Fetal
25. Mulder KA, Elango R, Innis SM. Fetal DHA inadequacy and the impact on child
neurodevelopment: a follow-up of a randomised trial of maternal DHA supplementation in
26. Mulder KA, King DJ, Innis SM. Omega-3 fatty acid deficiency in infants before birth identified
using a randomized trial of maternal DHA supplementation in pregnancy. PLoS One
27. Ostadrahimi A, Salehi-Pourmehr H, Mohammad-Alizadeh-Charandabi S, Heidarabady S,
Farshbaf-Khalili A. The effect of perinatal fish oil supplementation on neurodevelopment and
growth of infants: a randomized controlled trial. Eur J Nutr 2018;57(7):2387-97 doi:
10.1007/s00394-017-1512-1.
improves attention at 5 y of age: a randomized controlled trial. Am J Clin Nutr
Supplementation and Offspring Development at 18 Months: Randomized Controlled Trial.
30. Smithers LG, Gibson RA, Makrides M. Maternal supplementation with docosahexaenoic acid
during pregnancy does not affect early visual development in the infant: a randomized
potentials in Mexican infants are not affected by maternal supplementation with 400 mg/d
docosahexaenoic acid in the second half of pregnancy. J Nutr 2012;142(8):1577-81 doi:
10.3945/jn.112.162461.

Question: What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?

**Excluded articles**

The table below lists the articles excluded after full-text screening, and includes the categories of inclusion and exclusion criteria (see Table 1) that studies were excluded based on. At least one reason for exclusion is provided for each article, though this may not reflect all possible reasons for exclusion. Information about articles excluded after title and abstract screening is available upon request.

**Table 2. Articles excluded after full text screening with rationale for exclusion**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Rationale</th>
</tr>
</thead>
</table>

**Question:** What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?
Question: What is the relationship between omega-3 fatty acid supplements consumed during pregnancy and lactation and developmental milestones, including neurocognitive development?

<table>
<thead>
<tr>
<th>Citation</th>
<th>Rationale</th>
</tr>
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