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# Maternal fish consumption and child neurodevelopment in Nutrition 1 Cohort: Seychelles Child Development Study

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## Data Sharing

Data described in the manuscript, code book, and analytic code will be made available upon request pending [e.g., application and approval, payment, other].

## Declaration of Interests

All authors declare no conflicts of interest.

## Abstract

Maternal fish consumption exposes the foetus to beneficial nutrients and potentially adverse neurotoxicants. The current study investigated associations between maternal fish consumption and child neurodevelopmental outcomes. Maternal fish consumption was assessed in the Seychelles Child Development Study Nutrition Cohort 1 (NC1) (*n*=229) using four-day food diaries. Neurodevelopment was evaluated at nine and 30 months, and five and nine years with test batteries assessing 26 endpoints and covering multiple neurodevelopmental domains. Analyses used multiple linear regression with adjustment for covariates known to influence child neurodevelopment. This cohort consumed an average of 8 fish meals per week and the total fish intake during pregnancy was 106.8 (SD 61.9) g/d. Among the 26 endpoints evaluated in the primary analysis there was one beneficial association. Children whose mothers consumed larger quantities of fish performed marginally better on the KBIT (a test of nonverbal intelligence) at age 5 years (β 0.003, 95% CI 0 – 0.005). A secondary analysis dividing fish consumption into tertiles found no significant associations when comparing the highest and lowest consumption groups. In this cohort, where fish consumption is substantially higher than current global recommendations, maternal fish consumption during pregnancy was not beneficially or adversely associated with children's neurodevelopmental outcomes.

## Introduction

Fish and seafood are dietary staples for many populations worldwide and globally represent a major source of dietary protein (1). The Food and Agriculture Organization of the United Nations (FAO) estimates that aquatic foods account for at least 20% of average per capita intake of animal protein for 3.3 billion people (2). Fish is also a rich source of nutrients known to be essential for foetal neurodevelopment, in particular long chain polyunsaturated fatty acids (LCPUFA), iodine, and vitamin D (3). The LCPUFA docosahexaenoic acid (DHA) is critical for optimal visual and brain development and deficiencies during foetal growth may have lifelong adverse consequences for brain function (4). Women who consume fish throughout pregnancy are more likely to achieve optimal intakes of these essential nutrients (5). A large body of evidence supports the nutritional benefits of fish consumption throughout pregnancy (6–8). However, fish also contains small amounts of methylmercury (MeHg) and public health consumption guidelines have been formulated with the central aim of limiting possible risk from this naturally occurring environmental pollutant.

Public health advice to pregnant women has been variable. In their 2014 Opinion, the European Food Safety Authority concluded that three to four servings of fish per week (equivalent to >450 g or 16 oz per week) has nutritional benefits for neurodevelopment compared to no fish consumption (9). Similar guidance in the USA recommends that pregnant women should consume 8-12 oz (equivalent to approximately 227-340 g) of fish per week (10–12). The UK advice, last updated in 2004, recommends consuming two portions of fish per week (equivalent to ~280 g or 10 oz. per week) with at least one of these being oily (or fatty) fish (13). Each of these guidelines recommend on a precautionary basis that fish with a high MeHg content (such as shark or swordfish) should be limited or avoided altogether. In many countries, fish consumption in women of childbearing age is significantly below the recommended amounts (14,15). Public confusion about the benefits and risks of fish consumption in the USA contributed to some women avoiding fish altogether when pregnant (16). Limiting fish consumption during pregnancy has possible long-term adverse consequences given its nutritional contribution to the diet.

In 2019, an expert panel conducted a systematic review to evaluate the risks and benefits of seafood consumption (excluding sea mammals) during pregnancy (7). That study reported finding no evidence of an upper limit of intake at which adverse neurodevelopmental outcomes were present. The authors emphasised the benefits of consuming adequate amounts of a wide range of seafood for the greatest cognitive benefits to neurodevelopment, as well as the effect of beneficial nutrients to outweigh potential adverse effects of MeHg exposure (7,8).

Fish advisories in the USA are based on epidemiological studies of individuals consuming whales (Faroe Islands) and shark (New Zealand) with co-exposure to multiple other neurotoxicants and the precautionary principle (17). However, findings from the multi-cohort Seychelles Child Development Study (SCDS) support the conclusion that the beneficial effects of nutrients in fish outweigh the possible adverse effects of MeHg (18–22). The SCDS has studied a population that consumes on average more than eight fish meals per week, several times higher than global recommendations(9,11–13,19). The population has one of the highest prenatal MeHg exposures from fish consumption ever studied (> 5 ppm measured in maternal hair), consumes fish with MeHg concentrations similar to those in commercial fish in the UK and USA, and does not consume sea mammals(23). The study has followed three independent longitudinal cohorts over 24 years and found no consistent evidence of adverse associations between MeHg exposure and child neurodevelopmental outcomes (18–21). The SCDS has found beneficial associations between maternal LCPUFA status during pregnancy and early childhood neurodevelopment of offspring, with evidence that n-3 and n-6 PUFA may ameliorate negative outcomes from MeHg, if any are present, at this level of exposure (20,22).

Previous analyses of the SCDS cohorts focused on individual biomarkers of MeHg exposure and LCPUFA status. The aim of the current study is to investigate associations between maternal fish consumption (consumed as a whole food during pregnancy) and children's neurodevelopmental outcomes at nine and 30 months, and five and nine years. The advantage of this approach, as advised by the FDA in their 2014 report on net effects (10), is that it allows both the beneficial contributions of nutrients and potential adverse contributions of MeHg to be considered concurrently. Consequently, results should prove more meaningful for formulating accurate public health guidance.

## Subjects and Methods

### Population & Location

The SCDS is a longitudinal observational study being conducted in the Republic of Seychelles. The primary aim of the study is to investigate the influence of prenatal MeHg exposure from fish consumption during pregnancy on child neurodevelopmental outcomes (18). The Nutrition Cohort 1 (NC1) has the most comprehensive assessment of fish consumption during pregnancy of any SCDS maternal-child cohort to date and additionally comprehensive assessments of the children's neurodevelopment. In 2001 we enrolled a total of 300 healthy pregnant women. (22). A power calculation determined 250 participants were required to detect a 5-point difference on the BSID-II (primary outcome) between the low and high MeHg exposure groups (19).

Mothers were recruited during their first antenatal appointment (from 14 weeks of gestation) across the Island of Mahé, the main island of Seychelles. Inclusion criteria were over 16 years of age, native-born Seychellois and having a normal, healthy pregnancy.

Among the 300 women recruited to NC1, there were several exclusions owing to miscarriage/abortion (*n*=12), not being pregnant (*n*=4), illness (*n*=1), relocation (*n*=2) and noncompliance (*n*=8). Additionally, 44 participants had incomplete dietary data and are not included in this analysis (**Supplemental Figure 1**).

## Ethical approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving participants were reviewed and approved by the Seychelles Ethics Board and the Research Subjects Review Board at the University of Rochester. Written informed consent was obtained from all participants.

## Fish intake data

Dietary data were available at 28 weeks gestation for 229 mothers as detailed in Bonham *et al* (24). Mothers completed a four-day semi-quantitative food diary for two consecutive weekdays and two weekend days. The food diaries were available in both English and the native Kreol language and dietitians provided mothers with detailed information on how to complete them. Women were asked to record the amount and types of foods and beverages consumed. Diaries were reviewed locally by dietitians within one week of completion. Subsequently, nutritionists from Ulster University, Coleraine, reviewed them for any errors or omissions and requested clarification from participants. Food diary data were converted to weight in grams and analysed using dietary analysis software (WISP version 2.0; Tinuviel Software, Warrington, UK) allowing for quantitative food and nutrient intakes to be determined. WISP software was updated with recipe and food composition data for foods commonly eaten in Seychelles using a variety of food composition tables including *The Composition of South African Foods*(25) and *The Concise New Zealand Food Composition Tables*(26). The food diaries provide data on the amount (grams per day) of a range of fish consumed during pregnancy. Each fish meal (g/day) was categorised into: *fatty fish*, *lean fish*, *crustaceans*, *molluscs*, and *fish products and dishes*. Owing to a large number of non-consumers for the categories of *crustaceans*, *molluscs* and *fish products and dishes* in this cohort, these variables were excluded from analysis. Our analysis focused on the variable of fish consumption (g/day), calculated as the sum of *fatty fish* and *lean fish* consumed.

## Developmental assessment

Seychellois maternal child health nurses specially trained at the University of Rochester administered all neurodevelopmental tests. Children completed testing at ages 9 and 30 months and 5 and 9 years. All tests were translated into Kreol. At nine and 30 months children completed the Bayley Scales of Infant Development II (BSID II) as described in Davidson *et al.* (27). At age five-years, the test battery included the following as described by Strain *et al.*(28): Finger Tapping (Dominant and Non-Dominant hand) (29) , the Preschool Language Scale (PLS) (Auditory Comprehension, Verbal Ability and Total Language) (30), the Woodcock-Johnson (WJ) Tests of Achievement (Applied Problems and Letter-Word Recognition)(31), the Achenbach Child Behaviour Checklist (CBCL) (Total score)(32) and the Kaufman Brief Intelligence Test (KBIT) (Verbal Knowledge and Matrices) (33). At age nine years, the Children's test battery included the following: CBCL (32), Bender Visual Motor Gestalt (34), Conners' Attention Deficit Hyperactivity Disorder (ADHD) Index (35), Expressive Vocabulary Test (EVT) (36), KBIT (Verbal Knowledge and Matrices) (33), Peabody Picture Vocabulary (PPV) test (37), Stroop (38), Trail Making Time (Part A and B) (39) and the WJ Tests of Achievement (Applied Problems and Letter-Word Recognition) (31).

## Covariates

Consistent with our previous work (18,20–22), multivariable regression analyses controlled for covariates already known to be associated with child neurodevelopment including: maternal age and IQ (KBIT), child sex, birthweight, and age at testing, socioeconomic status (the Hollingshead Four-Factor SES modified for use in Seychelles), family status (the presence of both parents living with the child), and the home environment (the Pediatric Review of Children's Environmental Support and Stimulation, PROCESS).

## Statistical Analysis

Descriptive analysis was performed, and all data were expressed as mean ± SD, median, interquartile range (IQR), and minimum and maximum values. The primary analysis was a series of multiple linear regressions where we separately examined associations between total fish consumption on a continuous scale (g/day) and child neurodevelopmental outcomes at each testing time point, while controlling for maternal age and KBIT, child sex, birthweight, and age at testing, family status, socioeconomic status, and PROCESS. To examine for any nonlinearity in the association of fish intake and endpoints we conducted a secondary set of analyses using tertiles of fish consumption, with the lowest tertile as the reference group. Owing to the high levels of fish consumption in our cohort it was not possible to categorise fish intakes with reference to the current FDA advice, above or below the lower cut point of 8 oz/week (equivalent to 32.4 g/d), as only 11 women reported consumption less than 8 oz (227 g)/week of seafood, the lower FDA recommendation, and three reported no seafood consumption. Therefore, we divided fish consumption into tertiles and examined their relationship with endpoints. Mothers in the lowest tertile consumed up to 74.5 g/d (median 55 g/d; equivalent to 14 oz/ wk) total fish. Mothers in the middle tertile consumed 74.6 – 118.6 g/d (median 97.3 g/d; equivalent to 24 oz/wk), and mothers in the highest tertile consumed 118.7 – 413.3 g/d (median 156.6 g/d; equivalent to 39 oz/wk). Analysis was performed with R statistical software and statistical significance in all analyses was considered a 2-sided P value <0.05.

## Results

A total of *n*=229 mother-child pairs had complete dietary, neurodevelopmental, and covariate data available. The average (SD) maternal age was 27.69 (5.88) years. The cohort comprised *n*=116 girls and *n*=113 boys. The average (SD) maternal total fish consumed in this cohort was 106.8 (61.9) g/d measured at 28 weeks' gestation as shown in **Table 1**. As different numbers of children completed each cognitive test, the *n* for each model differs and is shown within **Table 2**, which also displays summary statistics for the child outcomes at each time point.

The primary analysis using total fish consumption as a continuous variable and its association with child neurodevelopmental endpoints at each time point is presented in **Table 3**. Total fish consumption was positively associated with the KBIT Matrices score, a measure of nonverbal intelligence at age five years ($\beta$=0.003, 95% CI 0.000 – 0.005, *p*=0.03). There were no adverse associations with child neurodevelopmental outcome. However, if we had applied the Bonferroni correction for multiple testing and set p-values at less than 0.002 as statistically significant then no associations would have met that conservative threshold in primary analysis.

A secondary analysis examined fish consumption using tertiles (see Table 4). Among the 52 comparisons there were no significant associations between the highest and the lowest tertiles. At age five years, children of mothers in the middle tertile showed a statistically significant adverse difference in score on the WJ Applied Problems scores (a test of mathematical reasoning) from mothers in the lowest tertile. Scores were 1.16 points lower on average (95% CI -2.309 – -0.007) than those of mothers in the lowest tertile ($p$=0.049). We consider this a spurious finding because it was one of 52 comparisons and there was no association between the highest and lowest tertile on this test. In all models, reported associations did not meaningfully change when comparing the associations from models controlling for covariates to those from unadjusted models (data not shown). No associations would have been statistically significant if Bonferroni correction for multiple testing and a resultant p-value threshold of less than 0.002 used.

## Discussion

In the primary analysis examining the association of maternal fish consumption as a continuous variable with the 26 neurodevelopmental endpoints, we found one positive association. The children's KBIT Matrices, a test of nonverbal intelligence, at age five years improved as fish consumption increased. In a secondary analysis categorizing fish consumption by tertiles, we found no significant associations between the highest and lowest tertiles. However, there was a statistically significant adverse difference in score on the WJ Applied Problems scores in children from mothers in the middle tertile when compared with children from mothers in the lowest tertile. We interpret our study as providing no clear evidence in either the primary or secondary analysis of beneficial or adverse associations between maternal fish consumption and children's neurodevelopment. These results are consistent with our earlier findings in this cohort and findings of two recent systematic reviews which showed no adverse associations of fish consumption.

In our earlier assessment of this cohort, we found the mothers' total n-3 PUFA status (a proxy for fatty fish consumed during pregnancy) was positively associated with the PDI in this age group (22). This finding suggested that higher n-3 PUFA may be contributing to the improved psychomotor development of infants at this age. The guidance from fish advisories differs worldwide, but the most common advice during pregnancy is to consume fish two to three times per week, with at least one portion being fatty fish (9–12). The suggested benefits are believed to be mainly attributable to DHA, a crucial nutrient in pregnancy for brain neurodevelopment (4). The benefits of DHA for neurodevelopment are well established (4), but the evidence for prenatal DHA supplementation remains inconclusive (40).

In contrast, there is convincing evidence of the benefits of fish consumption in pregnancy for infant neurodevelopment from multiple studies that have evaluated fish as a whole food. Two rigorous scientific reviews of the evidence in this field concluded that there were no adverse associations of fish consumption with children's neurodevelopment (7,8). The reviews evaluated data from 44 publications where the range of beneficial outcomes included improved visual acuity, early language and communication skills, IQ and social skills in children (7,8). In these studies, fish consumption ranged from ~4 oz (113 g) per week up to > 100 oz (2835 g or ≥405 g/d) per week (7,8). Women in the SCDS NC1 consumed on average approximately 106 g/d (3.7 oz) fish, which is equivalent to 26 oz per week; these quantities are substantially more than the FDA advice to consume eight to 12 oz per week in pregnancy.

As the Seychellois are such a high fish-consuming population, exposure to MeHg is several times higher than in the USA or UK. However, it is important to note that MeHg concentrations in fish in the Seychelles (23) is the same as in countries such as USA (41); therefore, it is the high levels of fish consumption, rather than Seychelles fish containing higher MeHg that leads to higher MeHg exposure for the Seychellois population. Our results add further evidence to the existing reports which found no adverse associations with high fish consumption during pregnancy (7). We have previously reported that the nutrients, mainly LCPUFA, present in fish are likely to overcome any potential adverse toxic effects of prenatal MeHg exposure (20–22). Our findings add to the evidence supporting the safety of consuming fish that has only naturally acquired amounts of MeHg.

Strengths of our study include its prospective longitudinal double-blind exposure design and neurodevelopmental evaluations by specially trained nurse evaluators at multiple time points using a comprehensive battery of tests including measures of IQ and verbal development. Also detailed dietary data collected prospectively through the completion of four-day food diaries, a method which minimizes some of the errors typically associated with interviewer technique and memory recall(42). The dietary data were further strengthened by our update of the WISP dietary analysis software with food composition data for foods specific to Seychelles and extensive review of the data by dietitians in Seychelles and nutritionists at Ulster University. Additionally, in Seychelles consuming sea mammals is prohibited and there is no co-exposure to other pollutants which could potentially be detrimental to foetal neurodevelopment. Limitations of the study include it being an observational epidemiology study and unmeasured covariates might have been omitted and the sample size is relatively small.

## Conclusion

In this cohort, where fish consumption is substantially higher than current global recommendations, maternal fish consumption during pregnancy was not beneficially or adversely associated with children’s neurodevelopmental outcomes in primary or secondary analyses across numerous time points up to nine years of age.

## Acknowledgments

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## Conflict of Interest

All authors declare no conflicts of interest.

## Authorship

The authors GJM, CFS, PWD, GEW, EvW and JJS collaboratively designed the SCDS NC1 study (project conception, development of overall research plan, and study oversight), with the concept for the present paper conceptualised by GJM, EvW, and JJS. CFS, MSM, EMcS, GEW and JH conducted the research (hands-on conduct of the experiments and data collection). DW and TL analyzed the data and helped draft the manuscript. MCC, MW and AJY assisted with analyzing the data, interpretation of data and co-drafted the manuscript. All authors reviewed, edited and approved the final article. MCC and AJY had full access to all the data in the study and accept final responsibility for the decision to submit for publication. The funders had no involvement or restrictions in relation to publication of this manuscript.

## Data Sharing

Data described in the manuscript, code book, and analytic code will be made available upon request pending [e.g., application and approval, payment, other].

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**Table 1. Maternal characteristics of Nutrition Cohort 1 (NC1) with maternal fish consumption and any completed outcomes (*n*=229)**

| Covariates | Mean (SD) | Median (IQR) | Min, Max |
|---:|:---:|:---:|:---:|
| Maternal age (yrs) | 27.7 (5.9) | 27 (23,32) | 16, 43 |
| Hollingshead SES | 33.93 (11.01) | 33 (25,42) | 13, 63 |
| Maternal KBIT | 86.21 (14.19) | 89 (74,97) | 48, 117 |
| PROCESS | 152.14 (14.63) | 153 (141,161) | 113, 190 |
| Child birth weight (kg) | 3.24 (0.47) | 3.25 (2.92,3.56) | 1.87, 4.45 |
| Total fish consumption (g/d) | 106.8 (61.7) | 97.00 (61.00,131.67) | 0.00, 413.33 |

KBIT: Kaufmann Brief Intelligence Test; PROCESS: Pediatric Review of Children's Environmental Support and Stimulation

**Table 2. Summary statistics for Nutrition Cohort 1 (NC1) child cognitive outcomes at each time point**

| Time point | *n* | Mean | SD | Min | Max |
|---|---|---|---|---|---|
| *9 Months (n=229)* | | | | | |
| Child age (months) | 229 | 9.51 | 0.48 | 8.48 | 12.22 |
| MDI | 226 | 102.91 | 8.25 | 72.00 | 122.00 |
| PDI | 225 | 105.72 | 10.38 | 68.00 | 141.00 |
| *30 Months (n=228)* | | | | | |
| Child age (months) | 228 | 28.32 | 1.34 | 23.52 | 35.68 |
| MDI | 228 | 85.00 | 9.51 | 56.00 | 115.00 |
| PDI | 225 | 89.81 | 13.79 | 50.00 | 123.00 |
| *5 Years (n=222)* | | | | | |
| Child age (yrs) | 222 | 5.62 | 0.30 | 5.14 | 6.32 |
| FT Dominant | 222 | 23.49 | 5.72 | 5.40 | 39.60 |
| FT Non-Dominant | 222 | 21.30 | 4.87 | 8.60 | 34.80 |
| PLS Auditory Comprehension | 222 | 55.57 | 2.73 | 47.00 | 60.00 |
| PLS Verbal Ability | 222 | 63.10 | 3.25 | 51.00 | 68.00 |
| PLS Total Language | 222 | 118.68 | 5.39 | 100.00 | 128.00 |
| WJ Applied Problems | 222 | 15.09 | 4.14 | 2.00 | 24.00 |
| WJ Letter-Word Recognition | 222 | 10.95 | 6.06 | 1.00 | 24.00 |
| CBCL | 222 | 59.30 | 8.68 | 25.00 | 77.00 |
| KBIT Verbal | 222 | 11.79 | 2.77 | 6.00 | 18.00 |
| KBIT Matrices | 222 | 7.73 | 1.18 | 2.00 | 9.00 |
| *9 Years (n=216)* | | | | | |
| Child age (yrs) | 216 | 9.52 | 0.09 | 9.20 | 9.92 |
| CBCL | 215 | 37.59 | 19.34 | 3.00 | 103.00 |
| Bender Visual Motor Gestalt | 214 | 22.42 | 6.10 | 8.00 | 40.00 |
| ADHD Conners' Index | 215 | 7.66 | 8.11 | 0.00 | 36.00 |
| EVT | 214 | 79.94 | 11.80 | 51.00 | 126.00 |
| KBIT Verbal | 215 | 33.80 | 9.01 | 10.00 | 52.00 |
| KBIT Matrices | 215 | 24.03 | 5.97 | 12.00 | 39.00 |
| PPV test | 213 | 133.15 | 27.62 | 83.00 | 189.00 |
| Stroop | 206 | -21.02 | 8.97 | -61.00 | 1.00 |
| TM Part A | 215 | 66.47 | 29.20 | 23.00 | 246.00 |
| TM Part B | 214 | 157.46 | 66.32 | 52.00 | 361.00 |
| WJ Letter-Word Recognition | 212 | 66.94 | 16.03 | 11.00 | 76.00 |
| WJ Applied Problems | 215 | 28.97 | 4.53 | 22.00 | 44.00 |

NC1: Nutrition Cohort 1; MDI: Mental Developmental Index; PDI: Psychomotor Developmental Index; FT: Finger-Tapping; PLS: Preschool Language Scale; WJ: Woodcock Johnson; CBCL: Child Behavior Checklist; KBIT: Kaufman Brief Intelligence Test; ADHD: Attention Deficient Hyperactivity Disorder; EVT: Expressive Vocabulary Test, PPV: Peabody Picture Vocabulary, TM: Trail Making

**Table 3. Associations between maternal fish consumption (continuous) and child cognitive outcomes at each time point adjusted for maternal age and KBIT, child sex, birthweight, and age at testing, family status, socioeconomic status, and PROCESS**

| | | **Total fish (g/d)** | | | |
|---|---|---|---|---|---|
| | | | | **95% CI (LL, UL)** | |
| **Time point** | ***n*** | **β effect estimate** | **P value** | **LL** | **UL** |
| *9 Months* | | | | | |
| MDI | 226 | 0.000 | 0.986 | -0.017 | 0.017 |
| PDI | 225 | 0.005 | 0.645 | -0.017 | 0.027 |
| *30 Months* | | | | | |
| MDI | 228 | 0.006 | 0.556 | -0.013 | 0.025 |
| PDI | 225 | -0.001 | 0.934 | -0.029 | 0.026 |
| *5 Years* | | | | | |
| KBIT Verbal Knowledge | 222 | 0.001 | 0.665 | -0.004 | 0.007 |
| KBIT Matrices | 222 | **0.003** | **0.030** | **0.000** | **0.005** |
| PLS Auditory Comprehension | 222 | 0.001 | 0.658 | -0.004 | 0.006 |
| PLS Verbal Ability | 222 | 0.005 | 0.133 | -0.002 | 0.012 |
| PLS Total Language | 222 | 0.006 | 0.246 | -0.004 | 0.017 |
| WJ Applied Problems | 222 | 0.003 | 0.384 | -0.004 | 0.011 |
| WJ Letter-Word Recognition | 222 | 0.009 | 0.070 | -0.001 | 0.019 |
| CBCL | 222 | -0.002 | 0.837 | -0.020 | 0.016 |
| FT Dominant | 222 | 0.000 | 0.968 | -0.012 | 0.011 |
| FT Non-Dominant | 222 | 0.000 | 0.957 | -0.011 | 0.010 |
| *9 Years* | | | | | |
| KBIT Verbal Knowledge | 215 | -0.012 | 0.241 | -0.032 | 0.008 |
| KBIT Matrices | 215 | 0.005 | 0.446 | -0.008 | 0.018 |
| EVT | 214 | 0.006 | 0.609 | -0.018 | 0.031 |
| PPV Test | 213 | 0.021 | 0.496 | -0.039 | 0.080 |
| WJ Applied Problems | 215 | 0.004 | 0.398 | -0.006 | 0.014 |
| WJ Letter-Word Recognition | 212 | 0.012 | 0.484 | -0.022 | 0.047 |
| CBCL | 215 | 0.022 | 0.296 | -0.019 | 0.063 |
| Bender Visual Motor Gestalt | 214 | -0.010 | 0.134 | -0.023 | 0.003 |
| TM Part A | 215 | 0.004 | 0.904 | -0.059 | 0.067 |
| TM Part B | 214 | -0.083 | 0.255 | -0.227 | 0.061 |
| ADHD Conners' Index | 216 | 0.001 | 0.866 | -0.015 | 0.018 |
| Stroop | 206 | -0.005 | 0.608 | -0.025 | 0.015 |

PROCESS: Pediatric Review of Children’s Environmental Support and Stimulation; MDI: Mental Developmental Index; PDI: Psychomotor Developmental Index; FT: Finger-Tapping; PLS: Preschool Language Scale; WJ: Woodcock Johnson; CBCL: Child Behavior Checklist; KBIT: Kaufman Brief Intelligence Test; ADHD: Attention Deficient Hyperactivity Disorder; EVT: Expressive Vocabulary Test, PPV: Peabody Picture Vocabulary, TM: Trail Making. Multiple regression models were fit separately and adjusted for maternal age at birth, child age at testing, child sex, birthweight, socioeconomic status, family status, home environment, and maternal IQ

**Table 4. Associations between maternal total fish consumption (tertiles of intake) and child neurodevelopmental outcomes at each time point adjusted for maternal age and KBIT, child sex, birthweight, and age at testing, family status, socioeconomic status, and PROCESS**

| | | **Middle vs Low Tertile*** | | | | **High vs Low Tertile*** | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | **95% CI (LL, UL)** | | | | **95% CI (LL, UL)** | | |
| **Time point** | ***n*** | **β effect estimate** | **LL** | **UL** | **P value** | **β effect estimate** | **LL** | **UL** | **P value** |
| *9 Months* | | | | | | | | | |
| MDI | 226 | 0.674 | -1.857 | 3.205 | 0.600 | -0.089 | -2.615 | 2.437 | 0.945 |
| PDI | 225 | 1.947 | -1.355 | 5.249 | 0.246 | 1.741 | -1.538 | 5.020 | 0.297 |
| *30 Months* | | | | | | | | | |
| MDI | 228 | 1.054 | -1.845 | 3.953 | 0.474 | 0.920 | -1.959 | 3.799 | 0.529 |
| PDI | 225 | 1.148 | -3.057 | 5.353 | 0.591 | -1.160 | -5.300 | 2.981 | 0.582 |
| *5 Years* | | | | | | | | | |
| KBIT Verbal Knowledge | 222 | 0.189 | -0.683 | 1.061 | 0.670 | 0.004 | -0.852 | 0.859 | 0.994 |
| KBIT Matrices | 222 | -0.075 | -0.457 | 0.308 | 0.701 | 0.151 | -0.224 | 0.526 | 0.428 |
| PLS Auditory Comprehension | 222 | -0.057 | -0.879 | 0.766 | 0.892 | -0.175 | -0.981 | 0.632 | 0.670 |
| PLS Verbal Ability | 222 | 0.224 | -0.810 | 1.258 | 0.670 | 0.235 | -0.779 | 1.248 | 0.649 |
| PLS Total Language | 222 | 0.167 | -1.486 | 1.821 | 0.842 | 0.060 | -1.561 | 1.682 | 0.942 |
| WJ Applied Problems | 222 | **-1.158** | **-2.309** | **-0.007** | **0.049** | -0.040 | -1.169 | 1.089 | 0.945 |
| WJ Letter- Word Recognition | 222 | 0.686 | -0.868 | 2.241 | 0.385 | 0.775 | -0.750 | 2.300 | 0.317 |
| CBCL | 222 | 0.813 | -1.943 | 3.570 | 0.561 | -0.119 | -2.823 | 2.584 | 0.931 |
| FT Dominant | 222 | 1.130 | -0.689 | 2.949 | 0.222 | 0.553 | -1.231 | 2.336 | 0.542 |
| FT Non-Dominant | 222 | 0.614 | -1.018 | 2.246 | 0.459 | 0.216 | -1.385 | 1.817 | 0.790 |
| *9 Years* | | | | | | | | | |
| KBIT Verbal Knowledge | 215 | 0.302 | -2.749 | 3.353 | 0.845 | -2.363 | -5.394 | 0.667 | 0.126 |
| KBIT Matrices | 215 | 0.048 | -1.962 | 2.057 | 0.963 | -0.005 | -2.001 | 1.991 | 0.996 |
| EVT | 214 | 0.919 | -2.944 | 4.782 | 0.640 | 0.072 | -3.753 | 3.896 | 0.971 |
| PPV Test | 213 | 0.993 | -8.298 | 10.284 | 0.833 | 2.401 | -6.813 | 11.615 | 0.608 |
| WJ Applied Problems | 215 | 0.608 | -0.886 | 2.102 | 0.423 | 0.479 | -1.005 | 1.964 | 0.525 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| WJ Letter- Word Recognition | 212 | 2.606 | -2.765 | 7.977 | 0.340 | 1.059 | -4.309 | 6.427 | 0.698 |
| CBCL | 215 | 2.256 | -4.043 | 8.554 | 0.481 | 5.613 | -0.643 | 11.869 | 0.078 |
| Bender Visual Motor Gestalt | 214 | 0.751 | -1.252 | 2.754 | 0.461 | -0.958 | -2.950 | 1.035 | 0.344 |
| TM Part A | 215 | -4.741 | -14.465 | 4.983 | 0.338 | 2.547 | -7.111 | 12.206 | 0.604 |
| TM Part B | 214 | -2.587 | -24.908 | 19.734 | 0.819 | -4.541 | -26.814 | 17.732 | 0.688 |
| ADHD Conners' Index | 216 | -0.036 | -2.617 | 2.545 | 0.978 | 0.980 | -1.594 | 3.553 | 0.454 |
| Stroop | 206 | 1.363 | -1.674 | 4.400 | 0.377 | 0.399 | -2.656 | 3.454 | 0.797 |

PROCESS: Pediatric Review of Children's Environmental Support and Stimulation MDI: Mental Developmental Index; PDI: Psychomotor Developmental Index; FT: Finger-Tapping; PLS: Preschool Language Scale ; WJ: Woodcock Johnson; CBCL: Child Behavior Checklist; KBIT: Kaufman Brief Intelligence Test; ADHD: Attention Deficient Hyperactivity Disorder; EVT: Expressive Vocabulary Test, PPV: Peabody Picture Vocabulary, TM: Trail Making; *tertile median g/day (tertile range g/d); range of fish intake for each tertile at each time point is as follows: 9 months: low (n=77) = 55.0g/day (0- 74·5), middle (n=76) = 97·3g/d (74·6- 118·6), high (n=76) = 156·6g/d (118·7- 413·3); 30 months: low (n=76) = 55.0g/d (0- 74·3), middle (n=76) = 97·3g/d (74·4- 118·8), high (n=76) = 156·6g/d (118·9- 413·3); 5 years: low (n=74) = 55.0g/d (0- 74·7), middle (n=74) = 96·8g/d (74·8- 118·4), high (n=74) = 155·3g/d (118·5-413·3); 9 years: low (=72) = 55·4g/d (0- 74·3), middle (n=72) = 97·6g/d (74·4- 118·8), high (n=72) = 155·3g/d (118·9- 413·3).