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Periconceptional seafood intake and fetal growth

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Abstract

Background—Previous reports of associations of maternal seafood intake with fetal growth were inconsistent. Further, little is known whether associations differ across seafood subtypes or fetal growth indices.

Methods—Among 3,141 participants of the Omega study, a pregnancy cohort study, we investigated associations of periconceptional shell-, lean-, and fatty-fish intake with fetal growth indices. We categorized food frequency questionnaire reported seafood intake into frequencies of: <0.2 servings/month, 0.2 servings/month–<0.5 servings/week, 0.5–1 servings/week, and >1 servings/week. We abstracted birthweight, birth length, and head circumference from medical records. Using generalized linear models with a log link, the Poisson family, and robust standard errors, we estimated relative risks and 95% confidence intervals (CIs) for low birthweight (LBW, <2500 g) and linear regression models to estimate mean differences for continuous fetal growth indices across seafood intake categories.

Results—Medians (interquartile ranges) of shell-, lean-, and fatty-fish intake were 0.3 (0–0.9), 0.5 (0–1.0), and 0.5 (0.1–1.0) servings/week, respectively. Lean fish intake of >1 servings/week (versus <0.2 servings/month) was associated with a 2.2-fold higher risk of LBW [95% CI: 1.2, 4.1]. Shellfish intake of >1 servings/week (versus <0.2 servings/month) was associated with a 0.6 kg/m³ higher mean ponderal index [95% CI: 0.0, 1.2 kg/m³]. There was no evidence for associations of total seafood or seafood subtype intake with other fetal growth indices.

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Conclusions—Higher intakes of lean- and shell-fish were associated with a higher risk of LBW and higher mean ponderal index, respectively. Findings highlight the importance of considerations of seafood subtype in similar investigations.

Maternal periconceptional seafood intake may have diverse effects on fetal growth. Seafood is a source of many beneficial nutrients that include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA and DHA influence eicosanoid hormone profiles, important for regulating inflammation and maternal-fetal blood flow^{1, 2}, and normal cell membrane development and function³, important for optimal fetal growth and development. On the other hand, seafood intake may lead to exposure to heavy metals or contaminants such as polychlorinated biphenyls (PCBs), which may adversely impact fetal development.

Higher maternal seafood intake has been associated with higher fetal growth indices including birthweight⁴⁻⁶, birth length⁶ and head circumference⁴⁻⁶, and lower risk of low birthweight or small for gestational age^{5, 7, 8} status in some but not all studies^{9, 10}. Besides these inconsistencies, findings also suggest associations of seafood intake during pregnancy and fetal growth may depend on several factors such as the timing of intake (whether during early or late pregnancy), the type of seafood (including the seafood species and how it is prepared)^{5, 8, 9, 11}, and underlying population characteristics⁷. These factors were heterogeneous across previous studies and depend on geographic location. Few investigators have examined associations of early pregnancy seafood intake across seafood subtypes with fetal growth in the US¹⁰, where intake is generally lower relative to intake among most of the previously studied populations. Prior investigations have primarily focused on birthweight and less is known about the associations of seafood intake with other fetal growth indices.

Research supports that intrauterine growth and development of female and male fetuses differ¹², as reflected by sex differences in birthweight. Further, accumulating evidence supports potential sex-specific differences in associations of *in utero* exposures with fetal growth¹³, including nutrients (e.g. DHA¹⁴, Vitamin D¹⁵) and contaminants (e.g. cadmium¹⁶, PCBs¹⁷) found in seafood. Despite this evidence, we are unaware of prior studies of periconceptional seafood intake and fetal growth associations across infant sex.

In the Omega study, a pregnancy cohort study, we investigated associations of maternal periconceptional seafood intake with fetal growth indices: birthweight, birth length, ponderal index, and head circumference. We hypothesized that associations of seafood intake and fetal growth vary by seafood subtype. In addition, among a subset of study participants, we examined associations of maternal erythrocyte EPA+DHA and fetal growth indices. In secondary analyses, we examined whether associations of maternal seafood intake and fetal growth indices differ by infant sex.

METHODS

Study population

The Omega study is a prospective cohort study of dietary and metabolic risk factors associated with adverse pregnancy outcomes. Participants were recruited among women

attending prenatal care clinics affiliated with Swedish Medical Center and Tacoma General Hospital in Seattle and Tacoma, Washington, respectively¹⁸. Eligible participants, pregnant women who initiated prenatal care at or before 20 weeks gestation, were aged 18 years, able to speak and read English, planned to carry the pregnancy to term, and to deliver at either of the two hospitals. The protocol for the study was approved by the Institutional Review Boards of Tacoma General Hospital and Swedish Medical Center. All participants provided informed consent.

During the study period (1996-2008), 5,063 eligible women were approached, 4,000 (79%) consented to participate, and 3,892 (97%) completed study follow-up. For the current study, we excluded the following participants: 118 with multifetal pregnancies, 72 with implausible total energy intake of <500 or >3500 kcal/day, 34 with pregnancies complicated by fetal demise (after 20 weeks of gestation), 124 participants missing labor and delivery information, 14 participants missing information on all fetal growth indices, and 389 who were missing seafood intake information. A total of 3,141 participants remained for analyses.

Data collection

At 16 weeks gestation on average, trained interviewers conducted in-person interviews (45-60 minutes in length) to collect data on socio-demographic characteristics, reproductive and medical histories, height and pre-pregnancy weight, recreational physical activity, alcohol and tobacco intake. Participants completed a self-administered, validated, semi-quantitative food-frequency questionnaire (FFQ) to assess periconceptional (the three months before and the first three months of index pregnancy)¹⁸ diet. The FFQ had been developed for and used in the Women's Health Initiative Clinical Trial¹⁹. FFQs were analyzed using food composition values obtained from the University of Minnesota Nutrition Coding Center nutrient database²⁰. In addition, participants completed a Seafood Intake Scale (SIS) FFQ²¹ to determine usual intake of 35 types of seafood available in the Pacific Northwest during the prior three-month period and provided non-fasting peripheral blood samples at this initial visit. Blood samples from a randomly selected subset (60%) of early participants (enrolled from 1996-2000, $n = 534$) were analyzed for erythrocyte membrane EPA and DHA¹⁸. After delivery, trained personnel abstracted maternal and infant medical records to ascertain course and outcomes of pregnancy.

Seafood intake

Seafood was categorized into shell-, lean-, or fatty-fish groups as described in the Supporting Information, Table S1. Shellfish included crab, lobster, shrimp or prawns, clams, mussels, oysters, scallops, abalone, octopus, and squid. Lean fish included regular canned tuna, catfish, cod, flounder or sole, haddock, halibut, mahi mahi, snapper or rockfish, shark, imitation crab, imitation lobster, and fish sticks. Fatty fish included anchovies, herring (pickled or regular), kipper snacks, salmon (canned, fresh or smoked), sardines, albacore tuna, swordfish, rainbow trout, smelt, and mackerel. Using the SIS FFQ, we calculated the monthly intake of seafood by multiplying the usual monthly frequency of intake by the serving size. We defined a single serving of seafood to equal 3 ounces (85 g) based on

American Heart Association guidelines²². The lowest SIS FFQ reportable amount of seafood was <0.2 servings/month.

Fetal growth indices

Infant birthweight, birth length, and head circumference measures were abstracted from medical records. Low birthweight (<2500 g), normal birthweight (2500-3999 g), and macrosomia (≥ 4000 g) categories were defined according to the World Health Organization²³. Ponderal index was calculated as birthweight (kg) divided by the birth length cubed (m³)¹².

Statistical analysis

We examined frequency distributions of maternal characteristics across categories of seafood intake. We chose categories of <0.2 servings/month (reference), 0.2 servings/month-0.5 servings/week, 0.5-1 servings/week, and >1 servings/week, to allow for approximately equal frequencies of participants across seafood intake categories.

To estimate relative risks (RRs) and 95% confidence intervals (CIs) for low birthweight relative to normal birthweight infants associated with each non-referent category of seafood intake, we fit generalized linear models with a log link, Poisson family (a “Log-Poisson” regression model), and robust standard errors. This model allows estimation of RRs for prospective studies with binary outcome data²⁴. Macrosomic infants were excluded from analyses of low birthweight. To estimate mean differences and 95% CIs for continuous indices of fetal growth across each category of seafood relative to the reference group, we fit linear regression models. In these models, each non-reference category of seafood intake was modeled as an indicator variable and compared with the reference category. Model fit was assessed by examination of regression residual diagnostics. Based on prior literature that suggests potential linear trends across higher seafood intake categories and EPA+DHA levels^{4, 5, 10}, we calculated Wald p-values for grouped linear terms of seafood intake. Adjusted models for seafood subtypes as the exposure included non-referent indicator variables for intake of shell-, lean-, and fatty-fish simultaneously. For example, to observe associations of lean fish with fetal growth, independent of shell- or fatty-fish, we included non-referent indicator variables for all three seafood subtypes.

The following variables were identified *a priori* and considered as potential confounding variables and were included in all our adjusted models as binary variables: non-Hispanic white race/ethnicity, high school or less education, unmarried status, nulliparity, habitual recreational physical activity during index pregnancy based on activity in the week prior to interview, alcohol intake, cigarette smoking during index pregnancy. Male infant sex was included as a precision variable. Three non-referent indicator variables for pre-pregnancy body mass index (BMI), based on the National Institute of Health definitions of underweight (referent, <18.5 kg/m²), normal weight (18.5-24.9 kg/m²), overweight (25-29.9 kg/m²), and obese (≥ 30 kg/m²)²⁵ status, were included in our adjusted model. Maternal age (years), total energy consumed (kcal/day), and intakes of red and processed meats (servings/day) were included in all adjusted models as continuous variables.

In addition to our main analysis, we examined whether associations of seafood intake with fetal growth indices were sensitive to further adjustment for gestational week at delivery (modeled continuously). We did not include gestational week at delivery in our main analysis due to the potential for reversal of exposure-outcome associations as described by Wilcox *et al.*²⁶ In another sensitivity analysis, we examined whether our results were materially altered by excluding those who experienced any of the following: preeclampsia, gestational hypertension, gestational diabetes, or preterm birth (birth <37 weeks gestation).

Among a subset of study participants ($n = 534$) we examined mean change (95% CIs) in fetal growth indices associated with maternal quartile of erythrocyte EPA+DHA. In secondary analyses, we also examined whether associations of seafood intake with fetal growth indices varied across infant sex by repeating the analyses described above, stratified by infant sex.

The Wald test was used to calculate p-values for the seafood-infant sex interaction terms. All p-values were 2-sided and defined to be significant at p-value <0.05. Analyses were carried out using Stata Software (version 10.1; StataCorp LP, College Station, TX).

RESULTS

Most study participants were non-Hispanic white (88%), married (90%), nulliparous (62%), and educated beyond high-school (97%). A minority smoked cigarettes (5%), consumed alcohol (26%) during the index pregnancy or indicated intake of fish oil supplements (1%). Mean (standard deviation, SD) maternal age was 32.7 (4.3) years. Medians (IQRs) of shell-, lean-, and fatty-fish intake were 0.3 (0-0.9), 0.5 (0-1.0), and 0.5 (0.1-1.0) servings/week, respectively. Among 1,552 female and 1,588 male infants, 63 female and 60 male (4%) were low birthweight infants (one infant was missing sex information). There were 449 (14%) macrosomic infants. Means (SDs) of birthweight, birth length, head circumference, and ponderal index for all infants were 3460.4 (534.6) g, 50.9 (3.1) cm, 34.7 (2.2) cm, and 26.5 (5.3) kg/m³, respectively.

Compared to included participants, excluded participants due to missing seafood intake information or implausible seafood/energy intake ($n = 461$) were less likely to be non-Hispanic white (71% versus 88%), nulliparous (40% versus 62%), or married (59% versus 90%) and more likely to be obese (17% versus 8%). Included and excluded participants were similar across indices of fetal growth.

Maternal characteristics across seafood intake are described in Tables 1-2. Briefly, women with seafood intake (regardless of type) of >1 servings/week compared to <0.2 servings/month reported higher daily total energy and red/processed meat intake. Women with higher intake of total seafood, shell-, lean- and fatty-fish had higher rates of post high-school education and Hispanic and/or non-white race/ethnicity (except for fatty-fish).

Lean fish intake of >1 servings/week compared to intake of <0.2 servings/month was associated with a 2.2-fold higher risk of low birthweight [95% CI: 1.21, 4.09], linear trend p-value across higher intake categories = 0.02 (Figure 1, Supporting Information Table S2).

Higher intakes of total seafood, shell-, and fatty-fish were not associated with risk of low birthweight.

Except for associations of shellfish intake with ponderal index, we found limited evidence for associations of higher total seafood or seafood subtypes with continuous fetal growth indices (Tables 3-4). Intake of >1 servings/week of shellfish versus intake of <0.2 servings/month (reference) was associated with a 0.6 kg/m³ higher mean ponderal index [95% CI: 0.0, 1.2 kg/m³], linear trend p-value = 0.07 (Table 3).

In sensitivity analyses, when we further adjusted for gestational week of delivery or excluded 780 infants born to mothers who experienced a pregnancy complication during the index pregnancy, our results were not materially altered. We did not observe evidence of an association between maternal quartile of erythrocyte EPA+DHA and fetal growth indices (Supporting Information Table S3). We observed several potential associations in the secondary, sex-stratified analyses of seafood intake with fetal growth indices. Adjusted RRs [95% CIs] for associations of lean fish intake of >1 servings/week compared to <0.2 servings/month (reference) with low birthweight, were 1.77 [0.76, 4.14] and 3.26 [1.36, 7.82] for female and male infants, respectively (Supporting Information Table S4). However, the Wald p-value for lean fish (grouped linear variable)-infant sex interaction was 0.43. Among females, shellfish intake of >1 servings/week (versus <0.2 servings/month) was associated with a 1.1 kg/m³ higher mean ponderal index [95% CI: 0.3, 1.9 kg/m³] (linear trend p-value = 0.02) (Supporting Information Table S5). The corresponding mean ponderal index among male infants was 0.2 kg/m³ higher [95% CI: -0.7, 1.2 kg/m³] (linear trend p-value = 0.66). However, the shellfish (grouped linear variable)-infant sex interaction term Wald p-value was 0.17. Associations of higher total seafood, fatty-, or lean-fish and ponderal index or seafood intake with other fetal growth indices did not vary across infant sex (Supporting Information Tables S4-6).

Using residual diagnostic procedures, we identified several potential outlying and influential points. Except for shellfish intake and ponderal index, further examination of these observations did not suggest erroneous characteristics for these participants and our main study findings were robust when we excluded these observations. Of note, we found that the 23 infants with ponderal indices of ≥ 40 kg/m³ were influencing the association of higher shellfish intake and higher mean ponderal index. After we excluded these infants and compared to intake of <0.2 servings/month of shellfish, mean differences in ponderal index [95% CIs] corresponding to intake of 0.2/month-<0.5/week, 0.5-1/week, >1/week servings were 0.3 higher [-0.1, 0.6], 0.2 higher [-0.1, 0.6], and 0.2 higher [-0.1, 0.6] kg/m³, linear trend p-value = 0.25.

COMMENTS

In this study, we found associations of higher maternal periconceptional lean fish intake with higher risk of low birthweight and higher shellfish intake with higher mean ponderal index. Also, our results suggest that associations of maternal seafood intake and fetal growth may vary by infant sex, although our tests for interaction were not statistically significant.

We note that our observed results were in a population with a median intake of shell-, lean- and fatty-fish of half a serving or less per week. Generally the intake among our study participants is much less than in other populations, especially populations outside the US, where a positive association between seafood consumption and fetal growth has been observed⁴⁻⁶.

We are aware of only one previous US cohort study of early pregnancy seafood intake and fetal growth. Among 2,109 maternal infant pair participants of Project Viva, Oken *et al.* reported mean difference in birthweight of -70 g [95% CI: 18, -158 g] (p-value for trend = 0.05) comparing the highest first-trimester seafood intake category (>2 servings/week) to the lowest intake category (<1 serving/month)¹⁰. Oken *et al.* also reported a 94 g lower mean birthweight [95% CI: -23, -166 g] (p-value for trend = 0.01) comparing the highest (mean = 0.36 g/day) to the lowest (mean = 0.02 g/day) quartile of EPA+DHA intake. Both of these results support our main finding that higher lean fish intake is associated with higher risk of low birthweight. However, risk of low birthweight was not associated with total seafood or EPA+DHA intake and associations with seafood subtypes were not examined in the study by Oken *et al.* Contrary to this previous report, we did not observe associations of total seafood intake or EPA+DHA with mean birthweight. Intakes of total seafood, assuming 1 serving = 3 ounces in both studies, and EPA+DHA were similar in both studies^{10, 27}. Despite these similarities, the contribution of seafood subtypes to overall intake differed and may account for some of the differences in findings. For example, of total seafood (excluding canned tuna), shell- and fatty-fish intake was lower among participants in the study by Oken *et al.* compared to participants in our study, 25% and 17% versus 31% and 25%, respectively²⁷.

There are several possible explanations for the association of higher lean fish intake with higher risk of low birthweight observed in our study, even though this finding has not been reported previously^{9, 11}. For example, generally fried fish includes lean fish species rather than fatty- or shell-fish and there is evidence that trans-fats, often used in frying, are associated with low birthweight²⁸. Also, frying can oxidize and lower EPA+DHA content²⁹. Another possibility may be that lean fish in our study was related to higher methylmercury (MeHg) exposure, which has been previously associated with lower birthweight¹¹. In our study, few (4%) women reported intake of predatory fish (shark [categorized as lean fish], mackerel and swordfish [categorized as fatty fish]), which the Food and Drug Administration recommends pregnant women avoid due to higher MeHg levels²². Our results were not materially altered when we excluded those who reported predatory fish intake (results not shown). However, since we lacked information on seafood preparation and contaminant content, we were unable to determine whether the higher lean fish intake-higher low birthweight risk-association in our study could be explained by these factors.

We are unaware of prior investigations of seafood subtype associations with ponderal index. Ponderal index is commonly used to capture infant body composition or proportionality and is similar to BMI³⁰. High ponderal index has been associated with high BMI in early adulthood³¹. The difference in mean ponderal index observed in our study was modest, 0.6 kg/m³ higher comparing servings of shellfish intakes of >1/week to <0.2/month, and it is unclear whether these results have clinical significance.

Importantly, our examination of model fit using regression residual diagnostics, revealed 23 infants with ponderal indices of 40 to 100 kg/m³ who were influencing the association of higher shellfish intake and higher mean ponderal index. Although the ponderal indices for these participants were high, their birthweights and birth lengths were within plausible ranges (results not shown). Since we could not be certain whether these values of ponderal index were erroneous, we retained them in the analyses.

While available evidence strongly supports different intrauterine growth patterns, trajectories, and birth size differences between female and male infants¹², prior studies of early pregnancy seafood intake have not examined the potential for differences across infant sex. Recent evidence supports the possibility for fetal sex specific differences in associations of nutrient and xenobiotic exposure with fetal growth and adulthood disease^{13, 32}. For instance, Kilari *et al.* reported that maternal erythrocyte DHA levels at delivery were significantly lower among low birthweight infants versus normal birthweight infants only among female infants (p-value <0.05), although the p-value for infant sex interaction was not reported¹⁴. We observed associations of higher lean fish intake with low birthweight that were statistically significant only among male infants and statistically significant associations for higher intake of shellfish and higher mean ponderal index only among females. However, these findings should be interpreted with caution since our tests for interaction were not statistically significant and our current study may be underpowered to formally assess statistical interaction.

Our findings should be interpreted in view of several potential limitations. We cannot rule out the possibility of exposure or outcome measurement error or residual confounding due to unmeasured or imprecisely measured confounding factors. It is understood that among the fetal growth indices that we examined, birthweight, though imperfect, is the most commonly reported and reliable anthropometric measures obtained at delivery³³. For instance, birth length and head circumference can be biased by the degree of flexion and head molding, respectively, which varies over time. Second, we evaluated associations between multiple exposures and outcomes and did not adjust for multiple comparisons, which may lead to increased type I error. Third, our overall study statistical power may be limited, particularly for the maternal erythrocyte EPA+DHA or infant sex-interactions analyses. Fourth, although we used indicator variables to model seafood intake to allow for some flexibility to observe non-linear associations, we did not statistically examine threshold effects. Threshold effects have been observed for modest intake of seafood (or up to approximately 250-500 mg/day EPA+DHA) and cardiovascular outcomes in men and non-pregnant women³⁴. Finally, our study participants were mostly non-Hispanic white, married, highly educated, and with normal pre-pregnancy BMI. Therefore, our results may not generalize to women of different race/ethnicity, socioeconomic status, or pre-pregnancy BMI.

Our study strengths included detailed information on seafood intake, collected prospectively, which we used to investigate a research gap on the potential varied effects of seafood subtypes. Blood samples from a subset of participants permitted assessment of associations of maternal erythrocyte EPA+DHA with fetal growth and to evaluate correlations of erythrocyte EPA+DHA with self-reported EPA+DHA intake (based on seafood intake), covering the periconceptional period (EPA+DHA $r = 0.53$, p-value <0.001).

Correlations were as high as prior reports³⁵. Our well-characterized cohort had high participation and follow-up rates, which allowed us to control for many previously reported confounding factors and to determine that our results were robust in several sensitivity analyses.

In sum, our study is the first to examine maternal periconceptional intake of seafood subtypes in a US cohort in relation to fetal growth. Our findings suggest that higher lean fish intake is associated with higher risk of low birthweight, and higher shellfish intake is associated with higher mean ponderal index. We did not observe a statistically significant change in mean birthweight or ponderal index with higher lean- or shell-fish intake. Our results also suggest that associations of seafood intake with fetal growth indicators may vary by infant sex, though our sex-specific associations should be interpreted with caution since interactions were not statistically significant. Future studies in different study populations as well as studies that examine the role of seafood preparation, contaminants, infant sex, and potential mechanisms for observed associations are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Relative risks (95% confidence intervals) of low birthweight associated with levels of seafood intake ^a

^aRelative risks (shown on a logarithmic scale) were calculated using generalized linear models with a log link, Poisson family, and robust standard errors. Relative risks were adjusted for maternal age (years), non-Hispanic white race, post high-school education, unmarried marital status, pre-pregnancy body mass index (indicator variables 18.5-24.9, 24-29.9, 30 kg/m²), total energy (kcal/day), current recreational physical activity, current smoking, current alcohol intake, nulliparity, intake of red/processed meats (servings/day), and male infant sex. For shell-, lean-, and fatty-fish analyses, alternate seafood subtypes (indicator variables for non-reference categories) were also included.

Table 1

Selected maternal characteristics according to amount of total seafood and shellfish intake

Characteristics	Total seafood intake (servings)				Shellfish intake (servings)			
	<0.2/mo (n = 286)	0.2/mo-<0.5/wk (n = 300)	0.5-1/wk (n = 521)	>1/wk (n = 2034)	<0.2/mo (n = 1038)	0.2/mo-<0.5/wk (n = 685)	0.5-1/wk (n = 739)	>1/wk (n = 679)
Non-Hispanic white, %	91	89	88	87	91	87	88	82
High school/less, %	6	6	4	2	5	2	2	2
Unmarried, %	13	10	8	10	10	9	10	11
Nulliparous, %	65	58	59	63	58	60	65	66
Pre-pregnancy body mass index								
<18.5 (kg/m ²), %	7	4	3	4	4	5	4	4
18.5-<25.0 (kg/m ²), %	65	70	74	72	70	75	72	69
25.0-<30.0 (kg/m ²), %	19	17	14	16	17	12	17	19
30.0 (kg/m ²), %	9	9	9	8	8	8	8	8
Current smoking, %	8	5	5	5	6	4	6	6
Current alcohol intake, %	22	22	23	28	21	28	28	29
No current recreational physical activity, %	20	20	20	17	19	19	17	16
Fish oil supplement use, %	0	2	1	2	1	2	1	1
Age (years), mean, SD	31.6, 4.8	32.0, 4.6	32.5, 4.2	33.0, 4.2	32.3, 4.5	32.7, 4.2	32.8, 4.2	33.1, 4.2
Gestational age at delivery (weeks), mean, SD	38.9, 1.8	38.8, 1.8	38.9, 1.6	38.9, 1.7	38.9, 1.7	38.8, 1.8	39.0, 1.6	38.9, 1.7
Erythrocyte EPA+DHA (%/total fatty acids), mean, SD	4.3, 1.2	4.8, 0.9	4.9, 0.8	5.6, 1.1	4.9, 1.1	5.2, 1.0	5.6, 1.1	5.9, 1.2
Dietary EPA+DHA (g/wk), median, IQR	0.0, 0.0-0.0	0.1, 0.0-0.1	0.3, 0.1-0.4	0.9, 0.6-1.3	0.2, 0.0-0.5	0.4, 0.2-0.8	0.7, 0.4-1.1	1.2, 0.8-1.8
Total energy (kcal/day), median, IQR	1515, 1193-1964	1471, 1125-1871	1545, 1256-1910	1720, 1387-2106	1600, 1273-1997	1543, 1211-1945	1671, 1360-2061	1779, 1470-2196
Red/processed meat (servings/day), median, IQR	0.4, 0.1-0.7	0.5, 0.3-0.8	0.5, 0.3-0.8	0.6, 0.3-0.9	0.5, 0.2-0.8	0.5, 0.3-0.8	0.6, 0.3-0.9	0.7, 0.4-1.0

EPA+DHA, eicosapentaenoic acid and docosahexaenoic acid; SD, standard deviation; IQR, interquartile range

Table 2

Selected maternal characteristics according to level of lean and fatty fish intake

Characteristics	Lean fish intake (servings)				Fatty fish intake (servings)			
	<0.2/mo (n = 800)	0.2/mo-<0.5/wk (n = 781)	0.5-1/wk (n = 857)	>1/wk (n = 825)	<0.2/mo (n = 742)	0.2/mo-<0.5/wk (n = 797)	0.5-1/wk (n = 855)	>1/wk (n = 747)
Non-Hispanic white, %	91	87	86	86	86	87	89	88
High school/less, %	4	4	3	2	7	3	1	2
Unmarried, %	11	9	10	11	14	9	7	11
Nulliparous, %	64	56	64	63	63	62	62	61
Pre-pregnancy body mass index								
<18.5 (kg/m ²), %	6	4	4	3	5	3	4	4
18.5-<25.0 (kg/m ²), %	69	73	72	71	66	75	74	70
25.0-<30.0 (kg/m ²), %	17	16	17	15	18	15	15	17
30.0 (kg/m ²), %	8	7	8	10	11	7	7	8
Current smoking, %	7	5	6	5	7	6	4	5
Current alcohol intake, %	23	25	27	29	22	27	26	28
No current recreational physical activity, %	21	19	16	16	19	20	18	14
Fish oil supplement use, %	1	2	2	1	1	2	2	2
Age (years), mean, SD	32.4, 4.5	32.6, 4.3	32.9, 4.3	32.8, 4.2	31.6, 4.6	32.5, 4.3	33.0, 4.0	33.6, 4.2
Gestational age at delivery (weeks), mean, SD	38.9, 1.7	38.9, 1.7	39.0, 1.6	38.9, 1.9	38.8, 1.8	38.9, 1.6	38.9, 1.7	39.0, 1.7
Erythrocyte EPA+DHA (%/total fatty acids), mean, SD	4.9, 1.3	5.2, 1.0	5.5, 1.1	5.6, 1.1	4.6, 1.0	5.1, 0.9	5.6, 1.0	6.0, 1.2
Dietary EPA+DHA (g/wk), median, IQR	0.1, 0.0-0.5	0.4, 0.2-0.8	0.7, 0.4-1.1	1.1, 0.7-1.6	0.0, 0.0-0.1	0.3, 0.2-0.5	0.8, 0.6-0.9	1.4, 1.1-2.0
Total energy (kcal/day), median, IQR	1567, 1266-1970	1585, 1252-1977	1621, 1292-2035	1837, 1502-2201	1543, 1212-1956	1558, 1237-1931	1686, 1364-2086	1797, 1456-2205
Red/processed meat (servings/day), median, IQR	0.5, 0.2-0.8	0.5, 0.3-0.9	0.6, 0.3-0.9	0.6, 0.4-1.0	0.5, 0.2-0.9	0.5, 0.3-0.8	0.6, 0.3-0.9	0.6, 0.3-0.9

EPA+DHA, eicosapentaenoic acid and docosahexaenoic acid; SD, standard deviation; IQR, interquartile range

Table 3

Mean change [95% confidence intervals] in fetal growth indices associated with levels of total seafood and shellfish intake^a

	Total seafood intake (servings)				Shellfish intake (servings)			
	<0.2/mo ^b (n = 286)	0.2/mo-<0.5/wk (n = 300)	0.5-1/wk (n = 521)	>1/wk (n = 2034)	<0.2/mo ^b (n = 1038)	0.2/mo-<0.5/wk (n = 685)	0.5-1/wk (n = 739)	>1/wk (n = 679)
BW (g), n	286	300	521	2034	1038	685	739	679
Mean, SE	3469.9, 30.3	3465.1, 34.5	3449.3, 22.9	3461.2, 11.8	3468.2, 16.6	3435.3, 21.3	3460.3, 18.5	3474.0, 21.0
Unadjusted	0.0	-4.8 [-91.5, 81.9]	-20.6 [-97.7, 56.6]	-8.7 [-74.9, 57.5]	0.0	-32.8 [-84.4, 18.8]	-7.9 [-58.3, 42.6]	5.9 [-45.9, 57.6]
Adjusted ^c	0.0	-12.3 [-99.3, 74.6]	-19.9 [-97.7, 58.0]	-14.9 [-82.3, 52.5]	0.0	-20.4 [-74.0, 33.2]	-4.6 [-58.7, 49.5]	23.7 [-35.8, 83.1]
BL (cm), n	283	295	515	2008	1025	674	732	670
Mean, SE	50.7, 0.2	50.9, 0.2	50.9, 0.1	50.9, 0.1	50.9, 0.1	50.7, 0.1	50.9, 0.1	50.8, 0.1
Unadjusted	0.0	0.2 [-0.3, 0.7]	0.3 [-0.2, 0.7]	0.2 [-0.2, 0.6]	0.0	-0.3 [-0.6, 0.0]	0.0 [-0.3, 0.2]	-0.1 [-0.4, 0.2]
Adjusted ^c	0.0	0.2 [-0.3, 0.7]	0.2 [-0.2, 0.7]	0.1 [-0.3, 0.5]	0.0	-0.3 [-0.6, 0.1]	-0.1 [-0.5, 0.2]	-0.2 [-0.5, 0.2]
HC (cm), n	278	292	512	1981	1012	669	722	660
Mean, SE	34.9, 0.2	34.7, 0.1	34.7, 0.1	34.8, 0.0	34.8, 0.1	34.7, 0.1	34.8, 0.1	34.7, 0.1
Unadjusted	0.0	-0.2 [-0.5, 0.2]	-0.3 [-0.6, 0.1]	-0.2 [-0.4, 0.1]	0.0	-0.1 [-0.3, 0.1]	0.0 [-0.2, 0.3]	0.0 [-0.2, 0.2]
Adjusted ^c	0.0	-0.2 [-0.6, 0.2]	-0.3 [-0.6, 0.1]	-0.2 [-0.4, 0.1]	0.0	-0.1 [-0.3, 0.2]	0.1 [-0.2, 0.3]	0.1 [-0.2, 0.3]
PI (kg/m³), n	283	295	515	2008	1025	674	732	670
Mean, SE	27.0, 0.4	26.4, 0.3	26.2, 0.2	26.5, 0.1	26.4, 0.2	26.6, 0.2	26.4, 0.2	26.6, 0.2
Unadjusted	0.0	-0.6 [-1.5, 0.2]	-0.8 [-1.6, -0.1]	-0.5 [-1.2, 0.1]	0.0	0.2 [-0.3, 0.7]	0.0 [-0.5, 0.5]	0.2 [-0.3, 0.7]
Adjusted ^c	0.0	-0.7 [-1.6, 0.2]	-0.8 [-1.6, 0.0]	-0.5 [-1.1, 0.2]	0.0	0.3 [-0.2, 0.9]	0.2 [-0.4, 0.7]	0.6 [0.0, 1.2]

BW, birthweight; SE, standard error; BL, birth length; HC, head circumference; PI, ponderal index.

^aChange in mean fetal growth measures were calculated using linear regression, with non-robust standard errors.

^bReference category.

^cAdjusted for maternal age (years), non-Hispanic white race, post high-school education, unmarried marital status, pre-pregnancy body mass index (indicator variables: 18.5-24.9, 25-29.9, 30 kg/m²), current recreational physical activity, total energy (kcal/day), current smoking, current alcohol intake, nulliparity, intake of red/processed meats (servings/day), and male infant sex. For shellfish, alternate seafood subtypes (indicator variables for non-reference categories) were also included.

Table 4

Mean change [95% confidence intervals] in fetal growth indices associated with levels of lean and fatty fish intake^a

	Lean fish intake (servings)				Fatty fish intake (servings)			
	<0.2/mo ^b (n = 800)	0.2/mo-<0.5/wk (n = 781)	0.5-1/wk (n = 825)	>1/wk (n = 735)	<0.2/mo ^b (n = 742)	0.2/mo-<0.5/wk (n = 797)	0.5-1/wk (n = 855)	>1/wk (n = 747)
BW (g), n	800	781	825	735	742	797	855	747
Mean, SE	3472.6, 18.3	3453.6, 19.5	3466.5, 18.0	3447.6, 20.7	3465.2, 20.7	3456.4, 18.4	3451.1, 17.9	3470.6, 19.5
Unadjusted	0.0	-19.0 [-71.7, 33.8]	-6.1 [-58.1, 46.0]	-25.0 [-78.6, 28.6]	0.0	-8.8 [-62.3, 44.7]	-14.1 [-66.7, 38.5]	5.3 [-49.0, 59.7]
Adjusted ^c	0.0	-27.1 [-82.7, 28.5]	-15.8 [-71.4, 39.8]	-47.4 [-107.8, 13.0]	0.0	5.0 [-51.6, 61.5]	1.3 [-56.2, 58.7]	21.3 [-41.1, 83.7]
BL (cm), n	789	774	812	726	736	785	843	737
Mean, SE	51.0, 0.1	50.7, 0.1	50.8, 0.1	50.9, 0.1	50.7, 0.1	50.9, 0.1	50.9, 0.1	50.9, 0.1
Unadjusted	0.0	-0.2 [-0.5, 0.1]	-0.1 [-0.4, 0.2]	-0.1 [-0.4, 0.2]	0.0	0.2 [-0.2, 0.5]	0.2 [-0.1, 0.5]	0.2 [-0.1, 0.5]
Adjusted ^c	0.0	-0.2 [-0.6, 0.1]	-0.2 [-0.5, 0.1]	-0.2 [-0.5, 0.2]	0.0	0.2 [-0.1, 0.6]	0.3 [-0.1, 0.6]	0.3 [-0.1, 0.7]
HC (cm), n	783	764	801	715	721	781	830	731
Mean, SE	34.7, 0.1	34.8, 0.1	34.7, 0.1	34.8, 0.1	34.8, 0.1	34.7, 0.1	34.8, 0.1	34.7, 0.1
Unadjusted	0.0	0.0 [-0.2, 0.2]	0.0 [-0.2, 0.2]	0.0 [-0.2, 0.2]	0.0	-0.1 [-0.3, 0.1]	0.0 [-0.2, 0.2]	-0.1 [-0.3, 0.1]
Adjusted ^c	0.0	0.0 [-0.2, 0.3]	0.0 [-0.2, 0.2]	0.1 [-0.2, 0.3]	0.0	-0.2 [-0.4, 0.1]	-0.1 [-0.3, 0.2]	-0.1 [-0.4, 0.2]
PI (kg/m³), n	789	774	812	726	736	785	843	737
Mean, SE	26.4, 0.2	26.7, 0.2	26.6, 0.2	26.3, 0.2	26.8, 0.2	26.4, 0.2	26.5, 0.2	26.3, 0.1
Unadjusted	0.0	0.4 [-0.2, 0.9]	0.2 [-0.3, 0.7]	-0.1 [-0.7, 0.4]	0.0	-0.4 [-0.9, 0.1]	-0.3 [-0.8, 0.2]	-0.5 [-1.0, 0.1]
Adjusted ^c	0.0	0.4 [-0.2, 0.9]	0.3 [-0.3, 0.8]	-0.1 [-0.8, 0.5]	0.0	-0.5 [-1.1, 0.1]	-0.4 [-1.0, 0.2]	-0.6 [-1.2, 0.0]

BW, birthweight; SE, standard error; BL, birth length; HC, head circumference; PI, ponderal index.

^aChange in mean fetal growth measures were calculated using linear regression, with non-robust standard errors.

^bReference category.

^cAdjusted for maternal age (years), non-Hispanic white race, post high-school education, unmarried marital status, pre-pregnancy body mass index (indicator variables: 18.5-24.9, 25-29.9, 30 kg/m²), current recreational physical activity, total energy (kcal/day), current smoking, current alcohol intake, nulliparity, intake of red/processed meats (servings/day), male infant sex, and alternate seafood subtypes (indicator variables for non-reference categories).