United States Department of Agriculture

Seafood Consumption during Childhood and Adolescence and Neurocognitive Development: A Systematic Review

2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee

Published date: July 15, 2020

Nutrition Evidence Systematic Review
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This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee in collaboration with the Nutrition Evidence Systematic Review (NESR) team at the Center for Nutrition Policy and Promotion, Food and Nutrition Service, U.S. Department of Agriculture (USDA). All systematic reviews from the 2020 Advisory Committee Project are available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews.

Conclusion statements drawn as part of this systematic review describe the state of science related to the specific question examined. Conclusion statements do not draw implications, and should not be interpreted as dietary guidance. This portfolio provides the complete documentation for this systematic review. A summary of this review is included in the 2020 Advisory Committee's Scientific Report available at www.DietaryGuidelines.gov.

Suggested citation for this systematic review: 2020 Dietary Guidelines Advisory Committee and Nutrition Evidence Systematic Review Team. Seafood Consumption during Childhood and Adolescence and Neurocognitive Development: A Systematic Review. 2020 Dietary Guidelines Advisory Committee Project. Alexandria, VA: U.S. Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, July 2020. Available at: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews.

Related citation: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

ACKNOWLEDGEMENTS

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USDA and HHS implemented a process to identify topics and scientific questions to be examined by the 2020 Dietary Guidelines Advisory Committee. The Committee conducted its review of evidence in subcommittees for discussion by the full Committee during its public meetings. The role of the Committee members involved establishing all aspects of the protocol, which presented the plan for how they would examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that met the criteria they set; deliberating on the body of evidence for each question; and writing and grading the conclusion statements to be included in the scientific report the 2020 Committee submitted to USDA and HHS. The NESR

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[i] Under contract with the Food and Nutrition Service, United States Department of Agriculture.

team with assistance from Federal Liaisons and Project Leadership, supported the Committee by facilitating, executing, and documenting the work necessary to ensure the reviews were completed in accordance with NESR methodology. More information about the 2020 Dietary Guidelines Advisory Committee, including the process used to identify topics and questions, can be found at www.DietaryGuidelines.gov. More information about NESR can be found at NESR.usda.gov.

The Committee and NESR staff thank USDA's Agricultural Research Service for coordinating the peer review of this systematic review, and the Federal scientist peer reviewers for their time and expertise.

FUNDING SOURCE: United States Department of Agriculture, Food and Nutrition Service, Center for Nutrition Policy and Promotion, Alexandria, VA

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INTRODUCTION

This document describes a systematic review conducted to answer the following question: What is the relationship between seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development? This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee, supported by USDA's Nutrition Evidence Systematic Review (NESR).

More information about the 2020 Dietary Guidelines Advisory Committee is available at the following website: www.DietaryGuidelines.gov.

NESR specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. More information about NESR is available at the following website: NESR.usda.gov.

NESR's systematic review methodology involves developing a protocol, searching for and selecting studies, extracting data from and assessing the risk of bias of each included study, synthesizing the evidence, developing conclusion statements, grading the evidence underlying the conclusion statements, and recommending future research. A detailed description of the methodology used in conducting systematic reviews for the 2020 Dietary Guidelines Advisory Committee is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews. In addition, starting on page 69 this document describes the final protocol as it was applied in the systematic review. A description of and rationale for any modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 9. Dietary Fats and Seafood.

List of abbreviations

Abbreviation	Full name
9-HPT	9-Hole Peg Test
ADD	Attention deficit disorder
ADHD	Attention-deficit/hyperactivity disorder
ALSPAC	Avon Longitudinal Study of Parents and Children
ASD	Autism spectrum disorder
CLASS	Children's Lifestyle and School Performance Study
DHA	Docosahexaenoic acid
EPA	Eicosapentaenoic acid
FFQ	Food frequency questionnaire
FINS-KIDS	Fish Intervention Studies-KIDS
FINS-TEENS	Fish Intervention Studies-TEENS
HHS	United States Department of Health and Human Services
IQ	Intelligence quotient
IQR	Interquartile range
MFQ	Moods and Feeling Questionnaire
n-3	Omega-3
NESR	Nutrition Evidence Systematic Review
PCS	Prospective cohort study
RCT	Randomized controlled trial
SD	Standard deviation
SDQ	Strengths and Difficulties Questionnaire
THHg	Total hair mercury concentration
U.K.	United Kingdom
U.S.	United States
USDA	United States Department of Agriculture

Abbreviation	Full name
WISC	Wechsler Intelligence Scale for Children
WPPSI	Wechsler Preschool and Primary Scales of Intelligence

WHAT IS THE RELATIONSHIP BETWEEN SEAFOOD CONSUMPTION DURING CHILDHOOD AND ADOLESCENCE (UP TO 18 YEARS OF AGE) AND NEUROCOGNITIVE DEVELOPMENT?

PLAIN LANGUAGE SUMMARY

What is the question?

- What is the relationship between seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development?

What is the answer to the question?

Developmental domains:

- **Cognitive development:** Insufficient evidence is available to determine whether there is a favorable relationship between seafood intake during childhood and adolescence and measures of cognitive development in children and adolescents. However, no unfavorable relationships were found between seafood consumption during childhood and adolescence and measures of cognitive development.
- **Language and communication development:** Insufficient evidence is available to determine whether there is a favorable relationship between seafood intake during childhood and adolescence and measures of language and communication development in children and adolescents. However, no unfavorable relationships were found between seafood consumption during childhood and adolescence and measures of language and communication development.
- **Movement and physical development:** Insufficient evidence is available to determine the relationship between seafood intake during childhood and movement and physical development in children.
- **Social-emotional and behavioral development:** Insufficient evidence is available to determine the relationship between seafood intake during childhood and adolescence and social-emotional and behavioral development in children and adolescents.

Attention deficit disorder and Attention-deficit/hyperactivity disorder: Insufficient evidence is available to determine the relationship between seafood consumption during childhood and adolescence and attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors.

Autism spectrum disorder: No evidence is available to determine the relationship between seafood intake during childhood and adolescence and autism spectrum disorder-like traits or behaviors or autism spectrum disorder diagnosis.

Academic performance: Insufficient evidence is available to determine the relationship between seafood intake during adolescence and academic performance in adolescents.

Anxiety and Depression: Insufficient evidence is available to determine the relationship between seafood consumption during childhood and adolescence and anxiety and depression.

Why was this question asked?

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.

How was this question answered?

- The 2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee, conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.

What is the population of interest?

- Generally healthy children and adolescents from birth to 18 years at the time of the exposure and children and adolescents from 2 years to 18 years and adults 19 years and older at the time of the outcome.

What evidence was found?

- This review includes 13 articles.
- Seafood intake during childhood and adolescence had a predominantly beneficial or null relationship across developmental domains, specifically in cognitive development, language and communication development, and movement and physical development.
- However, no conclusion regarding the relationship between seafood intake during childhood and adolescence and developmental domains could be drawn due to an inadequate number of studies, inconsistency in results, risk of bias in classification of exposures, and heterogeneity of outcome assessments.
- No conclusion regarding the relationship between seafood intake during childhood and adolescence and academic performance, attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD), anxiety and depression, and autism spectrum disorder (ASD) could be drawn due to an inadequate number of studies.

How up-to-date is this systematic review?

- This review searched for studies from January, 2000 to October, 2019.

TECHNICAL ABSTRACT

Background

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.
- The 2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- The goal of this systematic review was to examine the following question: What is the relationship between seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development?

Conclusion statements and grades

Developmental domains:

- **Cognitive development:** Insufficient evidence is available to determine whether there is a favorable relationship between seafood intake during childhood and adolescence and measures of cognitive development in children and adolescents. However, no unfavorable relationships were found between seafood consumption during childhood and adolescence and measures of cognitive development. (Grade: Grade not assignable)
- **Language and communication development:** Insufficient evidence is available to determine whether there is a favorable relationship between seafood intake during childhood and adolescence and measures of language and communication development in children and adolescents. However, no unfavorable relationships were found between seafood consumption during childhood and adolescence and measures of language and communication development. (Grade: Grade not assignable)
- **Movement and physical development:** Insufficient evidence is available to determine the relationship between seafood intake during childhood and movement and physical development in children. (Grade: Grade not assignable)
- **Social-emotional and behavioral development:** Insufficient evidence is available to determine the relationship between seafood intake during childhood and adolescence and social-emotional and behavioral development in children and adolescents. (Grade: Grade not assignable)

Attention deficit disorder and Attention-deficit/hyperactivity disorder: Insufficient evidence is available to determine the relationship between seafood consumption during childhood and adolescence and attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors. (Grade: Grade not assignable)

Autism spectrum disorder: No evidence is available to determine the relationship between seafood intake during childhood and adolescence and autism spectrum disorder-like traits or behaviors or autism spectrum disorder diagnosis. (Grade: Grade not assignable)

Academic performance: Insufficient evidence is available to determine the relationship between seafood intake during adolescence and academic performance in adolescents. (Grade: Grade not assignable)

Anxiety and Depression: Insufficient evidence is available to determine the relationship between seafood consumption during childhood and adolescence and anxiety and depression. (Grade: Grade not assignable)

Methods

- A literature search was conducted using four databases (i.e., PubMed, Cochrane, Embase, and CINAHL) to identify published literature that evaluated the intervention or exposure of seafood consumption during childhood and adolescence and the outcome of neurocognitive development. A manual search was conducted to identify articles that may not have been included in the electronic databases searched. Articles were screened by two NESR analysts independently for inclusion based on pre-determined criteria.
- Data extraction and risk of bias assessment were conducted for each included study, and both were checked for accuracy. The Committee qualitatively synthesized the body of evidence to inform development of conclusion statements, and graded the strength of evidence using pre-established criteria for risk of bias, consistency, directness, precision, and generalizability.

Summary of the evidence

- This review includes 13 articles, six articles from three randomized controlled trials (RCTs) and seven articles from six prospective cohort studies (PCSs), published between January 2000 and October 2019.
- The 2020 Dietary Guidelines Advisory Committee used the following seafood definition: marine animals that live in the sea and in freshwater lakes and rivers. Seafood includes fish (e.g., salmon, tuna, trout, and tilapia) and shellfish (e.g., shrimp, crab, and oysters).
- The majority of studies addressed developmental domains – cognitive development (seven articles), language and communication development (five articles), movement and physical development (two articles), and social-emotional and behavioral development (three articles).
- No conclusion regarding the relationship between seafood intake during childhood and adolescence and developmental domains could be drawn due to an inadequate number of studies, inconsistency in results, risk of bias in classification of exposures, and heterogeneity of outcome assessments.
    - Seafood intake during childhood and adolescence had a predominantly beneficial or null relationship across all domains, and had a few detrimental relationships, primarily in social-emotional and behavioral development.
        - Results from three RCTs found that three fatty fish meals per week (~50-80 grams per meal) compared to meat meals for 12 weeks in adolescents or 16 weeks in children had a predominantly null effect on developmental domain outcomes.

        - Results from three PCSs generally found a beneficial association between fish intake in children and adolescents and developmental domains.
    - The vast majority of analyses showed no detrimental relationship between seafood intake during childhood and adolescence and cognitive, language and communication, and movement and physical development.
- No conclusion regarding the relationship between seafood consumption during childhood and adolescence and academic performance, attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD), anxiety and depression, and autism spectrum disorder (ASD) could be drawn due to an inadequate number of studies and variation in outcome assessment and child age.

FULL REVIEW

Systematic review question

What is the relationship between seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development?

Conclusion statements and grades

Developmental domains:

Cognitive development: Insufficient evidence is available to determine whether there is a favorable relationship between seafood intake during childhood and adolescence and measures of cognitive development in children and adolescents. However, no unfavorable relationships were found between seafood consumption during childhood and adolescence and measures of cognitive development. (Grade: Grade not assignable)

Language and communication development: Insufficient evidence is available to determine whether there is a favorable relationship between seafood intake during childhood and adolescence and measures of language and communication development in children and adolescents. However, no unfavorable relationships were found between seafood consumption during childhood and adolescence and measures of language and communication development. (Grade: Grade not assignable)

Movement and physical development: Insufficient evidence is available to determine the relationship between seafood intake during childhood and movement and physical development in children. (Grade: Grade not assignable)

Social-emotional and behavioral development: Insufficient evidence is available to determine the relationship between seafood intake during childhood and adolescence and social-emotional and behavioral development in children and adolescents. (Grade: Grade not assignable)

Attention deficit disorder and attention-deficit/hyperactivity disorder: Insufficient evidence is available to determine the relationship between seafood consumption during childhood and adolescence and attention deficit disorder or attention-deficit/hyperactivity disorder-like traits or behaviors. (Grade: Grade not assignable)

Autism spectrum disorder: No evidence is available to determine the relationship between seafood intake during childhood and adolescence and autism spectrum disorder-like traits or behaviors or autism spectrum disorder diagnosis. (Grade: Grade not assignable)

Academic performance: Insufficient evidence is available to determine the relationship between seafood intake during adolescence and academic performance in adolescents. (Grade: Grade not assignable)

Anxiety and Depression: Insufficient evidence is available to determine the relationship between seafood consumption during childhood and adolescence and anxiety and depression. (Grade: Grade not assignable)

Summary of the evidence

- This review includes 13 articles,[1-13] six articles from three randomized controlled trials (RCTs) and seven articles from six prospective cohort studies (PCSs), published between January 2000 and October 2019.
- The 2020 Dietary Guidelines Advisory Committee used the following seafood definition: marine animals that live in the sea and in freshwater lakes and rivers. Seafood includes fish (e.g., salmon, tuna, trout, and tilapia) and shellfish (e.g., shrimp, crab, and oysters).
- The majority of studies addressed developmental domain outcomes – cognitive development (seven articles), language and communication development (five articles), movement and physical development (two articles), and social-emotional and behavioral development (three articles).
- No conclusion regarding the relationship between seafood intake during childhood and adolescence and developmental domains could be drawn due to an inadequate number of studies, inconsistency in results, risk of bias in classification of exposures, and heterogeneity of outcome assessments.
    - Seafood intake during childhood and adolescence had a predominantly beneficial or null relationship across all domains, and had a few detrimental relationships, primarily in social-emotional and behavioral development.
        - Results from three RCTs found that three fatty fish meals per week (~50-80 grams per meal) compared to meat meals for 12 weeks in adolescents or 16 weeks in children had a predominantly null effect on developmental domain outcomes.
        - Results from three PCSs generally found a beneficial association between fish intake in children and adolescents and developmental domains.
    - The vast majority of analyses showed no detrimental relationship between seafood intake during childhood and adolescence and cognitive, language and communication, and movement and physical development.
- No conclusion regarding the relationship between seafood consumption during childhood and adolescence and academic performance, attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD), anxiety and depression, and autism spectrum disorder (ASD) could be drawn due to an inadequate number of studies and variation in outcome assessment and child age.

Description of the evidence

This systematic review includes 13 articles[1-13] that examined the relationship between seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development. Six articles were randomized controlled trials (RCTs) and seven articles were prospective cohort studies (PCSs). The study characteristics are described in **Table 1**, and the results of RCTs and PCSs are described in **Table 2** and

Table 3, respectively.

The independent variable was seafood consumption during childhood and adolescence. Seafood was defined as marine animals that live in the sea and in freshwater lakes and rivers. Seafood included fish (e.g., salmon, tuna, trout, and tilapia) and shellfish (e.g., shrimp, crab, and oysters).[ii] Studies that compared different types, sources, and/or amounts of seafood consumed and different frequency of and/or timing of seafood consumption were included. Studies that did not report a measure of seafood consumption (e.g., only examined biomarkers of consumption), evaluated omega (n)-3 fatty acid intake from supplements but did not evaluate seafood consumption, and evaluated infant formula with added docosahexaenoic acid (DHA) and/or eicosapentaenoic acid (EPA) were excluded.

Several neurocognitive assessment tools administered in the included articles were widely used and have been validated in certain populations, such as Wechsler scales of intelligence, the Strengths and Difficulties Questionnaire (SDQ), and the Moods and Feelings Questionnaire (MFQ). The validity of the neurocognitive development assessment in a particular study depends on a variety of factors, including the population it is being used in, how the assessment is administered, and the training of study personnel administering the assessment. Although these details were not provided in all studies, several articles included in this review indicated that assessments were administered in controlled environments by study personnel well trained to administer the assessment.[2,3,10,12]

Neurocognitive development outcomes evaluated within this systematic review included the following:

Developmental domains

- Cognitive development (including intelligence quotient [IQ]) assessment indicators/scales and age at outcome assessment (7 articles: 4 from RCTs, 3 from PCSs)
    - Book-format random dot stereoacuity test at 3.5 years[12]
    - d2 test of attention and mental concentration at 14 to 15 years[3]
    - Intelligence tests in conjunction with the Swedish military service conscription examination at 18 years[1]
    - Wechsler Intelligence Scale for Children-Revised (WISC-R), Chinese version at 12 years[7]
    - Wechsler Preschool and Primary Scale of Intelligence, 3rd edition (WPPSI-III) at 4 to 6 years[2,6,10]
- Language and communication development (including verbal IQ) assessment indicators/scales and age at outcome assessment (5 articles: 3 from RCTs, 2 from PCSs)
    - Intelligence tests in conjunction with the Swedish military service conscription examination at 18 years[1]

[ii] U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at http://health.gov/dietaryguidelines/2015/guidelines/.

  - WISC-R at 12 years[7]
  - WPPSI-III at 4 to 6 years[2,6,10]

- Movement and physical development assessment indicators/scales and age at outcome assessment (2 articles: 2 from RCTs)
  - 9-hole peg test (9-HPT) (dominant and non-dominant hand) at ~4 to 6 years[2,10]

- Social-emotional and behavioral development assessment indicators/scales and age at outcome assessment (3 articles: 2 from RCTs, 1 PCS)
  - Strengths and Difficulties Questionnaire (SDQ) at 4 to 6 years[4]; at 4 to 10 years and 12 to 13 years[9]; at 14 to 15 years[11]

Academic performance (1 PCS)

- Total school grade (16 academic subjects expressing cumulative knowledge of 9 years of compulsory school) at 16 years[5]

Anxiety and Depression (2 from PCSs)

- Diagnosis of internalizing disorder (includes anxiety and depression) at ~10-14 years[8]
- Depressive symptoms via Moods and Feelings Questionnaire (MFQ) at 17 years[13]

Attention deficit disorder (ADD) and attention-deficit/hyperactivity disorder (ADHD)-like traits or behaviors (2 from RCTs)

- SDQ at 4 to 6 years[4] and 14 to 15 years[11]

Study characteristics

Randomized controlled trials

Six articles from three RCTs conducted in Norway[3,4,6,10,11] and Germany,[2] ranging in sample size from 170 to 426 participants, were included in this review. No trials directly reported race or ethnicity; however, one article reported that 11% of participants were non-Norwegian[11] and another article reported that 2.3% were immigrants.[3] The majority of participants' parents completed high school and a large proportion had completed some college or a college degree. Only one article controlled for mercury exposure in one analysis.[6] Descriptions of each trial are provided below:

- Fish Intervention Studies-KIDS (FINS-KIDS)[4,6,10]
  - Participants were schoolchildren with a mean age of 5.2 years (standard deviation [SD]=0.6, range 4-6 years).
  - Participants were randomized to receive one of two school lunch meals, 3 times per week for 16 weeks (N=170, n=81 fish meals, n=89 meat meals[4]; N=210, n=101 fish meals, n=109 meat meals[6]: N=218, n=105 fish meals, n=113 meat meals)[10]
    - Fatty fish lunch meals (50-80 grams of mackerel or herring)

        - Meat lunch meals (50-80 grams of chicken, beef, or lamb)
    - Research assistants, not otherwise involved in the study, served the meals and weighed the fish and meat before and after the lunch to monitor adherence.
        - Of the possible 48 study meals provided, children received, on average, 44 meals (SD=4).
        - Children in the meat group had significantly greater adherence (Mean=2,779 grams of meat consumed from the meals provided, SD=872) than children in the fish group (Mean=2,070 grams of fish consumed from the meals provided, SD=957).
    - The following outcomes were examined:
        - Cognitive development assessed using the WPPSI-III[6,10]
        - Language and communication development assessed using the WPPSI-III[6,10]
        - Movement and physical development assessed using the 9-HPT[10]
        - Social-emotional and behavioral development assessed using the SDQ[4]
        - ADD/ADHD-like traits or behaviors assessed using the SDQ[4]
    - Outcome assessment methods:
        - Nine medicine and nutrition students trained for 30 hours by a clinical child psychologist conducted WPPSI-III and 9-HPT assessments. Ten percent of tests were scored by two administrators and inter-class correlation ranged from 0.98 to 1.00. Testing occurred in a controlled classroom environment.
- Fish Intervention Studies-TEENS (FINS-TEENS)[3,11]
    - Participants were adolescents with a mean age of 14.6 (SD=0.3) years.
        - 61% of parents had completed college or university
        - Mean intake of fish for dinner at baseline was 1.5 meals (SD=1.0) per week (Fatty fish: 1.0 meals per week, SD=1.0)
    - Participants were randomized to receive different school lunch meals 3 times per week for 12 weeks (N=425, n=137 fish meals, n=145 meat meals[11]; N=426, n=137 fish meals, n=148 meat meals)[3]:
        - Fatty fish lunch meals (80-100 grams of salmon, mackerel, or herring)
        - Meat lunch meals (80-100 grams of chicken, turkey, beef, lamb or cheese)
    - Study staff estimated by eye the amount of fish/meat eaten using a scale of zero to four.
        - Dietary compliance significantly differed between groups: Proportion of participants who consumed at least half of the meals was 38% for the fish group and 66% for the meat group.
    - Outcomes assessed included:
        - Cognitive development assessed using the d2 test of attention and mental concentration.[3]
        - Social-emotional and behavioral development using the SDQ

(parental report).[11]
        - ADD/ADHD-like traits or behaviors measured using the SDQ (parental report).[11]
    - Outcome assessment methods:
        - The d2 attention test was administered by trained research staff who described the test according to standard instructions. The test was conducted under time pressure, as prescribed, in a controlled classroom environment.
- German RCT[2]
    - Participants were children with a median age of 5.0 years (interquartile range [IQR]=0.8).
    - Families were randomized to receive one of two types of meals which were delivered to the home 3 times per week for 16 weeks (n=96 salmon meals, n=93 meat meals):
        - Atlantic salmon meals (50 grams of salmon)
        - Meat lunch meals (50 grams of meat)
    - Meals were provided for each member of the family; families chose from five different meal options within the assigned meal type.
    - Compliance was assessed by parental report of how much of the study meal was consumed each day, other seafood meals eaten, if the child was sick, or if any supplements were taken.
        - Approximately 34 (Median, IQR=16.9) of 48 study meals were consumed by both groups (salmon meals: Median=33.6, IQR=20.3; meat group: Median=34.3, IQR=13.7).
        - Food Frequency Questionnaires (FFQ) indicated total weekly fish intake of ~315 grams and 70 grams in the salmon and meat groups, respectively.
        - The n-3 index (percent of total red blood cell membrane fatty acids that are EPA and DHA) significantly increased from 3.9% (SD=0.9%) to 5.2% (SD=1.3%) in the salmon group and was unchanged in the meat group (4.1%, SD=1.1% to 3.9%, SD=1.1%).
    - Outcomes assessed included:
        - Cognitive and language and communication development assessed using the German version of the WPPSI-III.
        - Movement and physical development assessed using the 9-HPT (time required for task completion); children started with the dominant hand, followed by the non-dominant hand.
    - Outcome assessment methods:
        - Cognitive assessments were conducted by nine testers with an academic background in education or psychology, who were trained for at least 2 days, and were blinded to the child’s group allocation. Tests were conducted in a kindergarten setting if possible or in a neutral room in the child’s home. The same assessor conducted the test and re-test.

Prospective cohort studies

Seven articles from six PCSs, conducted in the United Kingdom (U.K.),[9,12,13] Sweden,[1,5] China,[7] and Canada,[8] were included in this systematic review.

- Participants
  - Sample size
    - <1000 participants: 3 articles[7,12,13]
      - Avon Longitudinal Study of Parents and Children (ALSPAC) Cohort (N=435)[12]
      - China Jintan Child Cohort Study (N=541)[7]
      - ROOTS Cohort (N=603)[13]
    - ≥1000 participants: 4 articles[1,5,8,9]
      - Children's Lifestyle and School Performance Study (CLASS) Cohort (N=3,757)[8]
      - Swedish Cohort (N=3,972)[1]
      - ALSPAC Cohort (N=5,727)[9]
      - Allergy 2000 (N=9,448)[5]
  - Socioeconomic status
    - The majority of participants' parents completed high school and a large proportion had completed some college or a college degree.
  - Race and ethnicity
    - One study reported that 98% of participants were Caucasian.[9]
    - Six studies did not report race or ethnicity; however, two studies provided some information on immigration status: 22% immigrant,[1] 12% foreign descent.[5]
- Exposure
  - FFQs were used to assess child fish intake in articles from the ALSPAC and CLASS cohorts.
    - ALSPAC cohort (2 articles):
      - White fish, other fish, and shellfish intake (servings per week) at 38 months, reported by mother.[9]
      - Oily fish intake (Yes/No) at ≤36 months, assessed at unknown time, reported by mother.[12]
    - CLASS cohort (1 article):
      - Fish (servings per day) during the previous year assessed at 10 to 11 years via modified version of the validated Harvard Youth/Adolescent FFQ (modified to include Canadian food/product names).[8]
  - A 4-day diet diary, completed by the child, was used to assess child fish intake (servings per day) at 14 years in the ROOTS cohort. Fish was converted to daily servings, using a serving size of 140 grams for fish.[13]
  - Questionnaires with a single question assessing seafood intake, completed by child, were used in three articles to assess frequency of child fish intake (times per week).[1,5,7]

- Outcomes reported by cohort
    - Allergy 2000: academic performance based on total grade at 16 years representing a cumulative score encompassing 16 academic subjects over 9 years of compulsory school in Sweden.[5]
    - ALSPAC: two articles reported on the following outcomes:
        - Cognitive development via book-format random dot stereoacuity test at 3.5 years.[12]
        - Social-emotional and behavioral development via SDQ (parent report) at 4 to 13 years.[9]
    - CLASS: depression and anxiety based on diagnosis of internalizing disorders at ~10 to 14 years.[8]
    - China Jintan Child Cohort Study: cognitive and language and communication development using the WISC-R, Chinese version at 12 years.[7]
    - ROOTS: depression (depressive symptoms) using the MFQ at 17.5 years (self-report).[13]
    - Swedish cohort: cognitive and language/communication development (IQ) via intelligence tests administered in conjunction with the Swedish military service conscription examination at 18 years.[1]

Evidence synthesis

Results for this review were summarized and synthesized by outcome (developmental domains, ADD/ADHD-like behaviors or traits, academic performance, anxiety and depression) and, within each outcome, by study design (RCT and PCS).

Results and risk of bias assessments for RCTs are described in **Table 2** and **Table 4**, respectively. Results and risk of bias assessments for PCSs are described in **Table 3** and **Table 5**, respectively.

Developmental Domains

Cognitive Development

Four articles from three RCTs examined the relationship between child fish intake and cognitive development, in either children age 4 to 6 years[2,6,10] or in adolescents age 14.6 years.[3]

In children 4 to 6 years of age, two articles were from the FINS-KIDS trial,[6,10] conducted in Norway, and one was from an RCT conducted in Germany.[2] Both trials examined the effect of three fish meals per week for 16 weeks on cognitive development. Intervention meals differed slightly between trials. The FINS-KIDS provided 50-80 grams per meal of herring or mackerel in the fish group, and chicken, lamb, or beef in the meat group.[6,10] The RCT from Germany provided approximately 50 grams per meal of Atlantic salmon in the intervention group, or meat including turkey, ham or beef, in the control group.[2] FINS-KIDS was a school-based trial, whereas the RCT from Germany was a home-based trial that provided meals to be consumed at home. In both trials, compliance (described previously) was high, but was significantly higher in the meat group than fish group in the FINS-KIDS trial. In the German RCT, children in the salmon group had a significantly higher pre- to post-intervention increase in red blood cell n-3 index compared to children in the meat group.

Both the FINS-KIDS and German RCT used the WPPSI-III administered by trained testers blinded to the child's group allocation. However, only the German RCT assessed cognitive development, performance, and processing speed IQ scores (scaled scores; adjusted for pre-intervention score).[2] The German study found no statistically significant between-group differences in changes from pre- to post-intervention scores for full-scale IQ, performance IQ, or processing speed quotient among all participants, and among the subset of children who ate more than 70 percent of the study meals (salmon group n=46, meat group n=50). All three RCTs assessed between-group change from pre- to post-intervention for total raw score, and sub-scale raw scores for performance and processing speed, with two studies additionally reporting sub-test raw scores.[2,10] The German RCT found that children who consumed salmon meals, compared to children who consumed meat meals, had a statistically significantly greater pre- to post-intervention improvement in one (picture concepts) of three sub-tests contributing to performance raw score, and one (symbol search) of two sub-tests contributing to processing speed raw score.[2] However, when the sub-scale raw scores were examined, only the changes in performance raw score were statistically significant; no effect on processing speed raw score was detected.[2]

The FINS-KIDS trial found that herring and mackerel meals compared to meat meals had no effect on WPPSI-III raw scores when not adjusted for compliance.[6,10] After adjusting for compliance, both articles reported that WPPSI-III total raw scores were significantly higher or had greater increases among children who consumed herring and mackerel meals compared to those who ate meat meals.[6,10] Evidence from the model adjusted for compliance is weaker than the model not adjusted for compliance however, since those who comply with interventions may be systematically different from those who do not. One article[10] found similar results for the symbol search sub-test, which was also significant in the German RCT,[2] and for the block design sub-test. After adjusting for the interaction effect between treatment (intervention group) and compliance, this article found a statistically significant increase in WPPSI-III total raw score (1.2 points more per 100 grams of foods eaten) in the fish group compared to the meat group.[10] A similar statistically significant interaction effect, where processing speed raw score increased 0.8 points more per 100 grams of food eaten in the fish compared to the meat group was also detected.[10] FINS-KIDS found a statistically significant group difference in changes in mean total hair mercury concentration (THHg) from pre-intervention to post-intervention.[6] Specifically, THHg increased among children in the fish group (change: 0.162 mg/kg, 95% confidence interval: 0.111, 0.213) and decreased among children in the meat group, (change: −0.053 mg/kg, 95% confidence interval: −0.103, −0.002); however, analysis indicated that THHg had no significant relationship with WPPSI-III raw scores.

One article from the FINS-TEENS trial (described above) examined the effect of fatty fish meals (80-100 grams of salmon, mackerel, or herring), compared to meat meals (80-100 grams of chicken, turkey, beef, lamb, or cheese) three times per week for 12 weeks on cognitive function in adolescents age 14 to 15 years in a school setting.[3] The d2 test measured concentration performance, total performance, processing speed, omission errors, commission errors and total errors. In analyses adjusted for baseline score and in analyses adjusted for baseline score, age, and compliance, adolescents in the fish group had improved processing speed compared to the meat group. In the analysis adjusted for baseline score only, omission errors were statistically significantly higher among the fish group compared to the meat group; however, there were no between-group differences after adjusting for dietary compliance. No statistically significant between-group differences were found for concentration performance, total performance, commission errors, and total errors in either primary analyses or analyses adjusted for compliance.

Three articles from three PCSs examined child fish intake and cognitive development in preschool children 3.5 years of age enrolled in the ALSPAC cohort in the U.K.,[12] in school children 12 years of age from China,[7] or boys 18 years of age from Sweden.[1]

From the ALSPAC cohort, one article did not detect a statistically significant association between oily fish intake at 3 years of age and odds of achieving foveal stereoacuity at 3.5 years.[12]

Prospective cohort studies conducted in older children found a statistically significant, favorable association between child fish intake and total IQ score.[1,7] In a cohort from China, approximately 16% never or seldom (<2 times per month), 58% sometimes (2 to 3 times per month), and 25% often (at least once a week) consumed fish at 9 to 11 years of age.[7] This study found a statistically significant association between consumption of fish “sometimes” (n=315) or “often” (n=137) compared to “never or seldom” (reference, n=89) and higher full scale and performance IQ on the Chinese version of the WISC-R at 12 years, with the magnitude of association increasing with higher fish intakes.[7] The relationship for full scale IQ was no longer statistically significant when the analysis was adjusted for total sleep disturbance, indicating that the association was partially mediated by sleep quality. In a cohort from Sweden, approximately 22% reported eating fish less than once per week, 56% reported eating fish once a week and 20% reported eating fish more than once per week.[1] Compared to consumption of fish “less than once a week”, consumption of fish “once a week” and “greater than once a week” were both significantly associated with higher combined intelligence and visuospatial score on the Swedish military service conscription examination, with a greater magnitude of association with greater fish intake.[1]

Summary

- Seven articles (four articles from three RCTs and three articles from three PCSs) examined the relationship between seafood intake during childhood and adolescence and cognitive development in the child.
    - Among children age 4 to 6 years, three articles from two RCTs[2,6,10] found that 3 fatty fish meals per week (~50-80 grams per meal) compared to meat meals for 16 weeks had predominantly null effects on WPPSI-III raw scores.
        - Among the few significant effects reported, effects were predominantly beneficial[2,3,6,10] and primarily seen in analyses that controlled for compliance.[3,6,10]
    - One PCS from the ALSPAC cohort did not find a significant association

between oily fish intake at 3 years and odds of achieving foveal stereoacuity at 3.5 years.[12]

  - Among children 14 to 15 years of age, one RCT found that consumption of fish meals (80-100 grams of salmon, mackerel, or herring) compared to meat meals (80-100 grams of chicken, turkey, beef, lamb, or cheese) three times per week for 12 weeks resulted in a statistically significant improvement in processing speed, but had no significant effects on concentration performance, total performance, commission errors and total errors.[3]
  - Two PCSs found a significant association between greater frequency of fish intake among children 9 to 11 years[7] and among boys 15 years[1] and greater total IQ scores at 12 and 18 years, respectively.

Language and Communication Development

In children 4 to 6 years of age, one German RCT[2] and two articles from the Norwegian FINS-KIDS RCT[6,10] predominantly found that three fish meals per week for 16 weeks had no effect on language or communication development assessed using the WPPSI-III. For the majority of scales and sub-tests, no statistically significant between-group differences were found for changes in scaled or raw verbal IQ scores and sub-test scores in fully-adjusted analyses.[2,6,10] However, one article found that the fish group had statistically significantly greater improvements in vocabulary sub-test raw score (adjusted for pre-intervention score, age, and compliance) compared to the meat group.[10] Among all participants and the subset of children who ate at least 70% of the study meals, the German RCT found no difference in pre- to post-intervention score changes between groups and verbal IQ scale score.[2] In the full group, no between-group differences were found in total verbal raw score change or in information, vocabulary, and word reasoning sub-test raw score change.

Two PCSs examined the association between child seafood intake and language and communication development: one in Chinese school children at 12 years of age[7] and one in Swedish adolescent males at 18 years of age.[1] Language and communication outcomes assessment methods varied across the studies and included:

- WISC-R, Chinese version, at 12 years[7]
- Intelligence test administered in conjunction with the Swedish military service conscription examination at 18 years[1]

Higher fish intake was associated with better language and communication scores in both PCSs.[1,7] In the study conducted in China, the article reported a between-group difference with children who rarely or never consumed fish, compared to those who consumed fish sometimes at 9 to 11 years, and higher verbal IQ scores assessed at 12 years; however, this effect was partially mediated by sleep quality.[7] Finally, fish intake “once a week or greater”, when compared to “less than once” a week at 15 years in Swedish males was associated with higher verbal IQ scores at age 18 years.[1]

Summary

- Three articles from two RCTs found no effect in analyses adjusted for baseline score and predominantly null effects in analyses adjusted for baseline score, age, and compliance for child seafood intake and language and communication development. Two PCSs found a positive association between seafood intake during childhood and adolescence and language and communication development in the child.

  - One German RCT[2] and two articles from the Norwegian FINS-KIDS RCT[6,10] found that three fish meals per week for 16 weeks predominantly had no effect on language or communication development in children 4 to 6 years of age assessed using the WPPSI-III intelligence test.
  - Two PCSs found that higher fish intake in Chinese school children[7] and Swedish adolescent boys[1] was associated with improved language and communication development examined using three different assessment methods.

Movement and Physical Development

Two RCTs, one conducted in Germany and one in Norway, evaluated the effect of fish meals (~50 grams of Atlantic salmon or 50-80 grams of herring or mackerel) compared to meat (~50 or 50-80 grams of chicken, lamb, or beef), three times per week for 16 weeks during early childhood, and movement/physical development in the child.[2,10] In both studies, the populations were children 4 to 6 years of age. The outcomes were the time required for task completion of the 9-HPT in the dominant and non-dominant hand, with faster times indicating better child fine manual dexterity and fine motor coordination. Children were allowed to practice once before the actual test in one study.[2] No effect of consuming fish for lunch, compared to consuming meat, on 9-HPT scores was detected for the child's dominant hand in both studies. For the non-dominant hand, FINS-KIDS detected a significant effect of fish consumption, compared to meat consumption, on change in 9-HPT score in analyses that adjusted for pre-intervention score and age and as well as analyses that additionally adjusted for compliance.[10] Specifically, the fish group had a larger improvement in time to completion, compared to the meat group in both models. In the German RCT, there was no difference between the salmon and meat groups for 9-HPT scores with the non-dominant hand.[2]

Summary

- Two RCTs[2,10] found that fatty fish meals (~50 grams of Atlantic salmon or 50-80 grams of herring or mackerel), compared to meat (~50 or 50-80 grams of chicken, lamb or beef) meals, provided three times per week for 16 weeks had no effect on dominant hand fine manual dexterity and fine motor coordination assessed using the 9-HPT at 4 to 6 years of age.
  - One study found a significant effect of fish meals, compared to meat meals, on fine manual dexterity and fine motor coordination in the non-dominant hand.[10]
  - Both studies had relatively high levels of adherence to the intervention; however, FINS-KIDS weighed intake at each meal whereas the German RCT relied on parental report for compliance.[2]

Social-emotional and Behavioral Development

Two Norwegian studies, one each from the FINS-KIDS and FINS-TEENS RCTs, examined whether fatty fish meals, compared to meat meals, provided three times per week for 16 weeks for FINS-KIDS and 12 weeks for FINS-TEENS affected social-emotional and behavioral development.[4,11] The primary outcomes were pre- to post-intervention change in SDQ subscale scores for emotional problems, conduct problems, hyperactivity/inattention symptoms, peer relationship problems, total problem score (based on the sum of the previous scores) and pro-social behavior based on parent-report[4] and adolescent-report.[11] Results adjusted for pre-intervention scores and dietary compliance showed that school meals with fatty fish compared to similar meals with meat, had no statistically significant pre- to post-intervention effect on SDQ subscale and total scores among children with a mean age of 5.2 years and 16.6 years at assessment.[4,11]

Results in sub-analyses among participants with high behavioral symptoms at baseline (scores over the 80th percentile) differed by age group.[11] Among children 4 to 6 years of age, there was no statistically significant difference between groups in change in SDQ scores. Among adolescents, the fish-meal group improved significantly less than the meat-meal group in emotional problems (after adjusting for baseline scores and both for baseline scores and compliance) (n= 26 fish group, n=31 meat group) and total difficulties (when adjusted for baseline scores; not significant when further adjusted for compliance) (n=25 fish group; n=26 meat group).

One PCS from the ALSPAC cohort evaluated the association between fish intake (meals per week) and social-emotional and behavioral development.[9] The participants consumed approximately 1.3 servings per week at 3 years.[9] There was no difference in fish intake at 3 years between children who exhibited early-onset persistent conduct problem trajectories and children who exhibited low conduct problem trajectories from age 4 to 13 years.[9] The risk of selection bias was serious in this particular study because only children with the highest and lowest conduct problems were included and those with intermediate conduct problem trajectories were excluded from analyses.[9]

Summary

- Two RCTs from Norway, one conducted in 4 to 6-year-olds (FINS-KIDS)[4] and one conducted in 14 to 15-year-olds (FINS-TEENS),[11] did not find a significant effect of fish intake and change in behavioral symptoms measured with the SDQ in the full study sample. The studies compared consumption of fish meals to meat meals 3 times per week for 16 and 12 weeks, respectively.
    - In a small subset of adolescents with high behavioral symptoms at baseline in FINS-TEENS, adolescents consuming meat meals had a larger decrease in pre- to post-intervention scores in total difficulties and emotional problems, compared to adolescents consuming fish meals.[11]
- One PCS, from the ALSPAC cohort in the U.K., found no difference in fish intake at 3 years of age between children with early-onset persistent conduct problem trajectories and low conduct problem trajectories assessed from 4 to 13 years of age.[9]

ADD or ADHD-like behaviors or traits

Two RCTs, one from the FINS-KIDS and another from the FINS-TEENS cohort in Norway, did not find an effect of fish meals provided three times per week for 16 weeks (FINS-KIDS) or 12 weeks (FINS-TEENS) on hyperactivity/inattention scores among 4 to 6-year-old children[4] and 14 to 15-year-old children.[11] Both studies adjusted for baseline scores and dietary compliance, and used the validated parent-report SDQ to measure hyperactivity/inattention scores.

Academic performance

One PCS from the Swedish cohort, Allergy 2000, examined the relationship between fish intake at 15 years of age and total school grade at 16 years.[5] The exposure was frequency of fish intake, assessed using a single question in a questionnaire, completed by the child in cooperation with parents. The types, amounts, and preparation methods of the fish consumed were not reported. The comparator groups were fish intake <1 times per week (n=2,283), 1 time per week (n=5,341), and >1 times per week (n=1,824). The outcome was total grade at 16 years of age, which in Sweden is a cumulative score encompassing 16 academic subjects and describes cumulative knowledge of 9 years of compulsory school. A limitation of this study was that total school grade primarily represented academic performance prior to the measurement of the exposure. The study found a statistically significant association between fish intake once a week and greater than once a week compared to less than once a week at 15 years of age, and higher total school grade at 16 years.[5] The positive associations between higher fish intake frequencies and higher total school grades were similar across genders and parental education levels.

Anxiety and Depression

Two PCSs, one from the CLASS cohort in Canada and one from the ROOTS cohort in the U.K., examined the relationship between child fish intake and diagnosis of internalizing disorders, or depression symptoms.[8,13]

Both studies examined fish intake as the exposure but used different methods to assess and categorize fish intake. The CLASS cohort in Canada assessed child fish intake at 10 to11 years of age using a version of the Harvard Youth/Adolescent FFQ, modified to include Canadian food and product names, and categorized intake based on tertiles, not specifying fish intake levels represented within each category.[8] In addition, mean fish intake was not reported.[8] The ROOTS cohort in the U.K. assessed child fish intake via a four-day diet diary and analyzed child fish intake continuously in servings per day, with one serving equal to 140 grams (approximately 5 ounces).[13] Mean fish intake was 0.12 servings per day (SD=0.20) and median intake was 0.0 grams per day (IQR 0.00-24.29).[13]

In the CLASS cohort in Canada, diagnoses of internalizing disorders, which included anxiety and depression, were ascertained through Canadian administrative health data sets.[8] The outcome measure was based on the number of health-care provider contacts where a diagnosis of either a depressive episode, recurrent or persistent mood disorder, neurotic or general anxiety disorder, acute reaction to severe stress, or emotional disorder with onset specific to childhood was made.[8] Compared to the first (lowest) tertile of child fish intake, children in the third (highest) tertile of intake at 10 to

11 years had a statistically significantly lower incidence of internalizing disorder diagnoses by age 14 years (incidence rate ratio=0.59). The incidence of internalizing disorder diagnosis in children in the second tertile did not differ significantly from the first tertile.[8] In the ROOTS cohort, which assessed depressive symptoms using the validated self-report Moods and Feelings Questionnaire, child fish intake at 14.5 years of age was not significantly associated with depressive symptoms at 17.5 years of age.[13]

Assessment of the evidence[iii]

As outlined and described below, the body of evidence examining seafood intake during childhood and adolescence and neurocognitive development was assessed for the following elements used when grading the strength of evidence.

- **Risk of bias:**
  - There were some concerns of systematic errors resulting from the design and conduct of the studies that could have influenced the accuracy of the reported results across the body of evidence.
  - RCTs
    - Risk of bias due to deviation from intended interventions: In the FINS-TEENS trial, compliance to the fish meal was relatively low compared to the meat meal intervention (only 38% consumed at least half of the fish meals during the trial, compared to 66% in the meat group).[3,11]
    - Risk of bias due to outcome measurement: Outcomes for social-emotional and behavioral and ADD/ADHD assessments relied on parent or self-report for the SDQ.[3,4,9,11]
  - PCSs
    - Risk of bias due to confounding: All studies did not control for at least one key confounder.
    - Risk of bias in selection of participants into the study: one article from the ALSPAC cohort selected participants with high and low scores on the SDQ and excluded those with intermediate scores.[9]
    - Risk of bias due to classification of exposures: Most studies used poorly described FFQs, questionnaires, or surveys with no indication of validity or reliability to assess child seafood intake.
    - Risk of bias due to outcome measurement: one article from the ALSPAC cohort relied on parental report of social-emotional and behavioral development assessment tools.[9]
- **Consistency:**
  - Results were predominantly beneficial or null across all domains, with a few

[iii] A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

detrimental results in social-emotional and behavioral development.

  - Measures of language and communication development were heterogeneous.

- **Directness:**
  - All studies were designed to examine seafood intake in the child and neurocognitive outcomes in the child.
- **Precision:**
  - Evidence from three RCTs and six PCSs was described in 13 articles; several studies and sub-analyses were underpowered, and not all studies reported power calculations.
  - Variation in methods used to categorize seafood intake, outcome assessment types, scales or indices, and age at outcome assessment made evaluation of precision and comparison of magnitude of associations across studies difficult.
  - The CLASS cohort did not quantify fish exposure, making interpretation of results difficult.[8]
- **Generalizability:**
  - Majority of studies were conducted in northern Europe, particularly in Scandinavian countries. Few studies reported participants' race or ethnicity. Most participants had parents who were well-educated or with an above average level of education.

Other important considerations

- Publication bias: A large, comprehensive search was conducted in multiple databases for this systematic review. Although risk of publication bias is always of potential concern, both small and large studies were included in this review, reporting both null and statistically significant results. Therefore, risk of publication bias is likely low across this body of evidence.

Research recommendations

In order to better assess the relationship between child seafood consumption and child neurocognitive outcomes, additional research is warranted. Should research in this area be conducted, the following recommendations should be considered.

- Validated and reliable methods to assess the amount, frequency, type, source, and cooking method of seafood consumed in children.
- Increased usage of age-appropriate, objective outcome assessment tools that rely less on parent report or self-report, particularly for social-emotional and behavioral outcomes and use of standardized outcome assessment methods.
- Determine the point in time when benefits from breastfeeding diminish or are replaced by child seafood intake.

- Increased research in diverse populations.
- More research to examine seafood intake during childhood and adolescence and:
    - Academic performance, anxiety, depression, autism spectrum disorder (ASD)-like traits or behaviors, ASD diagnosis, ADD/ADHD-like traits or behaviors, and ADD/ADHD diagnosis in childhood
    - Cognitive decline, mild cognitive impairment, dementia, anxiety, or depression in adults.

Included articles

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11. Skotheim S, Handeland K, Kjellevold M, et al. The effect of school meals with fatty fish on adolescents' self-reported symptoms for mental health: FINS-TEENS - a randomized controlled intervention trial. *Food Nutr Res.* 2017;61(1):1383818.doi: 10.1080/16546628.2017.1383818.
12. Williams C, Birch EE, Emmett PM, Northstone K. Stereoacuity at age 3.5 y in children born full-term is associated with prenatal and postnatal dietary factors: a report from a population-based cohort study. *Am J Clin Nutr.* 2001;73(2):316-322.doi: 10.1093/ajcn/73.2.316.
13. Winpenny EM, van Harmelen AL, White M, van Sluijs EM, Goodyer IM. Diet quality and depressive symptoms in adolescence: no cross-sectional or prospective associations following adjustment for covariates. *Public Health Nutr.* 2018;21(13):2376-2384.doi: 10.1017/s1368980018001179.

Table 1. Study characteristics of randomized controlled studies and prospective cohort studies examining the relationship between seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development[iii]

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
Randomized controlled trials		
Demmelmair, 2019[2] **Randomized Controlled Trial** **Germany** Baseline N=205 Analytic N=189 (Attrition: 8%) **Participant characteristics:** • Child age: Median=5.0, IQR=0.8 • Female child: 50.3% • Race/Ethnicity: NR • SES: ○ SES score: Mother: Median=16.0, IQR=5.0; Father: Median=17.0, IQR=5.0 **Seafood exposure** • Total fish intake: post-test – pretest ○ Salmon group: Median=29.7 g/d, IQR=38.1 ○ Meat group: Median= -2.8 g/d, IQR=12.6 ○ Group difference: P<0.001 **Seafood nutrient exposure:** • n-3 index (EPA and DHA expressed as % of total fatty acids): ○ Salmon group: Pretest: 3.9, SD=0.9%, Post-test: 5.2, SD=1.3%, P<0.001 ○ Meat group: Pretest: 4.1, SD=1.1%, Post-test: 3.9, SD=1.1%, P=0.107 ○ Group difference: P<0.001 **Mercury exposure:** • Weekly intake of about 3 µg Hg (0.2 µg/kg/wk) and 140 pg toxic equivalent (TEQ) dioxin-like PCBs (7 pg/kg/wk)	**Intervention:** Two groups received 3 meals/wk for 16wk at 4-6y containing either (N=189): • Salmon group (n=96): ~50g Atlantic Salmon • Meat group (n=93): ~50g meat (turkey, ham, beef) Compliance: Median=34 of 48 study meals consumed, IQR=16.9; P>0.05 between groups Median fish intake in salmon group=45.3 **Outcomes and assessment methods:** Cognitive, language/communication development • WPPSI-III (Wechsler Preschool and Primary Scale of Intelligence), 3rd edition with norms for German children) at ~4-6y ○ Full-scale IQ (FIQ) scaled/raw score ○ Total raw score ○ Verbal IQ (VIQ) scaled/raw score ▪ Information sub-test raw score ▪ Vocabulary sub-test raw score ▪ Word reasoning sub-test raw score ○ Performance IQ (PIQ) scale/raw score ▪ Block design sub-test raw score ▪ Matrix reasoning sub-test raw score ▪ Picture concepts sub-test raw score ○ Processing speed quotient (PSQ) scaled /raw score ▪ Coding sub-test raw score ▪ Symbol search sub-test raw score Movement/Physical Development • 9-HPT (9-Hole Peg Test) with dominant and non-dominant hand at ~4-6y	**Limitations:** None **Funding source:** European Research Council Advanced Grant META-GROWTH

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
FINS-KIDS		

Hysing, 2018[4]
Randomized Controlled Trial
FINS-KIDS, Norway
Baseline N=232 Analytic N=170 (Attrition: 27%)
 	
Participant characteristics:
• Child age: Mean=5.2y, SD=0.6
• Female child: 53.8%
• Race/Ethnicity: NR
• SES:
  ○ Parental education: ~15.5y
  ○ Family income in NOK (100 NOK=$11): <200,000-749,999 ~25%, 750,000-1,249,999 ~59%, 1,250,000->2,000,000 ~16%
 	
Seafood intake:
• Mean=1.7 meals of fish/wk, SD=0.9
 	
Seafood nutrient exposure:
• EPA (% of fatty acids in RBC): Mean~0.9%
• DHA (% of fatty acids in RBC): Mean~6.5%
• n-3 index (content of EPA and DHA as % of total fatty acids): Mean=7.4%, SD=1.4% [Reference: low risk: >8%, intermediate risk:4-8%, high risk: <4%]
 	
Mercury exposure: NR
	Intervention:
	Two groups received 3 lunches/wk for 16wk at 5y containing either (N=170):
	• Fish meal (n=81): 50–80g fatty fish (herring/mackerel)
	• Meat meal (n=89): 50–80g meat (chicken/lamb/beef)
	
	Compliance: Mean=44 study meals of 48, SD=4
	
	Outcomes and assessment methods:
	Social-emotional/behavioral development; ADD/ADHD-like traits or behaviors
	• SDQ (Strengths and Difficulties Questionnaire) at 4-6y (parental report):
	  ○ Total problem score
	  ○ Emotional problems
	  ○ Conduct problems
	  ○ Hyperactivity/inattention
	  ○ Peer relationship problems
		Limitations:
		• SDQ relies on parental report
		• Study may have been underpowered (sufficient power at n=116 per group)
		
		Funding source:
		The Norwegian Seafood Research Fund; Pelagia A/S provided herring and mackerel used in the diets free of charge

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source

Kvestad, 2018[6]
Randomized Controlled Trial
FINS-KIDS, Norway
Baseline N=232 Analytic N=210-186 (Attrition: ~9%)
 	
Participant characteristics:
• Child age: Mean=5.2y, SD=0.6
• Female child: 52.4%
• Race/Ethnicity: NR
• SES:
  ○ Parental years of education: Mean=15.4, SD=1.6
  ○ Family income in NOK (100 NOK=$11): <200,000-749,999 26.9%, 750,000-1,249,999 57.0%, 1,250,000->2,000,000 16.1%
 	
Seafood exposure:
Pre-intervention consumption of seafood for dinner: ≤3x/mo 12.2%, 1x/wk 38.6%, 2-3x/wk 47.6%, ≥4x/wk 1.6%
 	
Seafood nutrient exposure:
RBC EPA (Mean): 0.02 mg/g, SD=0.01;
RBC DHA (Mean): 0.14 mg/g, SD=0.03
 	
Mercury exposure:
• THHg at baseline (Mean): 0.374 mg/kg, SD=0.204 (range: 0.015-1.017)
• Change in THHg from pre-intervention to post-intervention:
  ○ Fish: 0.162 (95% CI: 0.111, 0.213)
  ○ Meat: -0.052 (95% CI: -0.103, -0.002)
• THHg at end of study:
  ○ Fish vs meat P<0.001
• Total Hg exposure from study meals:
  ○ Fish: 53.3 µg (SD=24.3)
  ○ Meat: 5.40 µg (SD=1.7)
  P<0.001
	Intervention:
	Two groups received 3 lunches/wk for 16wk at 4-6y containing either (N=210):
	• Fish meal (n=101): 50–80g fatty fish (herring/mackerel)
	• Meat meal (n=109): 50–80g meat (chicken/lamb/beef)
	
	<u>Compliance:</u> Mean=44.0 of 48 study meals, SD=4.0
	
	Outcomes and assessment methods:
	Cognitive, language/communication development
	• WPPSI-III (Wechsler Preschool and Primary Scale of Intelligence III; translated and standardized to Norwegian population) at 4-6y:
	  ○ Raw total score
	  ○ Raw verbal score
	  ○ Raw performance score
	  ○ Raw processing speed score
		Limitations:
		• Utilized raw WPPSI-III scores for analysis (adjusted for age) instead of using scaled scores
		• Study did not adjust for pre-intervention scores
		• Study may be underpowered (sufficient power at n=116 per group)
		
		Funding source:
		The Norwegian Seafood Research Fund; Pelagia A/S provided herring and mackerel used in the diets free of charge

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source

Oyen, 2018[10]
Randomized Controlled Trial
FINS-KIDS, Norway
Baseline N=232 Analytic N=218 (Attrition: 6%)
 	
Participant characteristics:
• Child age: Mean=5.2y, SD=0.6
• Female child: 51.4%
• Race/Ethnicity: NR
• SES:
  ○ Mean parental education: 15.4y
  ○ Family income in NOK (100 NOK=$11): < 200,000–749,999 ~26%, 750,000–1,249,999 ~57%, 1,250,000– > 2,000,000~17%
 	
Seafood exposure:
• Background diet, dietary intake from FFQ
  ○ Seafood as dinner ~1.7 meals/wk
  ○ Mackerel as dinner 0.1 meals/wk
  ○ Herring as dinner 0.0 meals/wk
  ○ Fish as bread spread ~1.3 meals/wk
 	
Seafood nutrient exposure:
Children in the fish group had higher increased levels of EPA and DHA from pre- to post-intervention compared to the meat group.
 	
Mercury and environmental toxin exposure:
No participant exceeded 20% of the tolerable weekly intake for dioxin and dioxin-like PCBs from the study meals.
Hair Hg levels assessed
	Intervention:
	Two groups received 3 lunches/wk for 16wk at 5y containing either (N=218):
	• Fish meal (n=105): 50–80g fatty fish (herring/mackerel)
	• Meat meal (n=113): 50–80g meat (chicken/lamb/beef)
	
	Compliance: Mean of 44 of 48 study meals served, SD=4
	
	Outcomes and assessment methods:
	Cognitive, language/communication development
	• WPPSI-III (Wechsler Preschool and Primary Scale of Intelligence, 3rd edition) at 4-6y
	  ○ Total raw score change
	  ○ Verbal raw score change
	    ▪ Information sub-test raw score
	    ▪ Vocabulary sub-test raw score
	    ▪ Word Reasoning sub-test score
	  ○ Performance raw score change
	    ▪ Block design sub-test raw score
	    ▪ Matrix reasoning sub-test raw score
	    ▪ Picture concepts sub-test raw score
	  ○ Processing Speed raw score change
	    ▪ Coding sub-test raw score
	    ▪ Symbol search sub-test raw score
	Movement/physical development
	• 9-HPT (9-Hole Peg Test) at 4-6y
		Limitations:
		• Sample size was slightly lower than calculated; however, the study had 78% power to detect an effect size of 0.37
		
		Funding source:
		• The Norwegian Seafood Research Fund, Pelagia A/S provided the herring and mackerel used in the diets free of charge

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
FINS-TEENS		

Handeland, 2017[3]
Randomized Controlled Trial
FINS-TEENS, Norway
Baseline N=478 Analytic N=426 (Attrition: 11%)
 	
Participant characteristics:
• Child age: Mean=14.6y, SD=0.3
• Female child: 52.1%
• Race/Ethnicity: Immigrant: 2.3% (both parents and themselves born outside Norway)
• SES:
  ○ Parental education: elementary/vocational school 39.3%, College/university 60.7%
  ○ Family income in NOK (100 NOK=$11): <200,000-749,999 21.3%, 750,000-1,249,999 51.1%, 1,250,000- >2,000,000 27.6%
 	
Seafood exposure:
• Mean intake of fish for dinner at baseline: 1.5 meals/wk, SD=1.0 (Fatty fish: 1.0 meals/wk, SD=1.0)
 	
Seafood nutrient exposure:
• Fish meals group (230 g/portion): 2.1 µg/100 g vitamin D, 4.9 µg/100 g Iodine, 152.3 mg/100 g EPA, 262.3 mg/100 g DHA, 39.9 mg/100 g
• Meat group (230 g/portion): < 1 µg/100 g vitamin D, 2.6 µg/100 g Iodine, 3.2 mg/100 g EPA, 5.0 mg/100 g DHA, 6 mg/100 g
 	
Mercury exposure: NR
	Intervention:
	Three groups received 3 lunches/wk for 12wk at 14y containing either (N=426):
	• Fatty fish meals (n=137): 80-100g salmon, mackerel, or herring
	• Meat meals (n=148): 80-100g chicken, turkey, beef, lamb, or cheese
	• n-3 supplements group (n=141; did not meet inclusion criteria)
	
	Compliance: % of participants who consumed at least half of fish/meat: fish 38%, meat 66%
	
	Outcomes and assessment methods:
	Cognitive development
	• d2 test of attention and mental concentration at 14-15y
	  ○ Concentration performance (Total target items correctly marked minus commission errors)
	  ○ Total performance (Total items processed minus total errors)
	  ○ Processing speed (Total items processed)
	  ○ Omission errors (Total target items missed)
	  ○ Commission errors (Total non-target items incorrectly marked)Total errors (Omission plus commission errors)
		Limitations:
		• Compliance to the fish meal intervention was relatively low (only 38% consumed at least half of the fish meals during the trial, compared to 66% in the meat group)
		
		Funding source:
		The Norwegian Seafood Research Fund; Marine Harvest A/S and Pelagia A/S provided fish for the study

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source

Skotheim, 2017[11]
Randomized Controlled Trial
FINS-TEENS, Norway
Baseline N=478 Analytic N=425 (Attrition: 11%)
 	
Participant characteristics:
• Child age: Mean=14.6y, SD=0.34
• Female child: 53%
• Race/Ethnicity: Non-Norwegian: 11%
• SES:
  ○ Maternal education: Elementary/high or vocational school 29%, College/University 71%
  ○ Paternal education: Elementary/high or vocational school 41%, College/University 59%
  ○ Household income (NOK): <200,000-749,999 21%, 750,000-1,249,999 51%, 1,250,000->2,000,000 28%
 	
Seafood exposure:
• Seafood for dinner (baseline, unit NR): Mean=4.1, SD=0.95
• Paper reports that participants consumed seafood once/wk for dinner
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
	Intervention:
	Three groups received 3 lunches/wk for 12 wk containing either (N=425):
	• Fish meal (n=137): 80-100 g fatty fish (salmon, mackerel, or herring)
	• Meat meal (n=145): 80-100 g meat (chicken, turkey, beef, or cheese)
	• n-3 LCPUFA supplement group (n=143)
	
	Compliance: Proportion of participants who consumed at least half of the meals: Fish 38%, Meat 66%
	
	Outcomes and assessment methods:
	Social-emotional/behavioral development; ADD/ADHD-like traits or behaviors
	• SDQ (Strengths and Difficulties Questionnaire) at 14-15y (child self-report):
	  ○ Total difficulties
	  ○ Emotional symptoms
	  ○ Conduct problems
	  ○ Hyperactivity/inattention symptoms
	  ○ Peer relationship problems
	  ○ Prosocial behavior
		Limitations:
		• SDQ relies upon child-self report
		• Compliance to the fish meal intervention was relatively low (only 38% consumed at least half of the fish meals during the trial, compared to 66% in the meat group)
		
		Funding source:
		Norwegian Seafood Research Fund/Research Council of Norway; Marine Harvest A/S; Leroy A/S; Pelagia A/S

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
Prospective cohort studies		

Aberg, 2009[1]
Prospective Cohort Study
Sweden
Baseline N=4,792 Analytic N=3,972 (Attrition: 17%)
 	
Participant characteristics:
• Child age at exposure: 15y
• Child age at outcome: 18y
• Female child: 0%
• Race/Ethnicity: NR (Born abroad: Immigrant 21.5%, Native 78.5%)
• SES:
  ○ Highest level of education of parents: Elementary school 9.6%, Senior high school (1–2 years) 21.8%, Senior high school (3 years) 18.9%, Residential college for adult education 4.3%, University 44.3%, Not answered 1.1%
  ○ Type of dwelling: House 79.4%. Apartment 20.6%
 	
Seafood intake:
Frequency of seafood intake: <once/wk 22.7%, once/wk 56.6%, >once/wk 20.2%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
	Exposure:
	Fish consumption (meals containing fish) assessed at 15y
	
	Exposure assessment method:
	One question in a questionnaire completed by the child
	
	Outcome and assessment method:
	Cognitive, language/communication development
	• Intelligence tests administered at age 18y in conjunction with the Swedish military service conscription examination:
	  ○ Full scale IQ
	  ○ Verbal IQ
	  ○ Visuospatial IQ
		Confounders accounted for:
		Child sex, child age, ethnicity, socioeconomic status (own dishwasher), parental education, family history of neurocognitive disorders, type and place of residence, frequency of physical exercise, BMI, dishwasher in home
		
		Limitations:
		• Several key confounders not accounted for: infant feeding mode, non-fish exposure to n-3 PUFAs, smoking
		• Did not account for child mercury exposure
		• Cannot determine the validity or reliability of the seafood assessment measure
		• No information provided on the type, preparation or amount of fish consumed
		
		Funding source:
		Swedish Society of Medicine; the Department of Public Health at the Vastra Gotaland Region; Swedish Science Council

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
ALSPAC Cohort		

Mesirow, 2017[9]
Prospective Cohort Study, Avon Longitudinal Study of Children and Parents (ALSPAC), U.K.
Baseline N=13,988 Analytic N=5,727 (Attrition: 59%)
 	
Participant characteristics:
• Child age at exposure: ~3y
• Child age at outcome: 4-13y
• Female child: 50.1%
• Race/Ethnicity: Caucasian/white ~98%
• SES:
  ○ Low-SES: ~9%
  ○ No educational qualifications (mother or partner): ~10%
  ○ Financial difficulties: ~19%
 	
Seafood exposure:
• Child fish intake at 3y (mean): ~1.3 servings/wk
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
	Exposure:
	Child fish intake (servings/wk) at 3y, assessed at 38mo
	
	Exposure assessment method:
	Fish intake (including white fish, other fish, and shellfish) measured via FFQ, completed by the mother. Fish/seafood items were summed to create continuous 3y "fish" variable. Fish fingers not included in fish assessment.
	
	Outcomes and assessment methods:
	Social-emotional/behavioral development
	• SDQ (Strengths and Difficulties Questionnaire) at 4-13y (parental report):
	  ○ Conduct problem
		Confounders accounted for:
		Child sex, child age, parental education, smoking, infant feeding mode; early parenthood, SES, no partner, lack of partner affection, major family problems, large family size, maternal psychopathology, substance use, criminal history, one or more birth complications (abruption, cervical suture, preterm rupture); preterm; low birth weight; multiparity
		
		Limitations:
		• Several key confounders not accounted for: race/ethnicity, non-fish dietary exposure to n-3
		• Did not account for child mercury exposure
		• SDQ relies on parental report
		• Serious risk of selection bias: participants selected based on high or low scores on the SDQ, those with intermediate scores excluded
		• No information provided on the amount and preparation of fish
		
		Funding source:
		NICHD

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source

Williams, 2001[12]
Prospective Cohort Study, ALSPAC, U.K.
Baseline N=641 (randomly selected subset of children born in last 6mo of cohort enrollment; Cohort N~12,000) Analytic N=435 (Attrition: 32%)
 	
Participant characteristics:
• Child age at exposure: NR
• Child age at outcome: Mean=3.5y, SD=0.6mo
• Female child: 47.9%
• Race/Ethnicity: NR
• SES:
  ○ Maternal education: Secondary 12.4%, Vocational 9.6%, O level 32.2%, A level 27.3%, Degree 18.5%
  ○ Financial difficulties: None 34.9%, Some 38.7%, Many 25.7%
 	
Seafood exposure:
• Child eats oily fish at 36mo: Yes 44.0%, No 56.0%
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
	Exposure:
	Child oily fish intake at ≤36mo assessed via FFQ
	
	Exposure assessment method:
	Oily fish (pilchards, sardines, mackerel, tuna, herring, kippers, trout, and salmon) measured via FFQ completed by mother
	
	Outcomes and assessment methods:
	Cognitive development
	Stereoacuity
	• Orthoptist administered book-format random dot stereoacuity test at 3.5y
		Confounders accounted for:
		Child sex, child age, SES, parental education, infant feeding mode, smoking
		
		Limitations:
		• Several key confounders not accounted for: race/ethnicity, non-fish dietary exposure to n-3 PUFA
		• Did not account for child mercury exposure
		• Cannot determine the validity or reliability of the seafood assessment measure
		• Stereopsis testing at 3.5y is difficult and repeatability of test was only moderately reliable (intraclass correlation coefficient=0.39)
		• No information provided on the amount, frequency, and preparation of fish
		
		Funding source:
		The Medical Research Council; the Wellcome Trust; The Ministry of Agriculture, Foods and Fisheries; the Departments of Health and the Environment; The South West Regional Health Authority; the National Eye Research Centre; Cow and Gate; and Milupa

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
Other cohorts		
Kim, 2010[5] **Prospective Cohort Study** **Allergy 2000, Sweden** Baseline N=10,837 Analytic N=9,448 (Attrition: 13%) **Participant characteristics:** • Child age at exposure: 15y • Child age at outcome: 16y • Female child: 50.5% • Race/Ethnicity: NR (Foreign descent [participants born abroad or both of their parents having been born abroad]: 11.7%) • SES: ○ Parents' education: elementary school 7.5%, secondary modern school 46.3%, College/University 44.5% ○ Type of housing: apartment 20.7%, detached/terrace house 79.3% **Seafood intake:** • Fish consumption: <1x/wk 24.2%, ~1x/wk 56.5%, >1x/wk 19.3% **Seafood nutrient exposure:** NR **Mercury exposure:** NR	**Exposure:** Frequency of child eating a meal containing fish at 15y. **Exposure assessment method:** One question in a questionnaire completed by the child **Outcome and assessment method:** Academic performance at 16y • Total school grade (16 participants expressing cumulative knowledge of 9 years of compulsory school)	**Confounders accounted for:** Child sex, child age, SES, parental education, physical activity, BMI, type of housing, residence area, dishwasher ownership **Limitations:** • Several key confounders not accounted for: infant feeding mode, smoking, non-fish dietary exposure to n-3 PUFA • Did not account for child mercury exposure • Cannot determine the validity or reliability of the seafood assessment measure • No information provided on the type, preparation or amount of fish consumed • Total school grades cover not only the prospective study period, but reflects grades from 9 years of compulsory education. **Funding source:** Swedish Society of Medicine, Department of Public Health Vastra Gotaland Region

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
Liu, 2017[7] **Prospective Cohort Study** **Jintan Child Cohort Study, China** Baseline N=1009 Analytic N=541 (Attrition: 46%) **Participant characteristics:** • Child age at exposure: Range: 9-11y • Child age at outcome: ~12y • Female child: 48.4% • Race/Ethnicity: NR • SES: ○ Mother's education: Less than high school 49.4%, High school 31.4%, College or higher 19.2% ○ Mother's occupation: Unemployed 26.6%, Worker 44.0%, Professional 29.4% ○ Father's education: Less than high school 34.6%, High school 34.4%, College or higher 31.1% ○ Father's occupation: Unemployed 4.4%, Worker 55.2%, Professional 40.4% **Seafood intake:** • Fish intake frequency: Never or seldom 16.5%, Sometimes 58.2%, Often 25.3% **Seafood nutrient exposure:** NR **Mercury exposure:** NR	**Exposure:** Child fish intake frequency (x/mo) at 9-11y of age. **Exposure assessment method:** Fish intake frequency assessed via self-administered FFQ with single question on fish **Outcome and assessment method:** Cognitive, language/communication development • WISC-R (Wechsler Intelligence Scale for Children-Revised), Chinese version, at 12y ○ Full-scale IQ ○ Verbal IQ ○ Performance IQ	**Confounders accounted for:** Child sex, child age, SES, parental education, infant feeding mode, siblings, home location, breakfast consumption habits, total sleep disturbance **Limitations:** • Several key confounders not accounted for: race/ethnicity, smoking, non-fish dietary exposure to n-3 PUFA • Did not account for child mercury exposure • Cannot determine the validity or reliability of the seafood assessment measure • No information provided on the type, preparation or amount of fish consumed **Funding source:** NIAA (intramural program)

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source

McMartin, 2012[8]
Prospective Cohort Study
Children's Lifestyle and School Performance Study (CLASS), Canada
Baseline N=5,200 Analytic N=3,757 (Attrition: 28%)
 	
Participant characteristics:
• Child age at exposure: ~10-11y
• Child age at outcome: ~10-14y
• Female child: 52%
• Race/Ethnicity: NR
• SES:
  ○ Parental education: Secondary school or less 31%, College 38%, University 31%; Parental marital status
  ○ Household income ($CAN): <20,000 11%, 20,001-40,000 23%, 40,001-60,000 27%, >60,000 39%
  ○ Married or common law 83%, Separated/divorced/ widowed/single 17%
 	
Seafood intake: NR
 	
Seafood nutrient exposure: NR
 	
Mercury exposure: NR
	Exposure:
	Child fish intake (servings/d) during the previous year assessed at 10-11y
	
	Exposure assessment method:
	Modified version of the validated Harvard Youth/Adolescent FFQ (modified to include Canadian food/product names) completed by child
	
	Outcome and assessment method:
	Depression and anxiety
	• Diagnosis of an internalizing disorder at ~10-14y based on ICD-9 and ICD-10 codes abstracted from the Medical Services Insurance (MSI) database and the Canadian Institute for Health Information Discharge Abstract Database (CIHI DAD)
		Confounders accounted for:
		Child sex, child age, SES, parental education, energy intake, parental marital status, body weight status, physical activity level, geographic area (urban or rural)
		
		Limitations:
		• Several key confounders not accounted for: race/ethnicity, non-fish dietary n-3 PUFA, infant feeding mode, smoking exposure, family history of neurocognitive disorder
		• Did not account for child mercury exposure
		• No information provided on the type, amount, frequency, or preparation of fish consumed
		
		Funding source:
		Canada Foundation for Innovation Leaders Opportunity Fund; Canadian Population Health Initiative; Canadian Institutes for Health Research; The Heart and Stroke Foundation of Canada

Article and Population Characteristics	Intervention/Exposures and Outcomes	Study Limitations and Funding Source
Winpenny, 2018[13] **Prospective Cohort Study, ROOTS, U.K.** Baseline N=1,238 Analytic N=603 (Attrition: 51%) **Participant characteristics:** • Child age: Mean=14.5y, SD=3.5mo • Female child: 60% • Race/Ethnicity: NR • SES: ○ A Classification of Residential Neighborhoods (ACORN) index: Low 11.1%, Medium 24.9%, High 64.0% **Seafood exposure:** • Fish intake (Mean): 0.12 servings/d, SD: 0.20, P<0.05 between males and females • Fish intake (Median): 0.0 g/d, IQR: 0.00, 24.29, P<0.04 between males and females **Seafood nutrient exposure:** NR **Mercury exposure:** NR	**Exposure:** Child fish intake (servings/d) at 14y **Exposure assessment method:** Fish intake assessed via 4d diet diary, including 2 weekdays and 2 weekend days, reporting estimated portion sizes (small, medium, or large), household measures or as individual items, completed by child. Fish was converted to daily servings, using a serving size of 140 g for fish. **Outcomes and assessment method:** Depression (depressive symptoms) • MFQ (Moods and Feelings Questionnaire) at 17y (self-report)	**Confounders accounted for:** Child sex, child age, SES, smoking, alcohol consumption, physical activity, sleep, friendship quality, self-esteem, family functioning, medication use, percentage body fat, total energy intake **Limitations:** • Several key confounders not accounted for: race/ethnicity, parental education, non-fish dietary exposure to n-3 PUFA, infant feeding mode, family history of depression • MFQ relies on self-report • Did not account for child mercury exposure • No information provided on the type, frequency or preparation of fish consumed **Funding source:** Wellcome Trust and National Institute of Health Research Collaboration for Leadership in Applied Research and Care East of England

[iii] Abbreviations: d – day(s), g – gram(s), Hg – mercury, IQR – interquartile range, kg – kilogram(s), LCPUFA – long chain polyunsaturated fatty acid, mg – milligram(s), mo – month(s), NOK – Norwegian kroner, NR – not reported, PCBs – polychlorinated biphenyls, PUFA – polyunsaturated fatty acid, RBC – red blood cell, SD – standard deviation, SES – socioeconomic status, wk – week(s), ug - microgram, x – times, y – year(s)

Table 2. Results of randomized controlled trials that examined the relationship between seafood consumption during childhood and adolescence and neurocognitive development[iv]

Article	Intervention	Outcome and Results (statistically significant results bolded)
Demmelmair, 2019[2] **Randomized Controlled Trial** **Germany** **Outcome domains:** cognitive, language/communication, movement/physical **Summary:** Salmon intake, when compared to meat intake, did not significantly improve IQ or child fine manual dexterity in preschool children after four months of intervention (3 meals per week containing ~50g Atlantic Salmon or 50g meat). However, improvement was observed in two sub-test raw scores related to non-verbal fluid intelligence. **Intervention Compliance:** Median=34 meals, IQR=16.9 of 48 study meals consumed; P>0.05 between groups **Baseline Seafood Intake:** Total fish intake pre-intervention: Salmon group: Median=16.2g/d, IQR=15.2 Meat group: Median=15.6g/d, IQR=14.1	Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=96) vs Meat intake (~50 g) 3x/wk for 16wk (n=93) Salmon meals (~50 g/meal): 1. Pasta filled with salmon pate 2. Salmon fillet in paprika sauce 3. Pasta sauce with salmon 4. Potato gratin with salmon 5. Salmon burger Meat meals (~50 g/meal): 1. Turkey fillet in paprika sauce 2. Tortellini with ham filling 3. Bolognese sauce 4. Potato gratin with turkey fillet 5. Beef burger **Age at intervention:** ~4-6y	*Higher scores on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) indicate better child performance* **WPPSI-III scale score change:** Between-group differences in pre- to post-intervention scale score change **Model adjustments:** Pre-intervention score **Age at outcome:** ~4-6y **Full-scale IQ (FIQ) scale score change** Salmon group: 1.2, 95% CI: 0.6, 3.1 Meat group: 1.0, 95% CI: -0.2, 2.2; Group difference, P=0.33 **Verbal IQ (VIQ) scale score change** Salmon group: -0.4, 95% CI: -1.8, 1.0 Meat group: -0.3, 95% CI: -1.6, 1.1; Group difference, P=0.92 **Performance IQ (PIQ) scale score change** Salmon group: 3.5, 95% CI: 1.8, 5.2 Meat group: 1.4, 95% CI: -0.3, 3.1; Group difference, P=0.08 **Processing speed quotient (PSQ) scale score change** Salmon group: 3.4, 95% CI: 1.3, 5.6 Meat group: 3.3, 95% CI: 1.1, 5.5; Group difference, P=0.93 Analyses repeated stratified for child sex or adjusting for SES and location of test (kindergarten or home), yielding similar results.

Article	Intervention	Outcome and Results (statistically significant results bolded)
Demmelmair, 2019 (CONTINUED) **Randomized Controlled Trial** **Germany**	Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=96) vs Meat intake (~50 g) 3x/wk for 16wk (n=93) **Age at intervention:** ~4-6y	**WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Pre-intervention score and age **Age at outcome:** ~4-6y **Total raw score change** Salmon group: 17.4, 95% CI: 14.8, 20.1 Meat group: 14.6, 95% CI: 11.9, 17.3; Group difference, P=0.14 **Verbal raw score change** Salmon group: 2.4, 95% CI: 1.5, 3.4 Meat group: 1.9, 95% CI: 0.9, 2.9; Group difference, P=0.44 **Information sub-test raw score change** Salmon group: 1.1, 95% CI: 0.6, 1.5 Meat group: 0.6, 95% CI: 0.2, 1.0; Group difference, P=0.14 **Vocabulary sub-test raw score change** Salmon group: 0.9, 95% CI: 0.2, 1.6 Meat group: 0.4, 95% CI: -0.3, 1.1; Group difference, P=0.33 **Word reasoning sub-test raw score change** Salmon group: 0.6, 95% CI: 0.1, 1.0 Meat group: 0.8, 95% CI: 0.4, 1.3; Group difference, P=0.41 **Performance raw score change** **Salmon group: 5.0, 95% CI: 3.8, 6.2** **Meat group: 3.2, 95% CI: 2.1, 4.4 ; Group difference, P=0.04** **Block design sub-test raw score change** Salmon group: 2.3, 95% CI: 1.4, 3.2 Meat group: 1.5, 95% CI: 0.6, 2.4; Group difference, P=0.22 **Matrix reasoning sub-test raw score change** Salmon group: 1.1, 95% CI: 0.7, 1.6 Meat group: 1.0, 95% CI: 0.6, 1.5; Group difference, P=0.72 **Picture concepts sub-test raw score change** **Salmon group: 1.5, 95% CI: 1.0, 2.1** **Meat group: 0.7, 95% CI: 0.1, 1.3; Group difference, P=0.04**

Article	Intervention	Outcome and Results (statistically significant results bolded)
Demmelmair, 2019 (CONTINUED) **Randomized Controlled Trial** **Germany**	Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=96) vs Meat intake (~50 g) 3x/wk for 16wk (n=93) **Age at intervention:** ~4-6y	**(CONTINUED)** **WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Pre-intervention score and age **Age at outcome:** ~4-6y **Processing speed raw score change** Salmon group: 10.1, 95% CI: 7.9, 12.3 Meat group: 9.4, 95% CI: 7.1, 11.6; Group difference, P=0.64 **Coding sub-test raw score change** Salmon group: 5.2, 95% CI: 3.3, 7.0 Meat group: 5.4, 95% CI: 3.6, 7.3; Group difference, P=0.83 **Symbol search sub-test raw score change** **Salmon group: 5.0, 95% CI: 4.1, 6.0** **Meat group: 3.6, 95% CI: 2.6, 4.6; Group difference, P=0.047** Analyses repeated stratified for child sex or adjusting for SES and location of test (kindergarten or home), yielding similar results.
Demmelmair, 2019 (CONTINUED) **Randomized Controlled Trial** **Germany**	**Subset of children who ate at least 70% of the study meals** Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=46) vs Meat intake (~50 g) 3x/wk for 16wk (n=50) **Age at intervention:** ~4-6y	**WPPSI-III scale score change:** Between-group differences in pre- to post-intervention scale score change **Model adjustments:** Pre-intervention score **Age at outcome:** ~4-6y **Full-scale IQ (FIQ) scale score change** Salmon group: 1.2, 95% CI: -1.0, 3.4 Meat group: -0.9, 95% CI: -3.3, 1.6; Group difference, P=0.21 **Verbal IQ (VIQ) scale score change** Salmon group: -1.0, 95% CI: -3.5, 1.5 Meat group: -0.9, 95% CI: -3.7, 1.8; Group difference, P>0.99 **Performance IQ (PIQ) scale score change** Salmon group: 3.6, 95% CI: 0.9, 6.3 Meat group: -0.1, 95% CI: --3.0, 2.9; Group difference, P=0.07 **Processing speed quotient (PSQ) scale score change** Salmon group: 3.4, 95% CI: -0.5, 7.3 Meat group: 1.0, 95% CI: -3.3, 5.2; Group difference, P=0.40 Analyses repeated stratified for child sex or adjusting for SES and location of test (kindergarten or home), yielding similar results.

Article	Intervention	Outcome and Results (statistically significant results bolded)
Demmelmair, 2019 (CONTINUED) **Randomized Controlled Trial** **Germany**	**Subset of children who ate at least 70% of the study meals** Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=46) vs Meat intake (~50 g) 3x/wk for 16wk (n=50) **Age at intervention:** ~4-6y	**WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Pre-intervention score and age **Age at outcome:** ~4-6y **Total raw score change** Salmon group: 16.9, 95% CI: 12.8, 21.1 Meat group: 11.3, 95% CI: 6.7, 15.9; Group difference, P=0.07 **Verbal raw score change** Salmon group: 2.0, 95% CI: 0.2, 3.9 Meat group: 1.7, 95% CI: -0.3, 3.8; Group difference, P=0.83 **Information sub-test raw score change** Salmon group: 1.0, 95% CI: 0.3, 1.6 Meat group: 0.6, 95% CI: -0.0, 1.3; Group difference, P=0.49 **Vocabulary sub-test raw score change** Salmon group: 0.4, 95% CI: -1.2, 2.0 Meat group: 0.5, 95% CI: -1.3, 2.3; Group difference, P=0.92 **Word reasoning sub-test raw score change** Salmon group: 0.7, 95% CI: -0.2, 1.5 Meat group: 0.7, 95% CI: -0.2, 1.6; Group difference, P=0.94 **Performance raw score change** **Salmon group: 5.4, 95% CI: 3.6, 7.1** **Meat group: 2.3, 95% CI: 0.4, 4.2; Group difference, P=0.02** **Block design sub-test raw score change** Salmon group: 2.4, 95% CI: 1.1, 3.8 Meat group: 0.9, 95% CI: -0.6, 2.3 ; Group difference, P=0.12 **Matrix reasoning sub-test raw score change** Salmon group: 1.0, 95% CI: 0.0, 1.9 Meat group: 0.6, 95% CI: -0.4, 1.6; Group difference, P=0.57 **Picture concepts sub-test raw score change** **Salmon group: 2.1, 95% CI: 1.2, 3.1** **Meat group: 0.6, 95% CI: -0.4, 1.6; Group difference, P=0.03**

Article	Intervention	Outcome and Results (statistically significant results bolded)
Demmelmair, 2019 (CONTINUED) **Randomized Controlled Trial** **Germany**	**Subset of children who ate at least 70% of the study meals** Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=46) vs Meat intake (~50 g) 3x/wk for 16wk (n=50) **Age at intervention:** ~4-6y	**(CONTINUED)** **WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Pre-intervention score and age **Age at outcome:** ~4-6y **Processing speed raw score change** Salmon group: 9.4, 95% CI: 5.6, 13.2 Meat group: 7.4, 95% CI: 3.3, 11.6; Group difference, P=0.48 **Coding sub-test raw score change** Salmon group: 3.2, 95% CI: -0.3, 6.7 Meat group: 5.3, 95% CI: 0.4, 8.1; Group difference, P=0.68 **Symbol search sub-test raw score change** Salmon group: 6.1, 95% CI: 4.0, 8.2 Meat group: 3.3, 95% CI: 1.0, 5.6; Group difference, P=0.07 Analyses repeated stratified for child sex or adjusting for SES and location of test (kindergarten or home), yielding similar results.
	Atlantic salmon intake (~50 g) 3x/wk for 16wk (n=96) vs Meat intake (~50 g) 3x/wk for 16wk (n=93) **Age at intervention:** ~4-6y	*Faster time on the 9-hole peg test (9-HPT) indicates better child fine manual dexterity and fine motor coordination* **9-HPT change:** Between-group in differences in pre- to post-intervention time change **Model adjustments:** Pre-intervention score **Age at outcome:** ~4-6y **9-HPT1 (dominant hand) change** Salmon group: -2.0, 95% CI: -2.9, -1.1 Meat group: -3.0, 95% CI: -3.8, -2.1; Group difference, P=0.15 **9-HPT2 (non-dominant hand) change** Salmon group: -3.6, 95% CI: -4.8, -2.4 Meat group: -3.6, 95% CI: -4.8, -2.4; Group difference, P=0.98 Analyses repeated stratified for child sex or adjusting for SES and location of test (kindergarten or home), yielding similar results except 9-HPT1 when adjusted for SES and location of test: Group difference, P=0.08

Article	Intervention	Outcome and Results (statistically significant results bolded)
[Kvestad, 2018](#)[6] **Randomized Controlled Trial** **FINS-KIDS; Norway** **Outcome Domains:** cognitive, language/communication **Summary:** Fish (herring/mackerel) meals 3x per week for 16 weeks, compared to meat (chicken/lamb/beef) meals, was significantly associated with better WPPSI-III total and processing speed raw scores at 4-6y, but only after adjustment for compliance. No difference between groups was detected for WPPSI-III verbal and performance raw scores. **Intervention Compliance:** Study meals served: Mean=44.0, SD=4.0 Intake by group: Total meat intake: Mean=2675 g, SD=850 Total fish intake: Mean=2070 g, SD=978 P<0.0001 **Baseline Seafood Intake:** Pre-intervention consumption of seafood for dinner: ≤3x/mo 12.2%, 1x/wk 38.6%, 2-3x/wk 47.6%, ≥4x/wk 1.6%	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=101) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=109) Model 1: N=210 Model 2: N=210 Model 3: N=186 **Age at intervention:** 4-6y	*Higher WPPSI-III raw scores indicate better cognitive development* **WPPSI-III raw score:** Between-group differences in post-intervention raw scores **Model adjustments**: Model 1: age; Model 2: model 1 + total hair mercury; Model 3: model 2 + fish/meat consumption + sex + SES **Age at outcome:** 4-6y **WPPSI-III Total Mean Raw Score** Fish group: 162.6, 95% CI: 156.5, 168.6 Meat group: 160.0, 95% CI: 154.1, 165.9; Group difference, P=0.48 (Model 1) Fish group: 160.4, 95% CI: 154.1, 166.7 Meat group: 161.8, 95% CI: 155.7, 167.8; Group difference, P=0.74 (Model 2) **Fish group: 164.5, 95% CI: 160.9, 168.1** **Meat group: 159.0, 95% CI: 155.6, 162.4; Group difference, P=0.008 (Model 3)** **WPPSI-III Verbal Mean Raw Score** Fish group: 60.2, 95% CI: 57.9, 62.5 Meat group: 60.1, 95% CI: 57.8, 62.3; Group difference, P=0.91 (Model 1) Fish group: 59.4, 95% CI: 57.0, 61.9 Meat group: 60.8, 95% CI: 58.5, 63.1; Group difference, P=0.45 (Model 2) Fish group: 61.1, 95% CI: 59.8, 62.4 Meat group: 59.9, 95% CI: 58.7, 61.1; Group difference, P=0.16 (Model 3) **WPPSI-III Performance Mean Raw Score** Fish group: 56.4, 95% CI: 54.9, 57.9 Meat group: 56.4, 95% CI: 55.0, 57.8; Group difference, P=0.97 (Model 1) Fish group: 56.4, 95% CI: 54.9, 57.9 Meat group: 56.4, 95% CI: 54.9, 57.8; Group difference, P=0.97 (Model 2) Fish group: 56.7, 95% CI: 55.2, 58.2 Meat group: 56.3, 95% CI: 54.9, 57.6; Group difference, P=0.66 (Model 3)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Kvestad, 2018 (CONTINUED) **Randomized Controlled Trial** **FINS-KIDS; Norway**	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=101) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=109) Model 1: N=210 Model 2: N=210 Model 3: N=186 **Age at intervention:** 4-6y	**(CONTINUED)** **WPPSI-III raw score:** Between-group differences in post-intervention raw scores **Model adjustments**: Model 1: age; Model 2: model 1 + total hair mercury; Model 3: model 2 + fish/meat consumption + sex + SES **Age at outcome:** 4-6y **WPPSI-III Processing Speed Mean Raw Score** Fish group: 45.1, 95% CI: 42.8, 47.4 Meat group: 44.3, 95% CI: 42.1, 46.5; Group difference, P=0.61 (Model 1) Fish group: 45.1, 95% CI: 41.8, 48.4 Meat group: 44.2, 95% CI: 41.0, 47.4; Group difference, P=0.70 (Model 2) **Fish group: 46.7, 95% CI: 44.0, 49.5** **Meat group: 43.0, 95% CI: 40.4, 45.6; Group difference, P=0.035 (Model 3)**
Hysing, 2018[4] **Randomized Controlled Trial** **FINS-KIDS; Norway** **Outcome Domains:** social-emotional/behavioral, ADD/ADHD-like traits/behaviors **Summary:** Among children 4-6y of age, consumption of fish meals 3x per week for 16 weeks did not result in more beneficial changes in emotional, conduct, peer, and total problems, and hyperactivity/inattention compared to meat meals 3x/week for 16 weeks. **Intervention Compliance:** Mean=44 study meals, SD=4; Total fish or meat consumed: Fish group: Mean=2070 g, SD=978 Meat group: Mean=2675 g, SD=850 (P<0.0001 between groups) **Baseline Seafood Intake:** Mean=1.7 meals of fish/wk, SD=0.9	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=81) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=89) **Age at intervention:** 4-6y	*Higher scores on the Strengths and Difficulties Questionnaire (SDQ) indicates greater emotional problems, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behavior.* **SDQ score change:** Between-group differences in pre- to post-intervention change **Model adjustments:** Model 1: Pre-intervention scores; Model 2: model 1 + dietary compliance **Age at outcome:** 4-6y **Total problems** Fish: 0.22, 95% CI: -0.47, 0.91 Meat: -0.37, 95% CI: -1.03, 0.30; Group difference, P=0.19 (Model 1) Fish: 0.29, 95% CI: -0.41, 0.99 Meat: -0.44, 95% CI: -1.11, 0.24; Group difference, P=0.13 (Model 2) **Emotional problems** Fish: -0.02, 95% CI: -0.29, 0.24 Meat: -0.08, 95% CI: -0.33, 0.17; Group difference, P=0.77 (Model 1) Fish: 0.02, 95% CI: -0.03*, 0.28 Meat: -0.11, 95% CI: -0.37, 0.14; Group difference, P=0.51 (Model 2) *Possibly an error in reporting

Article	Intervention	Outcome and Results (statistically significant results bolded)
Hysing, 2018 (CONTINUED) **Randomized Controlled Trial** **FINS-KIDS; Norway**	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=81) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=89) **Age at intervention:** 4-6y	**(CONTINUED)** **SDQ score change:** Between-group differences in pre- to post-intervention change **Model adjustments:** Model 1: Pre-intervention scores; Model 2: model 1 + dietary compliance **Age at outcome:** 4-6y **Conduct problems** Fish: 0.04, 95% CI: -0.22, 0.30 Meat: -0.07, 95% CI: -0.32, 0.18; Group difference, P=0.50 (Model 1) Fish: 0.05, 95% CI: -0.22, 0.31 Meat: -0.08, 95% CI: -0.33, 0.18; Group difference, P=0.48 (Model 2) **Hyperactivity/inattention** Fish: 0.10, 95% CI: -0.23, 0.42 Meat: -0.03, 95% CI: -0.35, 0.28; Group difference, P=0.54 (Model 1) Fish: 0.09, 95% CI: -0.25, 0.42 Meat: -0.02, 95% CI: -0.35, 0.31; Group difference, P=0.64 (Model 2) **Peer problems** Fish: 0.07, 95% CI: -0.15, 0.29 Meat: -0.16, 95% CI: -0.37, 0.05; Group difference, P=0.14 (Model 1) Fish: 0.11, 95% CI: -0.12, 0.34 Meat: -0.19, 95% CI: -0.41, 0.02; Group difference, P=0.06 (Model 2) Sub-analyses which included only participants with high total problem scores (>80th percentile) were also NS

Article	Intervention	Outcome and Results (statistically significant results bolded)
Oyen, 2018[10] **Randomized Controlled Trial** **FINS-KIDS; Norway** **Outcome Domains:** cognitive, language/communication, movement/physical **Summary:** Serving herring and mackerel 3x per week for 16 weeks to kindergarten children did not impact cognitive function measured by WPPSI-III but did significantly improve fine motor coordination in the non-dominant hand measured by the 9-HPT. After adjusting for treatment compliance interaction, herring and mackerel intake at 5y was significantly associated with improved total and processing speed raw scores and word reasoning, coding and symbol search sub-tests. **Intervention Compliance:** Study meals served: Mean=44.0, SD=4.0 Intake by group: Total meat intake: Mean=2675 g, SD=850 Total fish intake: Mean=2070 g, SD=978 P<0.0001 **Baseline Seafood Intake:** Background diet, dietary intake from FFQ Seafood as dinner ~1.7 meals/wk Mackerel as dinner 0.1 meals/wk Herring as dinner 0.0 meals/wk Fish as bread spread ~1.3 meals/wk	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=105) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=113) **Age at intervention:** 4-6y	*Higher scores on the Wechsler Primary Scales of Intelligence (WPPSI-III) indicate better child cognitive development* **WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Model 1: Pre-intervention score and age; Model 2: model 1 + compliance (amount of fish/meat consumed); Model 3: model 1 + interaction between treatment (intervention group) and compliance **Age at outcome:** 4-6y **WPPSI-III Total raw score change** Fish group: 17.7, 95% CI: 14.8, 20.7 Meat group: 17.8, 95% CI: 15.0, 20.6; Group difference: P=0.97 (Model 1) **Fish group: 20.4, 95% CI: 17.5, 23.3** **Meat group: 15.2, 95% CI: 12.4, 18.0; Group difference: P=0.01 (Model 2)** Fish group: 21.9, 95% CI: 19.4, 24.5 Meat group: 17.2, 95% CI: 14.7, 19.8; Group difference: NR (Model 3) **WPPSI-III Performance raw score change** Fish group: 6.0, 95% CI: 4.7, 7.3 Meat group: 5.6, 95% CI: 4.4, 6.8; Group difference: P=0.65 (Model 1) Fish group: 6.4, 95% CI: 5.2, 7.7 Meat group: 5.2, 95% CI: 4.0, 6.4; Group difference: P=0.16 (Model 2) Fish group: 6.6, 95% CI: 5.4, 7.9 Meat group: 5.4, 95% CI: 4.2, 6.6; Group difference: NR (Model 3) **WPPSI-III Processing speed raw score change** Fish group: 8.1, 95% CI: 5.9, 10.3 Meat group: 7.8, 95% CI: 5.7, 9.9; Group difference: P=0.83 (Model 1) Fish group: 9.3, 95% CI: 7.1, 11.4 Meat group: 6.7, 95% CI: 4.6, 8.8; Group difference: P=0.10 (Model 2) Fish group: 10.5, 95% CI: 8.4, 12.5 Meat group: 8.0, 95% CI: 6.0, 10.0; Group difference: NR (Model 3)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Oyen, 2018 (CONTINUED) **Randomized Controlled Trial** **FINS-KIDS; Norway**	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=105) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=113) **Age at intervention:** 4-6y	**(CONTINUED)** **WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Model 1: Pre-intervention score and age; Model 2: model 1 + compliance (amount of fish/meat consumed); Model 3: model 1 + interaction between treatment (intervention group) and compliance **Age at outcome:** 4-6y **Verbal raw score change** Fish group: 3.8, 95% CI: 2.6, 5.0 Meat group: 4.3, 95% CI: 3.1, 5.4; Group difference: P=0.59 (Model 1) Fish group: 4.7, 95% CI: 3.6, 5.8 Meat group: 3.4, 95% CI: 2.4, 4.5; Group difference: P=0.11 (Model 2) Fish group: 4.9, 95% CI: 3.8, 6.1 Meat group: 3.7, 95% CI: 2.6, 4.8; Group difference: NR (Model 3) **WPPSI-III Information Sub-test raw score change** Fish group: 1.0, 95% CI: 0.6, 1.4 Meat group: 1.1, 95% CI: 0.8, 1.5; Group difference: P=0.63 (Model 1) Fish group: 1.1, 95% CI: 0.7, 1.4 Meat group: 1.0, 95% CI: 0.7, 1.4; Group difference: P=0.90 (Model 2) Fish group: 1.1, 95% CI: 0.7, 1.4 Meat group: 1.0, 95% CI: 0.7, 1.4; Group difference: NR (Model 3) **WPPSI-III Vocabulary Sub-test raw score change** Fish group: 1.1 95% CI: 0.3, 1.9 Meat group: 1.1, 95% CI: 0.4, 1.9; Group difference: P=0.99 (Model 1) **Fish group: 1.7, 95% CI: 0.9, 2.4** **Meat group: 0.6, 95% CI: -0.1, 1.3; Group difference: 0.047 (Model 2)** Fish group: 1.7 95% CI: 1.0, 2.5 Meat group: 0.7, 95% CI: −0.1, 1.4; Group difference: NR (Model 3)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Oyen, 2018 (CONTINUED) **Randomized Controlled Trial** **FINS-KIDS; Norway**	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=105) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=113) **Age at intervention:** 4-6y	**(CONTINUED)** **WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Model 1: Pre-intervention score and age; Model 2: model 1 + compliance (amount of fish/meat consumed); Model 3: model 1 + interaction between treatment (intervention group) and compliance **Age at outcome:** 4-6y **WPPSI-III Word Reasoning Sub-test raw score change** Fish group: 1.8, 95% CI: 1.1, 2.4 Meat group: 2.1, 95% CI: 1.4, 2.7; Group difference: P=0.50 (Model 1) Fish group: 2.0, 95% CI: 1.4, 2.7 Meat group: 1.8, 95% CI: 1.1, 2.4; Group difference: P=0.54 (Model 2) Fish group: 2.2, 95% CI: 1.5, 2.8 Meat group: 1.9, 95% CI: 1.3, 2.6; Group difference: NR (Model 3) **WPPSI-III Block Design Sub-test raw score change** Fish group: 1.7, 95% CI: 1.3, 2.1 Meat group: 1.1, 95% CI: 0.7, 1.6; Group difference: P=0.07 (Model 1) **Fish group: 1.8, 95% CI: 1.3, 2.2** **Meat group: 1.1, 95% CI: 0.6, 1.5; Group difference: P=0.02 (Model 2)** Fish group: 1.9, 95% CI: 1.4, 2.3 Meat group: 1.1, 95% CI: 0.7, 1.6; Group difference: NR (Model 3) **WPPSI-III Matrix Reasoning Sub-test raw score change** Fish group: 2.5, 95% CI: 1.8, 3.1 Meat group: 2.2, 95% CI: 1.6, 3.1; Group difference: P=0.52 (Model 1) Fish group: 2.5, 95% CI: 1.8, 3.2 Meat group: 2.2, 95% CI: 1.5, 2.8; Group difference: P=0.48 (Model 2) Fish group: 2.5, 95% CI: 1.8, 3.2 Meat group: 2.2, 95% CI: 1.5, 2.8; Group difference: NR (Model 3)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Oyen, 2018 (CONTINUED) **Randomized Controlled Trial** **FINS-KIDS; Norway**	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=105) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=113) **Age at intervention:** 4-6y	**(CONTINUED)** **WPPSI-III raw score change:** Between-group differences in pre- to post-intervention raw score change **Model adjustments:** Model 1: Pre-intervention score and age; Model 2: model 1 + compliance (amount of fish/meat consumed); Model 3: model 1 + interaction between treatment (intervention group) and compliance **Age at outcome:** 4-6y **WPPSI-III Picture Concepts Sub-test raw score change** Fish group: 2.1, 95% CI: 1.1, 3.0 Meat group: 2.0, 95% CI: 1.1, 2.9; Group difference: P=0.91 (Model 1) Fish group: 2.4, 95% CI: 1.4, 3.3 Meat group: 1.7, 95% CI: 0.8, 2.6; Group difference: P=0.26 (Model 2) Fish group: 2.4, 95% CI: 1.5, 3.3 Meat group: 1.8, 95% CI: 0.9, 2.7; Group difference: NR (Model 3) **WPPSI-III Coding Sub-test raw score change** Fish group: 4.5, 95% CI: 2.9, 6.2 Meat group: 5.2, 95% CI: 3.6, 6.8; Group difference: P=0.58 (Model 1) Fish group: 5.4, 95% CI: 3.8, 7.0 Meat group: 4.4, 95% CI: 2.9, 6.0; Group difference: P=0.41 (Model 2) Fish group: 6.2, 95% CI: 4.6, 7.7 Meat group: 5.3, 95% CI: 3.8, 6.8; Group difference: NR (Model 3) **WPPSI-III Symbol Search Sub-test raw score change** Fish group: 3.6, 95% CI: 2.7, 4.5 Meat group: 2.6, 95% CI: 1.7, 3.5; Group difference: P=0.12 (Model 1) **Fish group: 3.9, 95% CI: 3.0, 4.8** **Meat group: 2.3, 95% CI: 1.4, 3.2, Group difference: P=0.02 (Model 2)** Fish group: 4.2, 95% CI: 3.3, 5.1 Meat group: 2.6, 95% CI: 1.7, 3.5; Group difference: NR (Model 3)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Oyen, 2018 (CONTINUED) **Randomized Controlled Trial** **FINS-KIDS; Norway**	Fish meal (50-80 g herring/mackerel) 3x/wk for 16wk (n=105) vs Meat meal (50-80 g chicken/lamb/beef) 3x/wk for 16 wk (n=113) **Age at intervention:** 4-6y	*Faster time on the 9-hole peg test (9-HPT) indicates better child fine manual dexterity and fine motor coordination* **9-HPT score change:** Between-group differences in pre- to post-intervention score change **Model adjustments:** Model 1: Pre-intervention score and age; Model 2: model 1 + compliance; Model 3: model 1 + interaction between treatment (intervention group) and compliance **Age at outcome:** 4-6y **9-HPT score change, dominant hand** Fish group: -2.7, 95% CI: −3.6, −1.8 Meat group: -1.8, 95% CI: −2.7, −1.0; Group difference: P=0.19 (Model 1) Fish group: -2.8, 95% CI: −3.7, −1.9 Meat group: -1.7, 95% CI: −2.6, −0.8; Group difference: P=0.09 (Model 2) Fish group: -2.9, 95% CI: −3.8, −1.9 Meat group: -1.8, 95% CI: −2.7, −0.8; Group difference: NR (Model 3) **9-HPT score change, non-dominant hand** **Fish group: -4.2, 95% CI: −5.3, −3.2** **Meat group: −2.7, 95% CI: −3.8, −1.7; Group difference, P=0.047 (Model 1)** **Fish group: -4.5, 95% CI: −5.6, −3.4** **Meat group: −2.5, 95% CI: −3.5, −1.4; Group difference, P=0.01 (Model 2)** Fish group: -4.8, 95% CI: −5.9, −3.6 Meat group: −2.8, 95% CI: −3.9, −1.7; Group difference: NR (Model 3)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Handeland, 2017[3] **Randomized Controlled Trial** **FINS-TEENS; Norway** **Outcome Domains:** cognitive **Summary:** Children who consumed fish meals 3x/wk for 12 weeks had improved processing speed, compared to the meat group. The meat group had greater decreases in the incidence rate ratio of omission errors compared to the fish group, but was no longer significant after adjusting for dietary compliance. No significant differences between groups were observed for concentration performance, commission errors, and total errors. **Intervention Compliance:** Percent of participants who consumed at least half of fish/meat: 38% fish group, 66% meat group **Baseline Seafood Intake:** Mean intake of fish for dinner at baseline: 1.5 meals/wk, SD=1.0	Fish meals (80-100 g salmon, mackerel, or herring) 3x/wk for 12wk (Ref, n=137) vs Meat meals (80-100 g chicken, turkey, beef, lamb, or cheese) 3x/wk for 12wk (n=148) **Age at intervention:** Mean=14.6y, SD=0.3	*Higher scores on the concentration performance, total performance, and processing speed scores on the d2 test of attention indicate better attention and mental concentration. Lower incidence rate ratios (IRR) for omission error, commission errors, and total errors on the d2 test of attention indicate better attention and mental concentration.* **d2 test of attention score change:** Between-group differences in pre- to post-intervention change (IRR = Difference between treatment groups, IRR < 1 indicates larger decrease in error rate compared to the Ref group) **Model adjustments:** Model 1: Baseline score; Model 2: model 1 + dietary compliance **Age at outcome:** 14-15y **d2 Test of attention - Concentration performance** Fish (Ref) vs Meat: -2.3, 95% CI: -6.8, 2.2, P=0.32 (Model 1) Fish (Ref) vs Meat: -3.4, 95% CI: -8.2, 1.3, P=0.16 (Model 2) **d2 Test of attention - Total performance** Fish (Ref) vs Meat: -7.9, 95% CI: -17.4, 1.6, P=0.10 (Model 1) Fish (Ref) vs Meat: -10.0, 95% CI: -20.1, 0.0, P=0.05 (Model 2) **d2 Test of attention - Processing speed** **Fish (Ref) vs Meat: -11.8, 95% CI: -23.3, -0.4, P=0.04 (Model 1)** **Fish (Ref) vs Meat: -13.3, 95% CI: -25.5, -1.2, P=0.03 (Model 2)** **d2 Test of attention - Omission errors** **Fish (Ref) vs Meat: IRR: 0.85, 95% CI: 0.74, 0.98, P=0.03 (Model 1)** Fish (Ref) vs Meat: IRR: 0.88, 95% CI: 0.76, 1.02, P=0.08 (Model 2) **d2 Test of attention - Commission errors** Fish (Ref) vs Meat: IRR: 0.91, 95% CI: 0.59, 1.39, P=0.65 (Model 1) Fish (Ref) vs Meat: IRR: 0.92, 95% CI: 0.60, 1.40, P=0.68 (Model 2) **d2 Test of attention - Total errors** Fish (Ref) vs Meat: IRR: 0.88, 95% CI: 0.75, 1.02, P=0.09 (Model 1) Fish (Ref) vs Meat: IRR: 0.91, 95% CI: 0.77, 1.07, P=0.25 (Model 2) Adjustment for parental education level, home use of n-3 supplements, and fatty fish intake (dinner and bread spread) at baseline did not affect the results (Data NR)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Skotheim, 2017[11] **Randomized Controlled Trial** **FINS-TEENS; Norway** **Outcome Domains:** social-emotional/behavioral, ADD/ADHD-like traits or behaviors **Summary:** Consumption of 3 lunches/wk containing 90 g fatty fish for 12 weeks did not improve self-reported behavioral symptoms (SDQ), compared to consumption of 3 lunches/wk containing 90 g meat. Among a small sub-sample with high SDQ scores at baseline, the fish group had smaller improvements in total difficulties and emotional problems scores compared to the meat group. **Intervention Compliance:** Dietary compliance (proportion of participants who consumed at least half of the meals): Fish group 38%, Meat group 66% **Seafood Intake:** Seafood for dinner (unit NR): Mean=4.1, SD=0.95; once/week for dinner	Fish meals (80-100 g salmon, mackerel, or herring) 3x/wk for 12wk (Ref; n=137) vs Meat meals (80-100 g chicken, turkey, beef, or cheese) 3x/wk for 12wk (n=145) Total N=425 **Age at intervention:** Mean=14.6y, SD=0.34	*Decrease in Strengths and Difficulties Questionnaire (SDQ) total difficulties and subscale scores (except prosocial) indicate improvement in self-reported behavioral symptoms* **SDQ score change:** Between-group differences in pre- to post-intervention change **Model adjustments:** Model 1: Baseline SDQ score; Model 2: model 1 + compliance **Age at outcome:** 14-15y **SDQ Total difficulties score change** Fish (Ref): Mean: -0.11, 95% CI: -0.65, 0.44 Meat: Mean: -0.33, 95% CI: -0.90, 0.20; Group difference, P=0.57 (Model 1) Fish (Ref): Mean: -0.12, 95% CI: -0.72, 0.48 Meat: Mean: -0.32, 95% CI: -0.85, 0.21; Group difference, P=0.62 (Model 2) **SDQ Emotional problems score change** Fish (Ref): Mean: 0.07, 95% CI: -0.18, 0.31 Meat: Mean: 0.03, 95% CI: -0.21, 0.27; Group difference, P=0.83 (Model 1) Fish (Ref): Mean: 0.12, 95% CI: -0.15, 0.39 Meat: Mean: 0.02, 95% CI: -0.22, 0.26; Group difference, P=0.61 (Model 2) **SDQ Conduct problems score change** Fish (Ref): Mean: -0.07, 95% CI: -0.27, 0.14 Meat: Mean: -0.27, 95% CI: -0.47, -0.07; Group difference, P=0.13 (Model 1) Fish (Ref): Mean: -0.08, 95% CI: -0.30, 0.14 Meat: Mean: -0.27, 95% CI: -0.47, -0.07; Group difference, P=0.19 (Model 2) **SDQ Hyperactivity/inattention score change** Fish (Ref): Mean: -0.10, 95% CI: -0.34, 0.16 Meat: Mean: 0.10, 95% CI: -0.15, 0.35; Group difference, P=0.28 (Model 1) Fish (Ref): Mean: -0.17, 95% CI: -0.44, 0.11 Meat: Mean: 0.11, 95% CI: -0.14, 0.35; Group difference, P=0.14 (Model 2) **SDQ Peer problems score change** Fish (Ref): Mean: -0.02, 95% CI: -0.22, 0.17 Meat: Mean: -0.16, 95% CI: -0.35, 0.03; Group difference, P=0.31 (Model 1) Fish (Ref): Mean: -0.03, 95% CI: -0.24, 0.18 Meat: Mean: -0.16, 95% CI: -0.35, 0.03; Group difference, P=0.37 (Model 2)

Article	Intervention	Outcome and Results (statistically significant results bolded)
Skotheim, 2017 (CONTINUED) **Randomized Controlled Trial** **FINS-TEENS; Norway**	Fish meals (80-100 g salmon, mackerel, or herring) 3x/wk for 12wk (Ref; n=137) vs Meat meals (80-100 g chicken, turkey, beef, or cheese) 3x/wk for 12wk (n=145) Total N=425 **Age at intervention:** Mean=14.6y, SD=0.34	**(CONTINUED)** **SDQ score change:** Between-group differences in pre- to post-intervention change **Model adjustments:** Model 1: Baseline SDQ score; Model 2: model 1 + compliance **Age at outcome:** 14-15y **SDQ Prosocial behaviour score change** Fish (Ref): Mean: -0.02, 95% CI: -0.25, 0.22 Meat: Mean: -0.03, 95% CI: -0.26, 0.19, P=0.93 (Model 1) Fish (Ref): Mean: 0.10, 95% CI: -0.16, 0.36 Meat: Mean: -0.04, 95% CI: -0.27, 0.19; Group difference, P=0.42 (Model 2)
	Subset of children with high SDQ scores at baseline (defined as those who scored at or above the 80th percentile based on Norwegian cut-off points: ≥15 on total difficulties, ≥5 on emotional symptoms, ≥4 on conduct problems, ≥6 on hyperactivity/inattention symptoms, and ≥4 on peer problems; ≤5 on prosocial behavior) Fish meals (80-100 g salmon, mackerel, or herring) 3x/wk for 12wk (Ref; n=13-33) vs Meat meals 3x/wk for 12wk (n=18-31) Total N (range: 44-93) varied by SDQ scale **Age at intervention:** Mean=14.6y, SD=0.34	**SDQ score change:** Between-group differences in pre- to post-intervention change **Model adjustments:** Model 1: Baseline SDQ score; Model 2: model 1 + compliance **Age at outcome:** 14-15y **SDQ Total difficulties score change** **Fish (Ref): Mean: -1.54, 95% CI: -3.01, 0.08** **Meat: Mean: -4.11, 95% CI: -5.55, -2.67; Group difference, P=0.02 (Model 1)** Fish (Ref): Mean: -1.88, 95% CI: -3.60, -0.15 Meat: Mean: -4.10, 95% CI: -5.54, -2.65; Group difference, P=0.06 (Model 2) **SDQ Emotional problems score change** **Fish (Ref): Mean: -0.31, 95% CI: -0.92, 0.30** **Meat: Mean: -1.20, 95% CI: -1.75, -0.64; Group difference, P=0.04 (Model 1)** **Fish (Ref): Mean: -0.21, 95% CI: -0.89, 0.47** **Meat: Mean: -1.20, 95% CI: -1.76, -0.63; Group difference, P=0.03 (Model 2)**

Article	Intervention	Outcome and Results (statistically significant results bolded)
Skotheim, 2017 (CONTINUED) **Randomized Controlled Trial** **FINS-TEENS; Norway**	**Subset of children with high SDQ scores at baseline** (defined as those who scored at or above the 80th percentile based on Norwegian cut-off points: ≥15 on total difficulties, ≥5 on emotional symptoms, ≥4 on conduct problems, ≥6 on hyperactivity/inattention symptoms, and ≥4 on peer problems; ≤5 on prosocial behavior) Fish meals (80-100 g salmon, mackerel, or herring) 3x/wk for 12wk (Ref; n=13-33) vs Meat meals (80-100 g chicken, turkey, beef, or cheese) 3x/wk for 12wk (n=18-31) Total N (range: 44-93) varied by SDQ scale **Age at intervention:** Mean=14.6y, SD=0.34	**(CONTINUED)** **SDQ score change:** Between-group differences in pre- to post-intervention change **Model adjustments:** Model 1: Baseline SDQ score; Model 2: Model 1 + compliance **Age at outcome:** 14-15y **SDQ Conduct problems score change** Fish (Ref): Mean: -1.64, 95% CI: -2.39, -0.89 Meat: Mean: -1.53, 95% CI: -2.16, -0.91; Group difference, P=0.83 (Model 1) Fish (Ref): Mean: -1.38, 95% CI: -2.23, -0.48 Meat: Mean: -1.56, 95% CI: -2.19, -0.93; Group difference, P=0.75 (Model 2) **SDQ Hyperactivity/inattention score change** Fish (Ref): Mean: -0.90, 95% CI: -1.44, -0.37 Meat: Mean: -0.44, 95% CI: -0.99, 0.11; Group difference, P=0.23 (Model 1) Fish (Ref): Mean: -0.88, 95% CI: -1.50, -0.26 Meat: Mean: -0.44, 95% CI: -1.00, 0.12; Group difference, P=0.28 (Model 2) **SDQ Peer problems score change** Fish (Ref): Mean: -1.47, 95% CI: -2.28, -0.65 Meat: Mean: -1.95, 95% CI: -2.70, -1.20; Group difference, P=0.78 (Model 1) Fish (Ref): Mean: -1.26, 95% CI: -2.15, -0.38 Meat: Mean: -1.95, 95% CI: -2.69, -1.22; Group difference, P=0.72 (Model 2) **SDQ Prosocial behaviour score change** Fish (Ref): Mean: 0.84, 95% CI: 0.15, 1.52 Meat: Mean: 1.05, 95% CI: 0.35, 1.75; Group difference, P=0.63 (Model 1) Fish (Ref): Mean: 0.88, 95% CI: 0.15, 1.61 Meat: Mean: 1.06, 95% CI: 0.35, 1.77; Group difference, P=0.69 (Model 2)

[iv] Abbreviations: CI – confidence interval, d – day(s), g – gram(s), IQR – interquartile range, IRR – incidence rate ratios, mo – month(s), NR – not reported, Ref – reference group, SD – standard deviation, SES – socioeconomic status, wk – week(s), x – time(s), y – year(s)

Table 3. Results of prospective cohort studies that examined the relationship between seafood consumption during childhood and adolescence and neurocognitive development[v]

Article	Exposure	Outcome and Results (statistically significant results bolded)
Aberg, 2009[1] **Prospective Cohort Study** **Sweden** **Outcome Domains:** cognitive, language/communication **Summary:** Fish intake once per week or greater, when compared to less than once per week, at age 15y in males was associated with higher cognitive performance at age 18y. **Baseline Seafood Intake:** Frequency of seafood intake: <once/wk 22.7%, once/wk 56.6%, >once/wk 20.2%	Frequency of fish consumption (meals containing fish): <once/wk (Ref) vs once/wk vs >once/wk Total N=3,972; N by intake group NR **Age at exposure:** 15y	*Higher scores on the Swedish military service conscription examination intelligence test indicate better performance.* **Intelligence scores:** Between-group differences in intelligence test scores **Model adjustments:** Parent's education, type and place of residence, ethnicity, socioeconomic variable (own dishwasher), BMI, frequency of exercise. **Age at outcome:** 18y **Combined intelligence score, Group differences** **<once/wk (Ref) vs once/wk: B: 0.36, 95% CI: 0.21, 0.51** **<once/wk (Ref) vs >once/wk: B: 0.58, 95% CI: 0.39, 0.77** **Verbal score, Group differences** **<once/wk (Ref) vs once/wk: B: 0.20 95% CI: 0.05, 0.34** **<once/wk (Ref) vs > once/wk: B: 0.46, 95% CI: 0.29, 0.64** **Visuospatial score, Group differences** **<once/wk (Ref) vs once/wk: B: 0.33, 95% CI: 0.18, 0.48** **<once/wk (Ref) vs > once/wk: B: 0.51, 95% CI: 0.32, 0.69**
Kim, 2010[5] **Prospective Cohort Study** **Sweden, Allergy 2000** **Outcome Domain:** academic performance **Summary:** Fish consumption among school children aged 15 years was significantly associated with higher cumulative school grades at 16 years. **Baseline Seafood Intake:** Fish consumption: <1x/wk 24.2%, ~1x/wk 56.5%, >1x/wk 19.3%	Fish consumption <1x/wk (Ref; n=2,283) vs 1x/wk (n=5,341) vs >1x/wk (n=1,824) Total N=9,448 **Age at exposure:** 15y	*Higher school grades indicate better academic performance.* **Total school grade:** Between-group differences in total school grade **Model adjustments:** Gender, foreign descent, parents' education, BMI, type of housing, residence area, dishwasher ownership, physical exercise during free time. **Age at outcome:** 16y **Total school grade, Group differences** **<1x/wk (Ref) vs 1x/wk: 14.5, 95% CI:11.8, 17.1, P<0.0001** **<1x/wk (Ref) vs >1x/wk: 19.9, 95% CI: 16.5, 23.3, P<0.0001**

Article	Exposure	Outcome and Results (statistically significant results bolded)
Kim, 2010 (CONTINUED) **Prospective Cohort Study** **Sweden, Allergy 2000**	Fish consumption <1x/wk (Ref) vs 1x/wk vs >1x/wk Stratified by parents' education (elementary school, secondary modern school, or college/university) Total N=9,448 **Age at exposure:** 15y	**Total school grade:** Between-group differences in total school grade **Model adjustments:** Gender, foreign descent, parents' education, BMI, type of housing, residence area, dishwasher ownership, physical exercise during free time. Stratified by parents' education (elementary school, secondary modern school, or college/university) **Age at outcome:** 16y **Total school grade, Stratified by parental education, Group differences** **Parental education: elementary school** **<1x/wk (Ref) vs 1x/wk: B: 12.5 95% CI: 2.9, 22.0, P<0.01** **<1x/wk (Ref) vs >1x/wk: B: 21.1 95% CI: 5.9, 36.2, P<0.0001** **Parental education: secondary modern school** **<1x/wk (Ref) vs 1x/wk: B: 15.4 95% CI: 11.7, 19.1, P<0.0001** **<1x/wk (Ref) vs >1x/wk: B: 21.5 95% CI: 16.5, 26.6, P<0.0001** **Parental education: college/university** **<1x/wk (Ref) vs 1x/wk: B: 13.7 95% CI: 9.4, 17.9, P<0.0001** **<1x/wk (Ref) vs >1x/wk: B: 18.7 95% CI: 13.8, 23.7, P<0.0001**
	Fish consumption <1x/wk (Ref) vs 1x/wk vs >1x/wk Stratified by child gender Total N=9,448 **Age at exposure:** 15y	**Total school grade:** Between-group differences in total school grade **Model adjustments:** Gender, foreign descent, parents' education, BMI, type of housing, residence area, dishwasher ownership, physical exercise during free time. Stratified by child gender **Age at outcome:** 16y **Total school grade, Boys, Group differences** **<1x/wk (Ref) vs 1x/wk: B: 14.6, 95% CI: 10.8, 18.5, P<0.0001** **<1x/wk (Ref) vs >1x/wk: B: 18.6, 95% CI: 13.9, 23.4, P<0.0001** **Total school grade, Girls, Group differences** **<1x/wk (Ref) vs 1x/wk: B: 14.1, 95% CI: 10.4, 17.9, P<0.0001** **<1x/wk (Ref) vs >1x/wk: B: 21.7, 95% CI: 16.9, 26.6, P<0.0001**

Article	Exposure	Outcome and Results (statistically significant results bolded)
Liu, 2017[7] **Prospective Cohort Study** **China, China Jintan Child Cohort Study** **Outcome Domains:** cognitive, language/communication **Summary:** More frequent fish intake at 9-11y of age (sometimes, often vs never or seldom) was associated with better performance on the WISC-R full scale, verbal, and performance IQ. These associations were partially mediated by sleep quality at 9-11y of age. **Baseline Seafood Intake:** Fish intake frequency: Never or seldom 16.5%, Sometimes 58.2%, Often 25.3%	Fish intake frequency: Never or seldom [<2x/mo] (Ref, n=89) vs Sometimes [2-3x/mo] (n=315) vs Often [≥once/wk] (n=137) Total N=541 **Age at exposure:** Range: 9-11y	*Higher scores on the Wechsler Intelligence Scales for Children, Revised (WISC-R Chinese version) Full scale, verbal, and performance IQ indicate greater child development* **WISC-R scores:** Between-group differences in WISC-R scores **Model adjustments:** Model 1: Child gender, father's education, mother's education, siblings, home location, breakfast consumption habits; Model 2: Model 1 + total sleep disturbance **Age at outcome:** Mean~12y **Full scale IQ, Group difference**s **Never or seldom (Ref) vs Sometimes: B: 3.31, SE: 1.45, Cohen's d: 0.567, P=0.023 (Model 1)** **Never or seldom (Ref) vs Often: B: 4.80, SE: 1.63, Cohen's d: 0.347, P=0.003 (Model 1)** *(fish intake - full scale IQ association partially mediated by sleep quality)* Never or seldom (Ref) vs Sometimes: B: 1.81, SE: 1.95, P=0.354 (Model 2) Never or seldom (Ref) vs Often: B: 3.64, SE: 2.13, P=0.088 (Model 2) **Verbal IQ, Group differences** **Never or seldom (Ref) vs Sometimes: B: 2.92, SE: 1.39, Cohen's d: 0.595, P=0.036 (Model 1)** **Never or seldom (Ref) vs Often: B: 4.75, SE: 1.55, Cohen's d: 0.317, P=0.002 (Model 1)** Never or seldom (Ref) vs Sometimes: B: 0.84, SE: 1.83, P=0.648 (Model 2) Never or seldom (Ref) vs Often: B: 1.84, SE: 2.00, P=0.359 (Model 2) *(fish intake - verbal IQ association partially mediated by sleep quality)* **Performance IQ, Group differences** Never or seldom (Ref) vs Sometimes: B: 2.52, SE: 1.51, Cohen's d: 0.416, P=0.097 (Model 1) **Never or seldom (Ref) vs Often: B: 3.79, SE: 1.69, Cohen's d: 0.236, P=0.026 (Model 1)** Never or seldom (Ref) vs Sometimes: B:2.39, SE: 2.01, P=0.236 (Model 2) **Never or seldom (Ref) vs Often: B: 5.31, SE: 2.20, P=0.016** (Model 2) *(fish intake - performance IQ association not mediated by sleep quality)*

Article	Exposure	Outcome and Results (statistically significant results bolded)
McMartin, 2012[8] **Prospective Cohort Study** **Canada, Children's Lifestyle and School Performance Study (CLASS)** **Outcome Domains:** depression, anxiety **Summary:** Higher fish intake, compared to lower fish intake, at ~10-11y was associated with lower risk of receiving an internalizing disorder diagnosis during the following ~3y **Baseline Seafood Intake:** NR	Child fish intake in tertiles: First (lowest) tertile (Ref) vs Second tertile vs Third (highest) tertile N=3,757 (N by intake tertile NR) **Age at exposure:** Range: ~10-11y	**Diagnosis of internalizing disorder:** Between-group differences (IRR) in diagnosis of an internalizing disorder **Model adjustments:** Energy intake, gender, household income, parental marital status, parental education, body weight status, physical activity level, geographic area **Age at outcome:** Range: ~10-14y **Diagnosis of Internalizing Disorder, Incidence Rate Ratio** First (lowest) vs Second tertile: IRR: 0.88, 95% CI: 0.56, 1.39 **First (lowest) vs Third (highest) tertile: IRR: 0.59, 95% CI: 0.41, 0.87**
Mesirow, 2017[9] **Prospective Cohort Study** **U.K., ALSPAC** **Outcome Domains:** social-emotional/behavioral **Summary:** There was no significant interaction between child fish intake at 3y and sex and conduct problem trajectory at 4-13 years. **Baseline Seafood Intake:** Child fish intake at 3y (mean): ~1.3 servings/wk	Child fish intake (mean servings/wk) modeled continuously EOP: n=348 boys, n=268 girls Low CP: n=2,312 boys, n=2,420 girls **Age at exposure:** ~3y	*EOP CP indicates an early-onset persistent conduct problem trajectory and Low CP indicates low conduct problems based on responses to the Strengths and Difficulties Questionnaire (SDQ).* **Mean fish intake by conduct problem trajectory:** Between conduct problem trajectory group differences in mean weekly fish intake **Model adjustments:** Total energy intake, Items from the Family Adversity Index (Early parenthood, inadequate housing, inadequate basic living conditions, housing defects, low educational attainment, no partner, lack of partner affection, major family problems, large family size, maternal psychopathology, substance use, criminal history), prenatal and birth risk factors included the following: one or more birth complications (abruption, cervical suture, preterm rupture); preterm birth (<37 weeks gestation); low birth weight (<2500 g at birth); never breastfed during first 6 months postnatal; multi parity; any smoking during pregnancy **Age at outcome:** Range: 4-13y **Mean weekly fish intake at 3y by conduct problem trajectory (EOP and Low CP) and sex at 4-13y**, Group differences Boys: EOP vs Low CP: Mean=1.11, SE=0.08 vs Mean=1.21, SE=0.03 Girls: EOP vs Low CP: Mean=1.25, SE=0.09 vs Mean=1.35, SE=0.03 Conduct problem trajectory: F: 2.46, P=0.12 **Mean weekly fish intake at 3y**, Group differences EOP vs Low CP: P>0.05 (Data NR)

Article	Exposure	Outcome and Results (statistically significant results bolded)
Williams, 2001[12] **Prospective Cohort Study** **U.K., ALSPAC** **Outcome Domains:** cognitive **Summary:** Child oily fish intake ≤36mo was not associated with achievement of foveal stereoacuity at 3.5y. **Baseline Seafood Intake:** Child eats oily fish at 36mo: Yes 44.0%, No 56.0%	Child oily fish intake ≤ 36mo Yes (N~248) No (N~195) **Age at exposure:** NR	*Achievement of foveal stereoacuity indicates maturation to adult or high-grade stereoacuity and reflects greater maturity of the visual cortex.* **Stereoacuity grade:** Between-group differences in proportion of children at each grade of stereoacuity **Model adjustments:** None **Age at outcome:** Mean=3.5y, SD=0.6mo **Proportion of 3 grades of stereoacuity** at 3.5y **Foveal stereo: Yes (38.2%) vs No (33.3%)** **Macular stereo: Yes (54.5%) vs No (50.7%)** **Peripheral stereo: Yes (7.3%) vs No (16.3%)** **P=0.039, unadjusted analysis** Association between child eating oily fish and stereoacuity was not significant using logistic regression analysis (Data NR).
Winpenny, 2018[13] **Prospective Cohort Study** **U.K., ROOTS** **Outcome Domains:** depression **Summary:** There was no significant association between fish intake at 14y and depressive symptoms at 17y. **Baseline Seafood Intake:** Fish intake (Mean): 0.12 servings/d, SD: 0.20, P<0.05 between males and females Fish intake (Median): 0.0 g/d, IQR: 0.00, 24.29, P<0.04 between males and females	Child fish intake (servings/d) modeled continuously All: N=603 Male: n=241 Female: n=362 1 serving=140 grams **Age at exposure:** Mean=14.5y, SD=3.5mo	*Higher Moods and Feelings Questionnaire (MFQ) scores indicate more depressive symptoms.* **MFQ score:** Difference in MFQ score per serving/d increase in fish intake **Model adjustments:** Model: sex, SES, smoking, alcohol consumption, physical activity, sleep, friendship quality, self-esteem, family functioning, medication use, % body fat, total energy intake **Age at outcome:** Mean=17.5y, SD=4.1mo **MFQ score, Difference per serving/d increase** All: B: 2.34, 95% CI: -1.15, 5.83, P>0.05 Male: B: -0.09, 95% CI: -4.44, 4.27, P>0.05 Female: B: 4.20, 95% CI: -1.32, 9.72, P>0.05

[v] Abbreviations: B – beta, BMI – body mass index, CI – confidence interval, CP – conduct problem, d – day(s), EOP CP – early-onset persistent conduct problem, IQR – interquartile range, IRR – incidence rate ratio, mo – month(s), NR – not reported, Ref – reference group, SD – standard deviation, SE – standard error, SES – socioeconomic status, wk – week, x – time(s), y – year(s)

Table 4. Risk of bias for randomized controlled trials examining seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development[vii,viii]

	Randomization	Deviations from intended interventions: Intention-to-treat	Deviations from intended interventions: Per protocol	Missing outcome data	Outcome measurement	Selection of the reported result
Demmelmair, 2019[2]	Low	Low	Low	Low	Low	Low
Handeland, 2017[3]	Low	Low	Some concerns	Low	Low	Low
Hysing, 2018[4]	Low	Low	Low	Low	Some concerns	Low
Kvestad, 2018[6]	Low	Low	Low	Low	Low	Low
Oyen, 2018[10]	Low	Low	Low	Low	Low	Low
Skotheim, 2017[11]	Low	Low	Some concerns	Low	Some concerns	Low

Table 5. Risk of bias for observational studies examining seafood consumption during childhood and adolescence (up to 18 years of age) and neurocognitive development[ix]

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Aberg, 2009[1]	Serious	Low	Serious	Low	Moderate	Low	Moderate
Kim, 2010[5]	Serious	Low	Serious	Low	Moderate	Low	Moderate
Liu, 2017[7]	Serious	Moderate	Serious	Low	No information	Low	Moderate
McMartin, 2012[8]	Serious	Moderate	Moderate	Low	Moderate	Low	Moderate
Mesirow, 2017[9]	Serious	Serious	Moderate	Low	Low	Moderate	Moderate
Williams, 2001[12]	Serious	Low	Moderate	Low	Low	Low	Moderate
Winpenny, 2018[13]	Serious	Low	Moderate	Low	Moderate	Low	Moderate

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[vii] A detailed description of the methodology used for assessing risk of bias is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

[viii] Possible ratings of low, some concerns, or high determined using the "Cochrane Risk-of-bias 2.0" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. *Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.)

[ix] Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

METHODOLOGY

The NESR team used its rigorous, protocol-driven methodology to support the 2020 Dietary Guidelines Advisory Committee in conducting this systematic review.

NESR's systematic review methodology involves:

- Developing a protocol,
- Searching for and selecting studies,
- Extracting data from and assessing the risk of bias of each included study,
- Synthesizing the evidence,
- Developing conclusion statements,
- Grading the evidence underlying the conclusion statements, and
- Recommending future research.

A detailed description of the methodology used in conducting this systematic review is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews, and can be found in the 2020 Dietary Guidelines Advisory Committee Report, Part C: Methodology.[x] This systematic review was peer reviewed by Federal scientists, and information about the peer review process can also be found in the Committee's Report, Part C. Methodology. Additional information about this systematic review, including a description of and rationale for any modifications made to the protocol can be found in the 2020 Dietary Guidelines Advisory Committee Report, Chapter 9. Dietary Fats and Seafood.

Below are details of the final protocol for the systematic review described herein, including the:

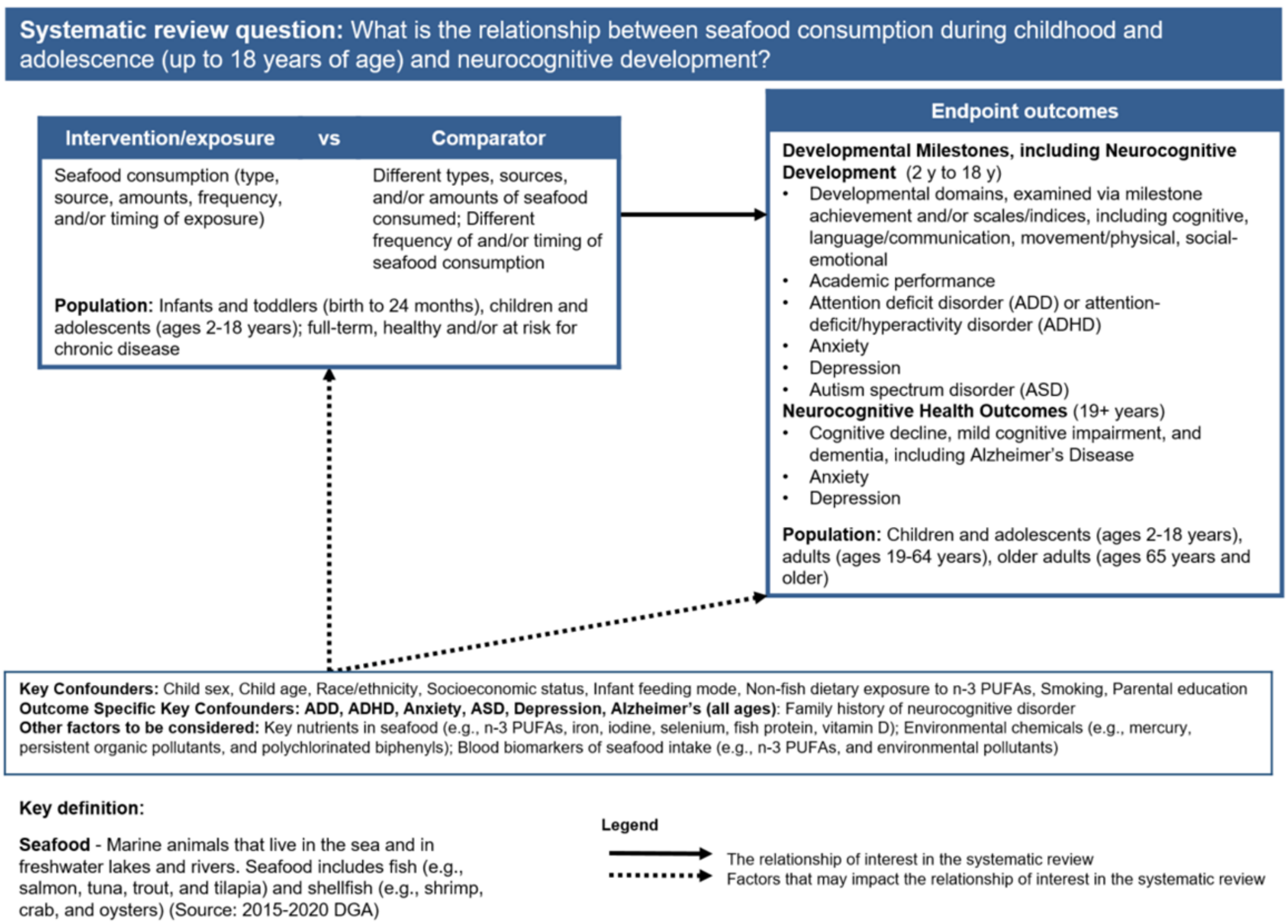
- Analytic framework
- Literature search and screening plan
- Literature search and screening results

[x] Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

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



LITERATURE SEARCH AND SCREENING PLAN

Inclusion and exclusion criteria

This table (**Table 6**) 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 6. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria
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 • Cross-sectional studies • Uncontrolled before-and-after studies • Narrative reviews • Systematic reviews • Meta-analyses
Intervention/ exposure	• Seafood consumption measured prior to outcome assessment ○ Type (e.g., salmon, tuna, bass) ○ Source (e.g., sea, fresh water, farmed, wild) ○ Amount/frequency of intake ○ Timing of exposure (e.g., age at intake) • Dietary intake (e.g., from food frequency questionnaires, dietary recall, fish/seafood screeners) may be validated with biomarkers for PUFA or methylmercury, but not substituted.	• No measure of seafood consumption (i.e., studies that only examined biomarkers for consumption) • n-3 supplement studies which do not evaluate seafood consumption • Studies evaluating infant formula with added DHA and/or EPA
Comparator	• Different types, sources, amounts, frequency, and/or timing of exposure of seafood consumption	• No comparator

Category	Inclusion Criteria	Exclusion Criteria
Outcomes	• Neurocognitive development (birth to 18 years): ○ Developmental milestones, including neurocognitive development ○ Developmental domains examined via milestone achievement and/or scales/indices, including: ▪ cognitive ▪ language/communication ▪ movement/physical ▪ social/emotional ○ Academic performance ○ Attention deficit disorder (ADD) or attention-deficit/hyperactivity disorder (ADHD) ○ Anxiety ○ Depression ○ Autism spectrum disorder (ASD) • Neurocognitive health (>18 years) ○ Cognitive decline, mild cognitive impairment, and dementia, including Alzheimer's Disease ○ Anxiety ○ Depression	• No measure of included neurocognitive development or neurocognitive health conditions
Date of publication	• January 2000 to October 2019	• Articles published prior to January 2000 or after October 2019
Publication status	• Articles that have been peer-reviewed	• Articles that have not been peer-reviewed and are not published in peer-reviewed journals, including unpublished data, manuscripts, reports, abstracts, and conference proceedings
Language of publication	• Articles published in English	• Articles published in languages other than English
Country[x]	• Studies conducted in countries ranked as high or very high human development	• Studies conducted in countries ranked as medium or lower human development
Study participants	• Human participants	• Non-human subjects (e.g., animal models or in-vitro models)

Category	Inclusion Criteria	Exclusion Criteria
Age of study participants	• Age at intervention or exposure: ○ Infants and toddlers (0-24 months) ○ Children and adolescents (2-18 years) • Age at outcome: ○ Children (2-12 years) ○ Adolescents (13-18 years) ○ Adults (ages 19-64 years) ○ Older adults (ages 65 years and older)	
Health status of study participants	• Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity • Studies that enroll **some** participants diagnosed with a disease or with the neurocognitive development and/or health outcomes of interest • Studies that enroll infants born full-term (≥37 weeks and 0/7 days gestational age) • Studies that enroll **some** infants born preterm (gestational age <37 weeks and 0/7 days), infants with low birth weight (<2500g), and/or infants born small for gestational age	• Studies that **exclusively** enroll participants diagnosed with a disease or hospitalized with an illness or injury. (For this criterion, studies that exclusively enroll participants with obesity will not be excluded.) • Studies that **exclusively** enroll participants with the neurocognitive development and/or health outcomes of interest • Studies that **exclusively** enroll infants born preterm (gestational age <37 weeks and 0/7 days), infants with low birth weight (<2500g), and/or infants born small for gestational age

[x] The Human Development classification was based on the Human Development Index (HDI) ranking (1) from the year the study intervention occurred or data were collected. 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 1990 to present. If a study was conducted in 2018 or 2019, the most current HDI classification was applied. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank (2) is used instead.

1. 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

2. 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

Listed below are the databases and search terms searched to identify all potentially relevant articles that have been published to address this systematic review question and a second systematic review question on seafood intake during pregnancy and lactation and neurocognitive development in the child.

PubMed

- Provider: U.S. National Library of Medicine
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#1 - "Pregnancy"[Mesh] OR pregnancy OR "Pregnant Women"[Mesh] OR "pregnant women" OR pregnant OR "Lactation"[Mesh] OR lactation OR "Breast Feeding"[Mesh] OR "breast feeding" OR "Maternal Health"[Mesh] OR "maternal health" OR "Prenatal Exposure Delayed Effects"[Mesh] OR "Maternal Exposure"[Mesh] OR pregnan*[tiab] OR pre-pregnancy[tiab] OR prenatal[tiab] OR maternal OR mother* OR postpartum OR perinatal OR peri-natal OR pre-conception OR preconception OR peri-conception OR periconceptional OR "Peripartum Period"[Mesh] OR peripartum[tiab] OR peri-partum[tiab] OR gestation* OR natal OR puerperium[tiab] OR "Maternal Nutritional Physiological Phenomena"[Mesh] OR "Infant"[Mesh] OR infant OR "Infant, Newborn"[Mesh] OR newborn OR baby OR babies OR "Fetus"[Mesh] OR fetus OR "Child"[Mesh] OR toddler* OR child OR children OR childhood OR "Child, Preschool"[Mesh] OR preschool OR teen* OR "Adolescent"[Mesh] OR adolescent* OR "Pediatrics"[Mesh] OR pediatric*

#2 - Seafood OR "Seafood"[Mesh] OR seafoods OR sea-food OR “sea food” OR sea-foods OR fish OR “fish consumption” OR "Fishes"[Mesh] OR fishes OR "Fish Proteins"[Mesh] OR “fish proteins” OR “fish products” OR “fish flour” OR “fatty fish” OR shellfish OR “shellfish proteins” OR “mercury poisoning” OR "Mercury Poisoning"[Mesh] OR methylmercury OR "Sharks"[Mesh] OR sharks OR swordfish OR "Tuna"[Mesh] OR tuna OR "Salmon"[Mesh] OR salmon OR sardines OR "Gadiformes"[Mesh] OR pollock OR "Flounder"[Mesh] OR flounder OR cod OR "Tilapia"[Mesh] OR tilapia OR shrimp OR "Ostreidae"[Mesh] OR oysters OR "Mya"[Mesh] OR "Bivalvia"[Mesh] OR clams OR "Pectinidae"[Mesh] OR scallops OR "Brachyura"[Mesh] OR crab OR "Perciformes"[Mesh] OR mackerel OR “Catfishes"[Mesh] OR catfishes OR "Trout"[Mesh] OR trout OR lobster OR "Decapodiformes"[Mesh] OR squid OR halibut OR “mahi mahi” OR crawfish OR anchov* OR herring OR rockfish OR marine product* OR "Fatty Acids, Omega-3"[Mesh]

#3 - "Mental Disorders"[Mesh] OR mental disorder*[tiab] OR "Cognition"[Mesh] OR cognition[tiab] OR cognitive[tiab] OR metacognition[tiab] OR neurocognitive[tiab] OR neurodevelop*[tiab] OR neurological[tiab] OR "Depression"[Mesh] OR depression[tiab] OR Alzheimer*[tiab] OR senility[tiab] OR senile[tiab] OR presenile[tiab] OR "Dementia"[Mesh] OR dementia[tiab] OR anxiety[tiab] OR "Psychomotor Performance"[Mesh] OR motor skill*[tiab] OR "Executive Function"[Mesh] OR executive function* OR attention deficit disorder*[tiab] OR ADHD[tiab] OR "Child Behavior Disorders"[Mesh] OR developmental disorder*[tiab] OR "Autism Spectrum Disorder"[Mesh] OR Autism[tiab] OR Asperger[tiab] OR language processing[tiab] OR language delay* OR "Child Development"[Mesh] OR child develop*[tiab] OR developmental delay[tiab] OR developmental disabilit*[tiab] OR motor skill*[tiab] OR "Problem Solving"[Mesh] OR developmental domain* OR academic performance[tiab] Or academic achievement[tiab] OR academic failure[tiab] OR academic success*[tiab] OR "Mental Health"[Mesh] OR mental health[tiab] OR "Mental Processes"[Mesh:NoExp]

#4 - (#1 AND #2 AND #3)

#5 - (#1 AND #2 AND #3) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti]) Filters: Publication date from 2000/01/01 to 2019/10/23; English

Cochrane Central Register of Controlled Trials (CENTRAL)

- Provider: John Wiley & Sons
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#1 - [mh "Pregnancy"] OR [mh "Pregnant Women"] OR [mh "Lactation"] OR [mh "Breast Feeding"] OR [mh "Maternal Health"] OR [mh "Prenatal Exposure Delayed Effects"] OR [mh "Maternal Exposure"] OR [mh "Peripartum Period"] OR [mh "Maternal Nutritional Physiological Phenomena"] OR [mh Infant] OR [mh "Infant, Newborn"] OR [mh Fetus] OR [mh Child] OR [mh "Child, Preschool"] OR [mh "Adolescent"] OR [mh "Pediatrics"]

#2 - (pregnan* OR lactation OR "breast feeding" OR "maternal health" OR pre-pregnancy OR prenatal OR maternal OR mother* OR postpartum OR perinatal OR peri-natal OR pre-conception OR preconception OR peri-conception OR periconceptional OR peripartum OR peri-partum OR gestation* OR natal OR puerperium OR infant OR newborn OR baby OR babies OR fetus OR toddler* OR child OR children OR childhood OR preschool OR teen* OR adolescent* OR pediatric*):ti,ab,kw

#3 - #1 OR #2

#4 - [mh "Seafood"] OR [mh "Fishes"] OR [mh "Fish Proteins"] OR [mh "Mercury Poisoning"] OR [mh "Sharks"] OR [mh "Tuna"] OR [mh "Salmon"] OR [mh "Gadiformes"] OR [mh "Flounder"] OR [mh "Tilapia"] OR [mh "Ostreidae"] OR [mh "Mya"] OR [mh "Bivalvia"] OR [mh "Pectinidae"] OR [mh "Brachyura"] OR [mh "Perciformes"] OR [mh "Catfishes"] OR [mh "Trout"] OR [mh "Decapodiformes"] OR [mh "Fatty Acids, Omega-3"]

#5 - (seafood OR seafoods OR sea-food OR “sea food” OR sea-foods OR fish OR “fish consumption” OR fishes OR “fish proteins” OR “fish products” OR “fish flour” OR “fatty fish” OR shellfish OR “shellfish proteins” OR methylmercury OR “mercury poisoning” OR sharks OR swordfish OR tuna OR salmon OR sardines OR pollock OR flounder OR cod OR tilapia OR shrimp OR oysters OR clams OR scallops OR crab OR mackerel OR catfishes OR trout OR lobster OR squid OR halibut OR “mahi mahi” OR crawfish OR anchov* OR herring OR rockfish OR marine product*):ti,ab,kw

#6 - #4 OR #5

#7 - [mh "Mental Disorders"] OR [mh "Cognition"] OR [mh "Depression"] OR [mh "Dementia"] OR [mh "Psychomotor Performance"] OR [mh "Executive Function"] OR [mh "Child Behavior Disorders"] OR [mh "Autism Spectrum Disorder"] OR [mh "Child Development"] OR [mh "Problem Solving"] OR [mh "Mental Health"] OR [mh ^"Mental Processes"]

#8 - (“mental disorder*” OR cognition OR cognitive OR metacognition OR neurocognitive OR neurodevelop* OR neurological OR depression OR Alzheimer* OR senility OR senile OR presenile OR dementia OR anxiety OR motor skill* OR “attention deficit disorder*” OR ADHD OR “developmental disorder*” OR Autism 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 “academic achievement” OR “academic failure” OR “academic success*” OR “mental health”):ti,ab,kw

#9 - #7 OR #8

#10 - #3 AND #6 AND #9" with Publication Year from 2000 to 2019, in Trials (Word variations have been searched)

Embase

- Provider: Elsevier
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#1 - 'pregnancy'/exp OR 'pregnant woman'/exp OR 'lactation'/exp OR 'breast feeding'/exp OR 'maternal welfare'/exp OR 'prenatal exposure'/exp OR 'mother'/exp OR 'perinatal period'/exp OR 'maternal nutrition'/exp OR 'infant'/exp OR 'newborn'/exp OR 'baby'/exp OR 'fetus'/exp OR 'child'/exp OR 'childhood'/exp OR 'preschool'/exp OR 'adolescent'/exp OR 'pediatrics'/exp

#2 - pregnan*:ab,ti OR lactation:ab,ti OR 'breast feeding':ab,ti OR 'prenatal exposure':ab,ti OR 'pre pregnancy':ab,ti OR prenatal:ab,ti OR maternal:ab,ti OR mother*:ab,ti OR postpartum:ab,ti OR perinatal:ab,ti OR 'peri natal':ab,ti OR 'pre conception':ab,ti OR preconception:ab,ti OR 'peri conception':ab,ti OR periconceptional:ab,ti OR peripartum:ab,ti OR gestation*:ab,ti OR natal:ab,ti OR puerperium:ab,ti OR infant:ab,ti OR newborn*:ab,ti OR childhood:ab,ti OR baby:ab,ti OR babies:ab,ti OR fetus:ab,ti OR child:ab,ti OR preschool:ab,ti OR adolescent:ab,ti OR teen*:ab,ti OR pediatric*:ab,ti

#3 - #1 OR #2

#4 - 'sea food'/exp OR 'fish'/exp OR 'fish consumption'/exp OR 'fish protein'/exp OR 'fish product'/exp OR 'fish meal'/exp OR 'fatty fish'/exp OR 'shellfish'/exp OR 'shellfish protein'/exp OR 'mercurialism'/exp OR 'methylmercury'/exp OR 'shark'/exp OR 'swordfish'/exp OR 'tuna'/exp OR 'salmonine'/exp OR 'sardine'/exp OR 'gadiformes'/exp OR 'flounder'/exp OR 'atlantic cod'/exp OR 'tilapia'/exp OR 'shrimp'/exp OR 'oyster'/exp OR 'mya'/exp OR 'bivalve'/exp OR 'clam'/exp OR 'scallop'/exp OR 'brachyura'/exp OR 'crab'/exp OR 'perciformes'/exp OR 'mackerel'/exp OR 'catfish'/exp OR 'lobster'/exp OR 'decapodiformes'/exp OR 'squid'/exp OR 'halibut'/exp OR 'crayfish'/exp OR 'anchovy'/exp OR 'herring'/exp OR 'rockfish'/exp OR 'omega 3 fatty acid'/exp

#5 - seafood*:ab,ti OR fish:ab,ti OR 'fish consumption':ab,ti OR 'fish protein*':ab,ti OR 'fish product*':ab,ti OR 'fish meal*':ab,ti OR 'fatty fish':ab,ti OR 'shellfish protein*':ab,ti OR mercurialism:ab,ti OR methylmercury:ab,ti OR shark:ab,ti OR swordfish:ab,ti OR tuna:ab,ti OR salmonine:ab,ti OR salmon:ab,ti OR sardine*:ab,ti OR gadiformes:ab,ti OR pollock:ab,ti OR flounder:ab,ti OR cod:ab,ti OR tilapia:ab,ti OR shrimp:ab,ti OR oyster*:ab,ti OR bivalve:ab,ti OR mya:ab,ti OR clam:ab,ti OR clams:ab,ti OR scallop*:ab,ti OR crab:ab,ti OR perciformes:ab,ti OR mackerel:ab,ti OR catfish:ab,ti OR trout:ab,ti OR lobster:ab,ti OR squid:ab,ti OR decapodiformes:ab,ti OR halibut:ab,ti OR 'mahi mahi':ab,ti OR crayfish:ab,ti OR crawfish:ab,ti OR achov*:ab,ti OR herring:ab,ti OR rockfish:ab,ti OR 'marine product*':ab,ti OR 'omega 3 fatty acid*':ab,ti

#6 - #4 OR #5

#7 - 'mental disease'/exp OR 'cognition'/exp OR 'depression'/exp OR 'dementia'/exp OR 'anxiety'/exp OR 'psychomotor performance'/exp OR 'executive function'/exp OR 'child development'/exp OR 'developmental disorder'/exp OR 'psychomotor disorder'/exp OR 'problem solving'/exp OR 'mental health'/exp OR 'mental function'/de

#8 - '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 alzheimer*:ab,ti OR senility:ab,ti OR senile:ab,ti OR presenile:ab,ti OR dementia:ab,ti OR anxiety:ab,ti OR 'motor skill*':ab,ti OR 'executive function':ab,ti OR 'attention deficit disorder':ab,ti OR adhd:ab,ti OR 'developmental disorder':ab,ti OR 'language processing':ab,ti OR 'language delay*':ab,ti OR 'child develop*':ab,ti OR autism:ab,ti OR asperger:ab,ti OR 'developmental delay':ab,ti OR 'developmental disabilit*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 OR 'mental health':ab,ti

#9 - #7 OR #8

#10 - #3 AND #6 AND #9

#11 - #3 AND #6 AND #9 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2000-2019]/py NOT ([conference abstract]/lim OR [conference review]/lim OR [conference paper]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

Cumulative Index of Nursing and Allied Health Literature (CINAHL Plus)

- Provider: EBSCO*host*
- Date(s) Searched: October 23, 2019
- Date range searched: January 1, 2000 - October 23, 2019
- Search Terms:

#S1 - (MH "Pregnancy") OR pregnancy OR (MH "Expectant Mothers") OR “expected mothers” OR pregnant OR (MH "Lactation") OR lactation OR (MH "Breast Feeding") OR breastfeeding OR (MH "Maternal-Child Health") OR “maternal child health” OR (MH "Prenatal Exposure Delayed Effects") OR (MH "Maternal Exposure") OR pregnan* OR pre-pregnancy OR prenatal OR maternal OR mother OR postpartum OR perinatal OR perinatal OR pre-conception OR preconception OR peri-conception OR periconceptional OR "peripartum period" OR peripartum OR peri-partum OR gestation* OR natal OR (MH "Puerperium") OR Puerperium OR (MH "Maternal Nutritional Physiology") OR (MH "Infant") OR infant OR (MH "Infant, Newborn") OR newborn OR baby OR babies OR (MH "Fetus") OR fetus OR (MH "Child") OR child OR (MH "Child, Preschool") OR toddler OR (MH "Adolescence") OR teen* OR adolescent OR (MH "Pediatrics") OR pediatrics

#S2 - seafood OR (MH "Seafood") OR seafood* OR sea-food OR “sea food” OR (MH "Fish") OR fish OR "fish consumption" OR fishes OR “fish protein*” OR “fish product*” OR “fish flour” OR “fatty fish” OR (MH "Shellfish") OR shellfish OR “shellfish proteins” OR “mercury poisoning” OR (MH "Mercury Poisoning") OR methylmercury OR shark* OR swordfish OR tuna OR salmon OR sardine* OR Pollock OR flounder OR cod OR tilapia OR shrimp OR oyster* OR clams OR scallops OR crab OR mackerel OR catfish* OR trout OR lobster* OR squid OR halibut OR “mahi mahi” OR crawfish OR achov* OR herring OR rockfish OR marine product* OR (MH "Fatty Acids, Omega-3")

#S3 - (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 "Alzheimer's Disease") OR “Alzheimer’s disease” OR (MH "Dementia, Senile") OR senile OR senility OR presenile OR (MH "Dementia") 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 developmental disorder* OR (MH "Autistic Disorder") OR autism OR Asperger OR “language processing” OR language delay* OR (MH "Child Development") OR child develop* OR (MH "Developmental Disabilities") OR developmental delay* OR developmental disabilit* OR (MH "Motor Skills Disorders") OR motor skill* OR (MH "Problem Solving") OR developmental domain* OR “academic performance” OR “academic achievement” OR “academic failure” OR academic success* OR (MH "Mental Health") OR "mental health" OR (MH "Mental Processes")

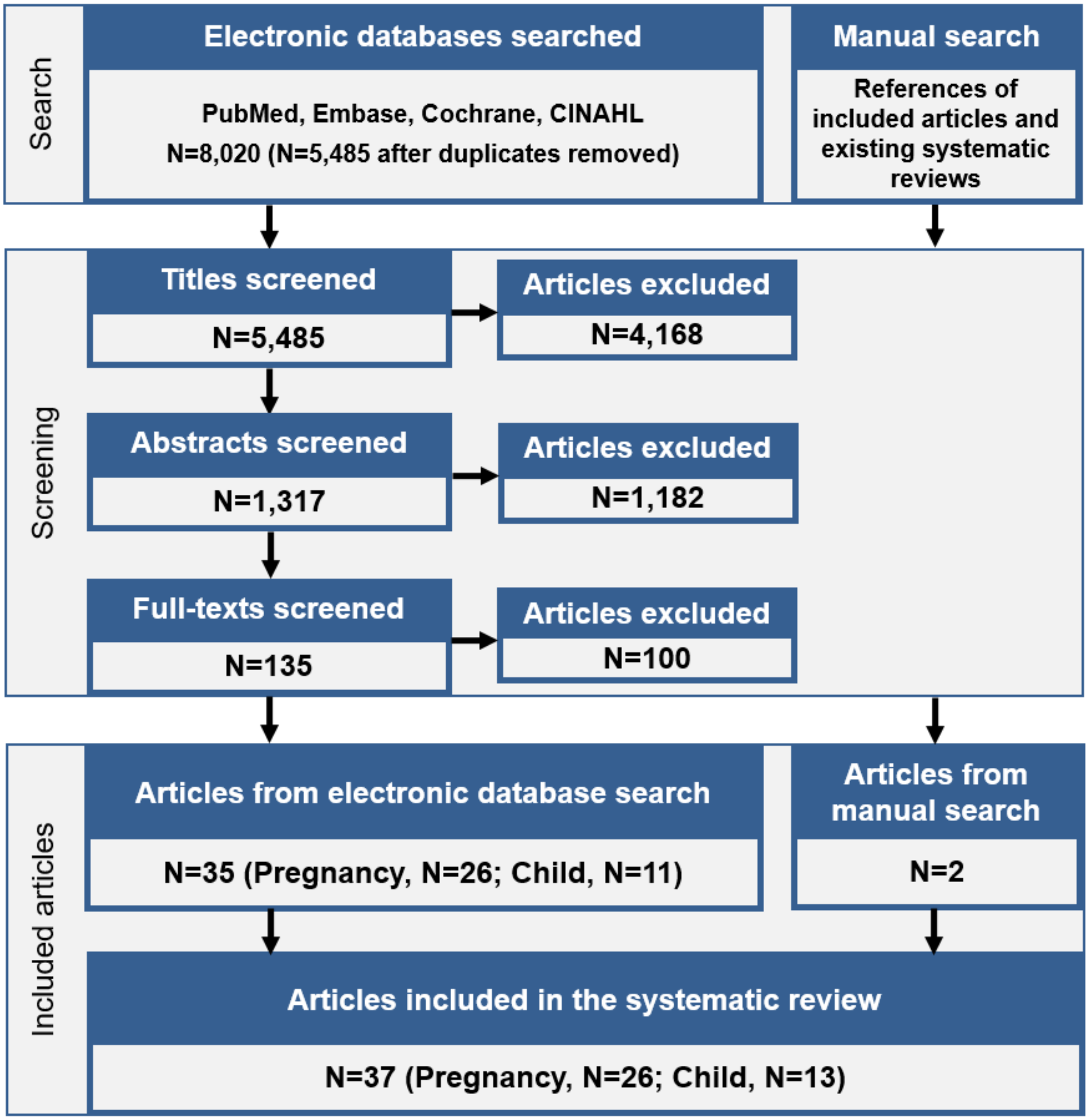
#S4 - S1 AND S2 AND S3

#S5 - S1 AND S2 AND S3 NOT (MH "Literature Review" OR MH "Meta Analysis" OR MH "Systematic Review" OR MH "News" OR MH "Retracted Publication" OR MH "Retraction of Publication”) Limiters - Publication Year: 2000-2019; Peer Reviewed; English Language; Human

LITERATURE SEARCH AND SCREENING RESULTS

The flow chart (**Figure 2**) below illustrates the literature search and screening results for articles examining this systematic review question and a second question on seafood consumption during pregnancy and lactation and neurocognitive development in the child. 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 7** for a list of excluded articles for the rationale for exclusion for each excluded full-text article. A manual search was conducted 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[xii]



[xii] Two articles were included in both the review for pregnancy and lactation and the review for childhood and adolescence

Excluded articles

The table below (**Table 7**) lists the articles excluded after full-text screening for this systematic review question and a second question on seafood consumption during pregnancy and lactation and neurocognitive development in the child, and includes columns for the categories of inclusion and exclusion criteria (see **Table 6**) that studies were excluded based on. At least one reason for exclusion is provided for each article, as indicated by an "X" in one of the columns, though this may not reflect all possible reasons for exclusion. Information about articles excluded after title and abstract screening is available upon request.

Table 7. Articles excluded after full-text screening with rationale for exclusion

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
1.	Al-Ghannami SS, Al-Adawi S, Ghebremeskel K, et al. Randomized open-label trial of docosahexaenoic acid-enriched fish oil and fish meal on cognitive and behavioral functioning in Omani children. *Nutrition.* 2019;57:167-172. doi:10.1016/j.nut.2018.04.008.					X	
2.	Andrew MJ, Parr JR, Montague-Johnson C, et al. Nutritional intervention and neurodevelopmental outcome in infants with suspected cerebral palsy: the Dolphin infant double-blind randomized controlled trial. *Dev Med Child Neurol.* 2018;60(9):906-913. doi:10.1111/dmcn.13586.	X					
3.	Boucher O, Muckle G, Ayotte P, Dewailly E, Jacobson SW, Jacobson JL. Altered fine motor function at school age in Inuit children exposed to PCBs, methylmercury, and lead. *Environ Int.* 2016;95:144-51. doi:10.1016/j.envint.2016.08.010.	X					
4.	Braarud HC, Markhus MW, Skotheim S, et al. Maternal DHA Status during Pregnancy Has a Positive Impact on Infant Problem Solving: A Norwegian Prospective Observation Study. *Nutrients.*2018;10(5). pii: E529. doi:10.3390/nu10050529.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
5.	Brouwer-Brolsma EM, van de Rest O, Godschalk R, Zeegers MPA, Gielen M, de Groot RHM. Associations between maternal long-chain polyunsaturated fatty acid concentrations and child cognition at 7 years of age: The MEFAB birth cohort. *Prostaglandins Leukot Essent Fatty Acids.* 2017;126:92-97. doi:10.1016/j.plefa.2017.09.012.	X					
6.	Budtz-Jorgensen E, Grandjean P, Weihe P. Separation of risks and benefits of seafood intake. *Environ Health Perspect.* 2007;115(3):323-7. doi:10.1289/ehp.9738.				X		
7.	Butler LJ, Janulewicz PA, Carwile JL, White RF, Winter MR, Aschengrau A. Childhood and adolescent fish consumption and adult neuropsychological performance: An analysis from the Cape Cod Health Study. *Neurotoxicol Teratol.* 2017;61:47-57. doi:10.1016/j.ntt.2017.03.001.				X		
8.	Carwile JL, Butler LJ, Janulewicz PA, Winter MR, Aschengrau A. Childhood Fish Consumption and Learning and Behavioral Disorders. *Int J Environ Res Public Health.* 2016;13(11):1069. doi:10.3390/ijerph13111069.				X		
9.	Chen MYY, Wong, WWK, et al. Quantitative risk-benefit analysis of fish consumption for women of child-bearing age in Hong Kong. *Food Addit Contam Part A Chem Anal Control Exp Risk Assess.* 2014;31(1):48-53. doi:10.1080/19440049.2013.855947.			X			
10.	Chien LC, Gao CS, Lin HH. Hair mercury concentration and fish consumption, Risk and perceptions of risk among women of childbearing age. *Environmental Research.* 2010;110(1):123-129. doi:10.1016/j.envres.2009.10.001.			X	X		
11.	Choi AL, Mogensen UB, Bjerve KS, et al. Negative confounding by essential fatty acids in methylmercury neurotoxicity associations. *Neurotoxicology and Teratology.* 2014;42,85-92. doi:10.1016/j.ntt.2014.02.003.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
12.	Davidson PW, Cory-Slechta DA, Thurston SW, et al. Fish consumption and prenatal methylmercury exposure, cognitive and behavioral outcomes in the main cohort at 17 years from the Seychelles child development study. *Neurotoxicology.* 2011;32(6):711-7. doi:10.1016/j.neuro.2011.08.003.	X	X				
13.	Davidson PW, Kost J, Myers GJ, Cox C, Clarkson TW, Shamlaye, C. F. Methylmercury and neurodevelopment, reanalysis of the Seychelles Child Development Study outcomes at 66 months of age. *JAMA.* 2001;285(10):1291-3. doi:10.1001/jama.285.10.1291.				X		
14.	Davidson PW, Leste A, Benstrong E, et al. Fish consumption, mercury exposure, and their associations with scholastic achievement in the Seychelles Child Development Study. *Neurotoxicology.* 2010;31(5):439-47. doi:10.1016/j.neuro.2010.05.010.	X					
15.	de Groot RH, Ouwehand C, Jolles J. Eating the right amount of fish, inverted U-shape association between fish consumption and cognitive performance and academic achievement in Dutch adolescents. *Prostaglandins Leukot Essent Fatty Acids.* 2012;86(3):113-7. doi:10.1016/j.plefa.2012.01.002.				X		
16.	Debes F, Budtz-Jorgensen E, Weihe P, White RF, Grandjean P. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. *Neurotoxicol Teratol.* 2006;28(5):536-47. doi:10.1016/j.ntt.2006.02.005.	X					
17.	Debes F, Weihe P, Grandjean P. Cognitive deficits at age 22 years associated with prenatal exposure to methylmercury. *Cortex.* 2016;74,358-69. doi:10.1016/j.cortex.2015.05.017.	X	X				

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
18.	Dorea JG, Marques RC, Abreu L. Milestone achievement and neurodevelopment of rural Amazonian toddlers (12 to 24 months) with different methylmercury and ethylmercury exposure. *J Toxicol Environ Health A.* 2014;77:1-13. doi:10.1080/15287394.2014.861335.	X			X		
19.	Dye D. Mother's omega-3 fatty acid deficit impairs infant's neurological development. *Life Extension.* 2008;14:28-28.						X
20.	Emmett PM. Dietary Patterns during Complementary Feeding and Later Outcomes. *Nestle Nutr Inst Workshop Ser.* 2016;85:145-54. doi:10.1159/000439505.	X			X		
21.	Emmett PM, Jones LR, Golding J. Pregnancy diet and associated outcomes in the Avon Longitudinal Study of Parents and Children. *Nutr Rev.* 2015;73(Suppl 3):154-74. doi:10.1093/nutrit/nuv053.				X		
22.	Freire C, Ramos R, Lopez-Espinosa MJ, et al. Hair mercury levels, fish consumption, and cognitive development in preschool children from Granada Spain. *Environ Res.* 2010;110(1):96-104. doi:10.1016/j.envres.2009.10.005.	X			X		
23.	Gao L, Cui SS, Han Y, Dai W, Su YY, Zhang X. Does periconceptional fish consumption by parents affect the incidence of Autism Spectrum Disorder and intelligence deficiency? A case-control study in Tianjin, China. *Biomed Environ Sci.* 2016;29(12):885-892. doi:10.3967/bes2016.118.				X		
24.	Gao L, Xi QQ, Wu J, et al. Association between prenatal environmental factors and child Autism: A case control study in Tianjin, China. *Biomed Environ Sci.* 2015;28(9):642-50. doi:10.3967/bes2015.090.				X		
25.	Gao Y, Yan CH, Tian Y, et al. Prenatal exposure to mercury and neurobehavioral development of neonates in Zhoushan City, China. *Environ Res.* 2007;105(3):390-9. doi:10.1016/j.envres.2007.05.015.	X				X	

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
26.	Gari M, Grimalt JO, Torrent M, Sunyer J. Influence of socio-demographic and diet determinants on the levels of mercury in preschool children from a Mediterranean island. *Environ Pollut.* 2013;182:291-8. doi:10.1016/j.envpol.2013.07.022.	X			X		
27.	Gignac F, Romaguera D, Fernandez-Barres S, Phillipat C, et al. Maternal nut intake in pregnancy and child neuropsychological development up to 8 years old: a population-based cohort study in Spain. *Eur J Epidemiol*. 2019;34(7):661-673. doi:10.1007/s10654-019-00521-6.	X					
28.	Gispert-Llaurado M, Perez-Garcia M, Escribano, et al. Fish consumption in mid-childhood and its relationship to neuropsychological outcomes measured in 7-9 year old children using a NUTRIMENTHE neuropsychological battery. *Clin Nutr.* 2016;35(6):1301-1307. doi:10.1016/j.clnu.2016.02.008.				X		
29.	Golding J, Gregory S, Ellis G, et al. Maternal prenatal external locus of control and reduced mathematical and science abilities in their offspring: A longitudinal birth cohort study. *Front Psychol.* 2019;10:194. doi:10.3389/fpsyg.2019.00194.	X				X	
30.	Golding J, Gregory S, Iles-Caven Y, Hibbeln J, Emond A, Taylor CM. Associations between prenatal mercury exposure and early child development in the ALSPAC study. *Neurotoxicology*. 2016;53:215-222. doi:10.1016/j.neuro.2016.02.006.					X	
31.	Golding J, Hibbeln JR, Gregory SM, Iles-Caven Y, Emond A, Taylor CM. Maternal prenatal blood mercury is not adversely associated with offspring IQ at 8 years provided the mother eats fish: A British prebirth cohort study. *Int J Hyg Environ* Health. 2017;220(7):1161-1167. doi:10.1016/j.ijheh.2017.07.004.	X				X	

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
32.	Groth E 3rd. Re: 'Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort'. *Am J Epidemiol*. 2008;168(2):236. doi:10.1093/aje/kwn172.				X		
33.	Haapala EA, Eloranta AM, Venalainen T, et al. Diet quality and academic achievement: a prospective study among primary school children. *Eur J Nutr.* 2017;56(7):2299-2308. doi:10.1007/s00394-016-1270-5.	X					
34.	Halldorsson TI, Thorsdottir I, Meltzer HM, Strom M, Olsen SF. Dioxin-like activity in plasma among Danish pregnant women: dietary predictors, birth weight and infant development. *Environ Res.* 2009;109(1):22-8. doi:10.1016/j.envres.2008.08.011.	X				X	
35.	Hamazaki T, Hirayama S. The effect of docosahexaenoic acid-containing food administration on symptoms of attention-deficit/hyperactivity disorder-a placebo-controlled double-blind study. *Eur J Clin Nutr.* 2004; 58(5):838. doi:10.1038/sj.ejcn.1601888.				X		
36.	Handeland K, Skotheim S, Baste V, et al. The effects of fatty fish intake on adolescents' nutritional status and associations with attention performance: Results from the FINS-TEENS randomized controlled trial. *Nutr J.* 2018;17(1):30. doi:10.1186/s12937-018-0328-z.				X		
37.	Hart SL, Boylan LM, Carroll SR, et al. Brief report: newborn behavior differs with decosahexaenoic acid levels in breast milk. *J Pediatr Psychol.* 2006;31(2):221-6. doi:10.1093/jpepsy/jsj069.	X			X		
38.	Henriksen C, Haugholt K, Lindgren, M, et al. Improved cognitive development among preterm infants attributable to early supplementation of human milk with docosahexaenoic acid and arachidonic acid. *Pediatrics.* 2008;121(6):1137-45. doi:10.1542/peds.2007-1511.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
39.	Hertz-Picciotto I, Green PG, Delwiche L, Hansen R, Walker C, Pessah IN. Blood mercury concentrations in CHARGE Study children with and without autism. *Environ Health Perspect.* 2010;118(1):161-6. doi:10.1289/ehp.0900736.	X			X		
40.	Hibbeln JR, Davis JM. Considerations regarding neuropsychiatric nutritional requirements for intakes of omega-3 highly unsaturated fatty acids. *Prostaglandins Leukot Essent Fatty Acids.* 2009;81(2-3):179-86. doi:10.1016/j.plefa.2009.06.005.	X			X		
41.	Hibbeln J, Gregory S, Iles-Caven Y, Taylor CM, Emond A, Golding J. Total mercury exposure in early pregnancy has no adverse association with scholastic ability of the offspring particularly if the mother eats fish. *Environ Int.* 2018;116:108-115. doi:10.1016/j.envint.2018.03.024.	X				X	
42.	Hoerr J, Fogel J, Van Voorhees B. Ecological correlations of dietary food intake and mental health disorders. *J Epidemiol Glob Health.* 2017;7(1):81-89. doi:10.1016/j.jegh.2016.12.001.				X	X	
43.	Hsi HC, Jiang CB, Yang TH, Chien LC. The neurological effects of prenatal and postnatal mercury/methylmercury exposure on three-year-old children in Taiwan. *Chemosphere.* 2014;100:71-6. doi:10.1016/j.chemosphere.2013.12.068.	X			X		
44.	Iles-Caven Y, Golding J, Gregory S, Emond A, Taylor CM. Data relating to early child development in the Avon Longitudinal Study of Parents and Children (ALSPAC), their relationship with prenatal blood mercury and stratification by fish consumption. *Data Brief.* 2016;9:112-22. doi:10.1016/j.dib.2016.08.034.				X	X	
45.	Innis SM, Friesen RW. Essential n-3 fatty acids in pregnant women and early visual acuity maturation in term infants. *Am J Clin Nutr.* 2008;87(3):548-557. doi:10.1093/ajcn/87.3.548.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
46.	Jacobson JL, Jacobson SW. Prenatal exposure to polychlorinated biphenyls and attention at school age. *J Pediatr.* 2003;143(6):780-8. doi:10.1067/S0022-3476(03)00577-8.	X					
47.	Jedrychowski W, Perera F, Jankowski J, et al. Fish consumption in pregnancy, cord blood mercury level and cognitive and psychomotor development of infants followed over the first three years of life, Krakow epidemiologic study. *Environ Int.* 2007;33(8):1057-62. doi:10.1016/j.envint.2007.06.001.	X				X	
48.	Jensen TK, Grandjean P, Jorgensen EB, White RF, Debes F, Weihe P. Effects of breast feeding on neuropsychological development in a community with methylmercury exposure from seafood. *J Expo Anal Environ Epidemiol.* 2005;15(5):423-30. doi:10.1038/sj.jea.7500420.	X					
49.	Kim Y, Ha EH, Park H, et al. Prenatal mercury exposure, fish intake and neurocognitive development during first three years of life, Prospective cohort mothers and Children's environmental health (MOCEH) study. *Sci Total Environ.* 2018;615:1192-1198. doi:10.1016/j.scitotenv.2017.10.014.	X				X	
50.	Kishi R, Araki A, Minatoya M, et al. The Hokkaido Birth Cohort Study on Environment and Children's Health, cohort profile-updated 2017. *Environ Health Prev Med*. 2017;22(1):46. doi:10.1186/s12199-017-0654-3.	X					
51.	Lam HS, Fok TF, Ng PC. Long-term neurocognitive outcomes of children prenatally exposed to low-dose methylmercury. *Hong Kong Med J.* 2012;18(Suppl 6):S23-4.	X	X				

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
52.	Lauritzen L, Jorgensen MH, Olsen SF, Straarup EM, Michaelsen KF. Maternal fish oil supplementation in lactation, effect on developmental outcome in breast-fed infants. *Reprod Nutr Dev.* 2005;45(5):535-47. doi:10.1051/rnd:2005044.	X				X	
53.	Llop S, Ballester F, Murcia M, et al. Prenatal exposure to mercury and neuropsychological development in young children, the role of fish consumption. *Int J Epidemiol.* 2017;46(3):827-838. doi:10.1093/ije/dyw259.	X				X	
54.	Loring PA, Duffy LK, Murray MS. A risk-benefit analysis of wild fish consumption for various species in Alaska reveals shortcomings in data and monitoring needs. *Sci Total Environ.* 2010;408(20):4532-41. doi:10.1016/j.scitotenv.2010.07.013.				X		
55.	Lyall K, Munger KL, O'Reilly EJ, Santangelo SL, Ascherio A. Maternal dietary fat intake in association with autism spectrum disorders. *Am J Epidemiol.* 2013;178(2):209-20. doi:10.1093/aje/kws433.	X	X				
56.	Lynch ML, Huang LS, Cox C, et al. Varying coefficient function models to explore interactions between maternal nutritional status and prenatal methylmercury toxicity in the Seychelles Child Development Nutrition Study. *Environ Res* 2011;111(1):75-80. doi:10.1016/j.envres.2010.09.005.	X			X		
57.	Mamalakis G, Kiriakakis M, Tsibinos G, Kafatos A. Depression and adipose polyunsaturated fatty acids in an adolescent group. *Prostaglandins Leukot Essent Fatty Acids.* 2004;71(5):289-94. doi:10.1016/j.plefa.2004.04.002.	X					
58.	Marques RC, Abreu L, Bernardi JV, Dorea JG. Traditional living in the Amazon, Extended breastfeeding, fish consumption, mercury exposure and neurodevelopment. *Ann Hum Biol.* 2016;43(4):360-70. doi:10.1080/03014460.2016.1189962.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
59.	Marques RC, Dorea JG, Leao RS, et al. Role of methylmercury exposure (from fish consumption) on growth and neurodevelopment of children under 5 years of age living in a transitioning (tin-mining) area of the western Amazon, Brazil. *Arch Environ Contam Toxicol.* 2012;62(2):341-50. doi:10.1007/s00244-011-9697-4.		X		X		
60.	Marques RC, Garrofe Dorea J, Rodrigues Bastos W, de Freitas Rebelo M, de Freitas Fonseca M, Malm O. Maternal mercury exposure and neuro-motor development in breastfed infants from Porto Velho (Amazon), Brazil. *Int J Hyg Environ Health.* 2007;210(1):51-60. doi:10.1016/j.ijheh.2006.08.001.	X					
61.	Matsudaira T. Attention deficit disorders--drugs or nutrition? *Nutr Health.* 2007;19(1-2):57-60. doi:10.1177/026010600701900206.				X		
62.	McGuire J, Kaplan J, Lapolla J, Kleiner R. The 2014 FDA assessment of commercial fish, practical considerations for improved dietary guidance. *Nutr J.* 2016;15(1):66. doi:10.1186/s12937-016-0182-9.				X		
63.	Milte CM, Sinn N, Buckley JD, Coates AM, Young RM, Howe PRC. Polyunsaturated fatty acids, cognition and literacy in children with ADHD with and without learning difficulties. *Journal of Child Health Care.* 2011;15(4):299-311. doi:10.1177/1367493511403953.	X					
64.	Myers GJ, Davidson PW. Maternal fish consumption benefits children's development. *Lancet.* 2007;369(9561):537-8. doi:10.1016/S0140-6736(07)60248-7.				X		
65.	Ng KH, Meyer BJ, Reece L, Sinn N. Dietary PUFA intakes in children with attention-deficit/hyperactivity disorder symptoms. *Br J Nutr.* 2009;102(11):1635-41. doi:10.1017/S0007114509990821.				X	X	

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
66.	Ninger LJ. Fish oil improves infants' cognitive and motor function. *Life Extension.* 2008;14,23-23.						X
67.	Noaghiul S, Hibbeln JR. Cross-national comparisons of seafood consumption and rates of bipolar disorders. *Am J Psychiatry.* 2003;160(12):2222-7. doi:10.1176/appi.ajp.160.12.2222.			X	X		
68.	Oddy WH, Allen KL, Trapp GSA, et al. Dietary patterns, body mass index and inflammation, Pathways to depression and mental health problems in adolescents. *Brain Behav Immun.* 2018;69:428-439. doi:10.1016/j.bbi.2018.01.002.	X					
69.	Oddy WH, Hickling S, Smith MA, et al. Dietary intake of omega-3 fatty acids and risk of depressive symptoms in adolescents. *Depress Anxiety.* 2011;28(7):582-8. doi:10.1002/da.20822.	X					
70.	Pawelczyk T, Trafalska E, Kotlicka-Antczak M, Pawelczyk A. The association between polyunsaturated fatty acid consumption and the transition to psychosis in ultra-high risk individual. *Prostaglandins Leukot Essent Fatty Acids.* 2016;108:30-7. doi:10.1016/j.plefa.2016.03.010.	X		X			
71.	Qi Y, Niu J. Does childhood nutrition predict health outcomes during adulthood? Evidence from a population-based study in China. *J Biosoc Sci.* 2015;47(5):650-66. doi:10.1017/S0021932014000509.	X			X		
72.	Rahbar MH, Samms-Vaughan M, Loveland KA, et al. Seafood consumption and blood mercury concentrations in Jamaican children with and without autism spectrum disorders. *Neurotox Res.* 2013;23(1):22-38. doi:10.1007/s12640-012-9321-z.				X		
73.	Rees AM, Austin MP, Parker GB. Omega-3 fatty acids as a treatment for perinatal depression, randomized double-blind placebo-controlled trial. *Aust N Z J Psychiatry.* 2008; 42(3):199-205. doi:10.1080/00048670701827267.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
74.	Rees A, Sirois S, Wearden A. Maternal docosahexaenoic acid intake levels during pregnancy and infant performance on a novel object search task at 22 months. *Child Dev.* 2014;85(6):2131-9. doi:10.1111/cdev.12280.	X	X				
75.	Rioux FM, Belanger-Plourde J, Leblanc CP, Vigneau F. Relationship between maternal DHA and iron status and infants' cognitive performance. *Can J Diet Pract Res.* 2011;72,76.	X					
76.	Samson K. Cognitive benefits of seafood during pregnancy outweigh risk, new study finds. *Neurology Today.* 2007;7(5):35-36.				X		
77.	Schell JD, Jr, Budinsky RA, Wernke MJ. PCBs and neurodevelopmental effects in Michigan children, an evaluation of exposure and dose characterization. *Regul Toxicol Pharmacol.* 2001;33(3):300-12. doi:10.1006/rtph.2001.1475.				X		
78.	Schmiedel V, Vogt H, Walach H. Are pupils' 'Programme for International Student Assessment (PISA)' scores associated with a nation's fish consumption? *Scand J Public Health.* 2018;46(7):675-679. doi:10.1177/1403494817717834.				X		
79.	Seafood in pregnancy: good or bad for the offspring? *Child Health Alert.* 2007;25:1-3.				X		
80.	Skotheim S, Dahl L, Handeland K, et al. Design of the FINS-TEENS study: A randomized controlled trial assessing the impact of fatty fish on cognitive performance in adolescents. *Scand J Public Health.* 2017; 45(6):621-629. doi:10.1177/1403494817717408.			X			

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
81.	Sorensen LB, Damsgaard CT, Dalskov SM, et al. Diet-induced changes in iron and n-3 fatty acid status and associations with cognitive performance in 8-11-year-old Danish children: secondary analyses of the Optimal Well-Being, Development and Health for Danish Children through a Healthy New Nordic Diet School Meal Study. *Br J Nutr.* 2015;114(10):1623-37. doi:10.1017/S0007114515003323.	X					
82.	Steuerwald U, Weihe P, Jorgensen PJ, et al. Maternal seafood diet, methylmercury exposure, and neonatal neurologic function. *J Pediatr.* 2000;136(5):599-605. doi:10.1067/mpd.2000.102774.	X		X			
83.	Stewart PW, Lonky E, Reihman J, Pagano J, Gump BB, Darvill T. The relationship between prenatal PCB exposure and intelligence (IQ) in 9-year-old children. *Environ Health Perspect.* 2008;116(10):1416-22. doi:10.1289/ehp.11058.	X					
84.	Strain JJ, Davidson PW, Thurston SW, et al. Maternal PUFA status but not prenatal methylmercury exposure is associated with children's language functions at age five years in the Seychelles. *J Nutr.* 2012;142(11):1943-9. doi:10.3945/jn.112.163493.	X	X				
85.	Surkan PJ, Wypij D, Trachtenberg F, et al. Neuropsychological function in school-age children with low mercury exposures. *Environ Res.* 2009;109(6):728-33. doi:10.1016/j.envres.2009.04.006.	X			X		
86.	Suzuki K, Nakai K, Sugawara T, et al. Neurobehavioral effects of prenatal exposure to methylmercury and PCBs, and seafood intake: neonatal behavioral assessment scale results of Tohoku study of child development. *Environ Res.* 2010;110(7):699-704. doi:10.1016/j.envres.2010.07.001.	X					

	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
87.	Tatsuta N, Murata K, Iwai-Shimada M, Yaginuma-Sakurai K, Satoh H, Nakai K. Psychomotor ability in children prenatally exposed to methylmercury: The 18-month follow-up of Tohoku Study of Child Development. *Tohoku J Exp Med.* 2017;242(1):1-8. doi:10.1620/tjem.242.1.	X					
88.	Tatsuta N, Nakai K, Sakamoto M, Murata K, Satoh H. Methylmercury exposure and developmental outcomes in Tohoku Study of Child Development at 18 months of age. *Toxics.* 2018;6(3). pii: E49. doi:10.3390/toxics6030049.	X				X	
89.	Theobald H. Oily fish and pregnancy. *Nutrition Bulletin.* 2003;28,247-251.	X			X		
90.	Timonen M, Horrobin D, Jokelainen J, Laitinen J, Herva A, Rasanen P. Fish consumption and depression: the Northern Finland 1966 birth cohort study. *J Affect Disord.* 2004;82(3):447-52. doi:10.1016/j.jad.2004.02.002.		X				
91.	Tomlinson D, Wilkinson H, Wilkinson P. Diet and mental health in children. *Child & Adolescent Mental Health.* 2009;14(3):148-55. doi:10.1111/j.1475-3588.2008.00520.x.				X		
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	Citation	Intervention /Exposure	Age	Outcome	Study Design	Comparator	Publication Status
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