ORIGINAL RESEARCH

CURRENT DEVELOPMENTS IN NUTRITION

Maternal and Pediatric Nutrition

Dietary Fat and Fatty Acid Intake in Nulliparous Women: Associations with Preterm Birth and Distinctions by Maternal BMI

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ABSTRACT

Background: Evidence documenting whether diet quality, particularly dietary fatty acids, is associated with preterm birth (PTB) is limited.

Objective: The aim was to measure associations between dietary fatty acid intake prior to pregnancy, specifically n–3 (ω-3) PUFAs and odds of PTB in US women and determine if associations differed by prepregnancy BMI.

Methods: We designed a secondary analysis of dietary intake in nulliparous women enrolled in a longitudinal cohort (NCT01322529). Participants completed an FFQ, modified to assess detailed PUFA intake, during the 3 mo preceding pregnancy. Inclusion in this analytic cohort required total energy intake within 2 SDs of the group mean. Prepregnancy BMI was categorized as underweight, normal, overweight, or obese. The primary exposure was estimated intake of EPA and DHA (combined EPA+DHA), in the context of a recommended intake of 250 mg. The primary outcome was PTB (<37 wk). Adjusted regression models controlled for maternal factors relevant to PTB and evaluated associations with PUFAs. Interaction terms estimated effect modification of BMI. A false discovery rate (FDR) correction accounted for multiple comparisons.

Results: Median daily intake of combined EPA+DHA in 7365 women was 70 mg (IQR: 32, 145 mg). A significant interaction term indicated the effects of EPA+DHA on odds of PTB were different for different BMI categories ($P < 0.01$). Specifically, higher intake of combined EPA+DHA was nominally associated with reduced odds of PTB in women with underweight (OR: 0.67; 95% CI: 0.46–0.98) and normal BMI (OR: 0.87; 95% CI: 0.78–0.96), yet was associated with increased odds of overweight BMI (OR: 1.21; 95% CI: 1.02–1.44). Associations remained significant after FDR correction.

Conclusions: Based on a cohort of US women designed to identify predictors of adverse pregnancy outcomes, dietary intake of combined EPA+DHA was considerably lower than recommended. Associations between intake of these recommended n–3 fatty acids and risk of PTB differ by maternal BMI. *Curr Dev Nutr* 2021;5:nzab074.

Keywords: maternal diet, body mass index, pregnancy, preterm birth, food-frequency questionnaire, diet quality, n-3 fatty acids, polyunsaturated fatty acids, fish intake

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Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/cdn/.

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Abbreviations used: AHEI-2010, Alternate Healthy Eating Index 2010; ALA, α-linolenic acid; DPA, docosapentaenoic acid; FDR, false discovery rate; LA, linoleic acid; nuMoM2b, Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be; PTB, preterm birth; SDA, stearidonic acid.

Introduction

Since 2014, rates of preterm birth (PTB) have increased in the United States to just above 10% (1). Multiple socioeconomic and environmental factors are associated with PTB, including preconception and prenatal diet quality (2). The rates of PTB in study populations vary considerably, ranging from 4.3% to 7.9% (3–5), perhaps in part due to variation in factors such as BMI and diet.

The associations of diet quality and specific fatty acid intake with PTB have not been well delineated. Current recommendations suggest pregnant and lactating women consume 250 mg of the PUFAs EPA (all-cis-5,8,11,14,17-icosapentaenoic acid; 20:5n–3) and DHA (all-cis-docosa-4,7,10,13,16,19-hexa-enoic acid; 22:6n–3) through dietary sources, especially low-mercury-containing fish and seafoods (6). This is because the trans-placental transfer of n–3 PUFAs suggests critical roles of the n–3 PUFAs in fetal development (7, 8). Also, as n–3 PUFAs

temper inflammatory responses, there has been a focus on their potential in enhancing the duration of gestation (9–11). Although a BMI (kg/m^2) >30 has been associated with adverse pregnancy outcomes including PTB (12, 13), recommendations for fatty acid intake are not stratified by BMI and yet relations of dietary patterns with health outcomes may vary by BMI (14–16).

The Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be (nuMoM2b) cohort was designed to identify predictors of adverse pregnancy outcomes, including PTB, in nulliparous women. The purpose of the present analysis was to assess intake of fatty acids and accompanying dietary patterns in relation to PTB. Finally, we aimed to assess whether there were differences in association between fatty acid intake and PTB based on prepregnancy BMI categories.

Methods

Women eligible to participate in nuMoM2b had a singleton pregnancy between 6 0/7 to 13 6/7 estimated weeks of gestation, confirmed by ultrasonography, and were enrolled from 2010 through 2013 (17). Participants reported having no previous pregnancy lasting 20 wk or longer. Prenatal care occurred at 24 hospitals affiliated with 8 primary US study centers, contributing diverse geographic representation of participants from coastal and central locations. All procedures occurred in accordance with the ethical standards of the responsible institutional committee on human experimentation. Institutional review boards of all participating centers approved the study prior to its initiation: Case Western Reserve University, Columbia University, Indiana University, Northwestern University, University of California–Irvine, University of Pennsylvania, University of Pittsburgh, and University of Utah. All participants gave written informed consent.

At the first of 4 study visits, women completed a self-administered Block FFQ (NutritionQuest) to report details of dietary intake during the 3 mo prior to pregnancy. The nuMoM2b FFQ assessed overall diet quality including enhanced survey of fatty acid intake, specifically n–3 PUFAs. This analysis focused on these dietary fatty acids. Methods for nutrient analysis from the nuMoM2b have been previously described in detail (18). The FFQ evaluates 52 nutrients as consumed in 120 foods and beverages. This included n–3 PUFA supplementation defined as any of α-linolenic acid (ALA; all-cis-9,12,15-octadecatrienoic acid; 18:3n−3), EPA, or DHA. Participants were reminded to document responses to both food frequency and portion size. NutritionQuest completed the FFQ analysis using their own database derived from the USDA Food and Nutrient Database for Dietary Studies. The Alternate Healthy Eating Index 2010 (AHEI-2010) was further calculated to evaluate global diet quality. The AHEI-2010 assesses intake specified in 11 food groups to discern their relative contributions to the total score (e.g., nuts and legumes, red meat). Questionnaires were available in both English and Spanish. At the initial study visit women self-reported prepregnancy height and weight, which were used to estimate prepregnancy BMI. We categorized women according to BMI as follows: underweight (BMI <18.5), normal weight (BMI: 18.5 to <25), overweight (BMI: 25 to <30), and obese (BMI ≥30) (19).

Women in the nuMoM2b cohort who reported daily total energy intake within 2 SDs of the mean response and had prepregnancy BMI and gestational age recorded at delivery were considered eligible for this analysis. Responses outside these boundaries were consider implausible and, along with missing responses, rendered participants ineligible for this analysis.

The primary exposure of interest was estimated dietary combined intake of EPA and DHA (combined EPA+DHA) in milligrams per day. For reference, and to account for variation in total energy intake, total fat and specific fatty acid intakes were also normalized to total energy intake and reported per 1000 kcal. The primary outcome for this analysis was PTB, defined as delivery prior to $37^{0/7}$ weeks of gestation. We also evaluated the outcome of PTB disaggregated into its subtypes, namely spontaneous PTB (i.e., after labor or premature rupture of membranes) and medically indicated PTB (i.e., due to conditions such as hypertensive disorders of pregnancy and fetal growth restriction).

In order to account for maternal covariates that have been associated with PTB, we recorded maternal education, self-identified race (White, Black, other), physical activity (number of times per week of activities including running, walking, aerobics, ball games, or gardening; reports of >10 times/wk were considered outliers and removed from statistical models), marital status, smoking (never; yes, have smoked in the last month; yes, have not smoked in the last month), primary health insurance provider (commercial, government, other), chronic hypertension, and pregestational diabetes. Primary health insurance provider was selected to estimate household socioeconomic status.

Statistical analysis

Descriptive statistics summarized all maternal covariates and dietary intake variables of interest, overall and by PTB. Differences in nutrient intake by BMI categories were assessed using Wilcoxon rank-sum, ANOVA, or chi-square tests, as appropriate. Unadjusted models measured the associations between primary and secondary predictor nutrients and the outcome of PTB. For all continuous predictors, higher order quadratic terms were considered. If the quadratic relation was not significant ($\alpha = 0.05$), the quadratic term was removed from the model and only the linear term was reported. Continuous variables that were heavily skewed were log transformed prior to model fitting. This transformation was performed for stearidonic (all-cis-octadeca-6,9,12,15-tetraenoic), eicosapentaenoic, docosapentaenoic, and docosahexaenoic acids. Adjusted logistic regression models were fitted exploring the interaction between independent dietary intake variables (e.g., individual nutrients, total energy intake, overall diet quality based on AHEI-2010 score) and BMI category, to determine whether the association between the exposures of interest and PTB varied in magnitude for different BMI groups. Interaction terms were removed from models when not significant ($\alpha = 0.05$). Models with significant interaction terms were reported as effects of independent variables within each category of BMI. All adjusted regression models included covariates as described above and the functional form of the dietary factor (linear or quadratic) was determined based on best fit in unadjusted models. A false discovery rate (FDR) correction was applied for each set of analyses to control for multiple testing across dietary intake variables of interest (20). Nominal and adjusted *P* values are reported. Sensitivity analyses considered separate models for spontaneous PTB and medically indicated PTB, as described above. A post hoc exploratory analysis compared the distributions of

AHEI-2010 between women with any reported fish intake and women with no reported fish intake using a 2-sample *t* test.

Results

Of the 10,037 women enrolled in nuMoM2b, 8259 women completed the FFQ and 7832 reported a total energy intake within 2 SDs, 1720 kcal/d. Either gestational age at delivery or BMI ($n = 157$) were not recorded for an additional 420 women and 47 women had pregnancy loss prior to 20 wk; these were excluded from the analytic cohort (**Figure 1**). The PTB rate for the subsequent 7365 women included in this report was 8.2%. Maternal characteristics are described in **Table 1**.

Dietary intake of MUFAs contributed most to total fat intake (**Table 2**, **Supplemental Table 1**). Fish intake of any type was reported by 79% of women ($n = 5850$). The AHEI-2010 scores were different between women with any reported fish intake [AHEI-2010 = mean ($\pm$ SD) 57.1 $\pm$ 12.3, $n = 5850$] and no reported fish intake (AHEI-2010 = 49.6 $\pm$ 11.4, $n = 1515$), with a P value <0.001 between groups. Shellfish, tuna, and salmon were most commonly consumed, followed by other whitefish (e.g., cod, sole, flounder, catfish, perch, or haddock). Diets including herring, mackerel, and sardines, rich sources of n–3 fatty acids, were uncommon (**Table 3**). Most women did not report routinely taking n–3 supplements.

Dietary intake differed according to prepregnancy BMI (**Table 4**). Women with a normal BMI reported the lowest intakes of total calories and, on average, n–3 PUFAs. More specifically, women with a normal BMI reported lower intake of ALA but higher intake of combined EPA+DHA than other women in this cohort. Fried-fish intake was most common among women with a prepregnancy BMI >25. Most differences between BMI groups remained after FDR correction.

In unadjusted models, multiple aspects of dietary fat were associated with odds of PTB at the nominal level. Significant quadratic log-odds relations existed for total fat and monounsaturated fat with PTB (Table 2). A significant linear log-odds relation existed between stearidonic acid (SDA; 18:4n-3), AHEI-2010 score, and AHEI-2010 vegetable component with PTB (Table 2). These linear relations suggest that greater SDA intake or having a higher score for the total AHEI-2010 (and specifically for the vegetable food group) was associated with reduced odds of PTB. Intake of any salmon, halibut, or trout was associated with reduced odds of PTB as well (Table 3). However, none of these relations remained statistically significant after applying the FDR correction.

In adjusted models at the nominal level, a linear association existed for intake of monounsaturated fats with PTB, such that greater intake was associated with lower odds of PTB (**Table 5**). Interactions with BMI, indicating the effect of the nutrient or AHEI-2010 score on the odds of PTB was different for different BMI groups, were present for the following dietary components: % of total calories as fat, % of total calories as carbohydrate, average daily total PUFAs, average daily intake of total n–6 and total n–3 PUFAs, linoleic acid (LA; 9,12-octadecadienoic acid; 18:2n–6), ALA, SDA, EPA, docosapentaenoic acid (DPA; all-cis-5,8,11,14,17-icosapentaenoic acid; 22:5n–3), DHA, combined EPA+DHA, and AHEI-2010 total score as well as its individual components for EPA and DHA intake, fruit, and polyunsaturated fat (Table 5). The BMI categories exhibiting the interactions differed by nutrient or score. For instance, a significant inverse linear association existed for combined EPA+DHA intake with distinct effects in underweight and normal BMI groups, and the overweight category showed a positive linear association. However, % of total calories as fat showed a significant inverse linear association only within the underweight BMI group. Intake of herring was associated with the odds of PTB in adjusted models (Table 3), and significant interactions by BMI category were present for fried fish, salmon, whitefish, and shellfish. The association between shellfish intake and odds of PTB remained for normal BMI after adjustment for multiple testing. Interaction terms remained significant for EPA, EPA+DHA, and AHEI-2010 score after applying the FDR correction. Otherwise, for main effects and all other interactions in adjusted models, applying the FDR correction eliminated statistical differences. Results were generally similar for the subtypes (spontaneous and medically indicated) of PTB, which also had no significant associations with fatty acids in multivariable analyses after applying FDR correction (data not shown).

Discussion

In this analysis, we found associations between intake of dietary EPA and DHA during the preconception period and risk of PTB in nulliparous US women. Associations differed by maternal prepregnancy BMI. Also, prepregnancy BMI was associated with differences in dietary fat intake. Specifically, women with higher BMI reported higher intake of total energy from fat and lower intakes of EPA with DHA. Underweight women reported the highest total PUFA intake.

In this population of nulliparous women, the median estimated combined periconceptional intake of EPA+DHA was <30% of current recommendations (6). This finding is consistent with population-based estimates for all US adults, as determined through the NHANES (21, 22). In contrast, the Norwegian Mother and Child Cohort Study estimated women's daily n–3 PUFA intake to be 450 mg while pregnant, almost double current US recommendations, which may be attributable to high rates of seafood intake (4). Notably, the PTB rate among those women was 5.4%, a rate approximately one-third lower than that of the nuMoM2b cohort. Risk-reducing effects of increased EPA and DHA may stem, in part, from regulation of placental angiogenesis (23) and favorably influencing inflammatory responses through EPA's and DHA's oxidation into specialized pro-resolving lipid mediators (24). We also found lower intakes of the essential fatty acids LA (n–6) and ALA (n–3) compared with amounts recommended in US dietary guidelines (6). This finding suggests that attention should be directed to the balance of PUFA intake. The estimated total energy intake in nuMoM2b women closely matches that reported by women in the Seattle region when asked to recall periconception intake (25), yet is lower than women in the New Hampshire Birth Cohort, who responded during their third trimester, and lower than reported to NHANES (26, 27). Aspects of dietary intake may remain similar between the preconception and prenatal time periods (28, 29), but variability can occur (30). This is especially true for alcohol and caffeinated beverage consumption in addition to relevant behaviors such as tobacco use (28). Regardless, dietary patterns in the preconception period predict not only pregnancy outcomes but also outcomes in offspring, for instance allergies in early childhood (31, 32).

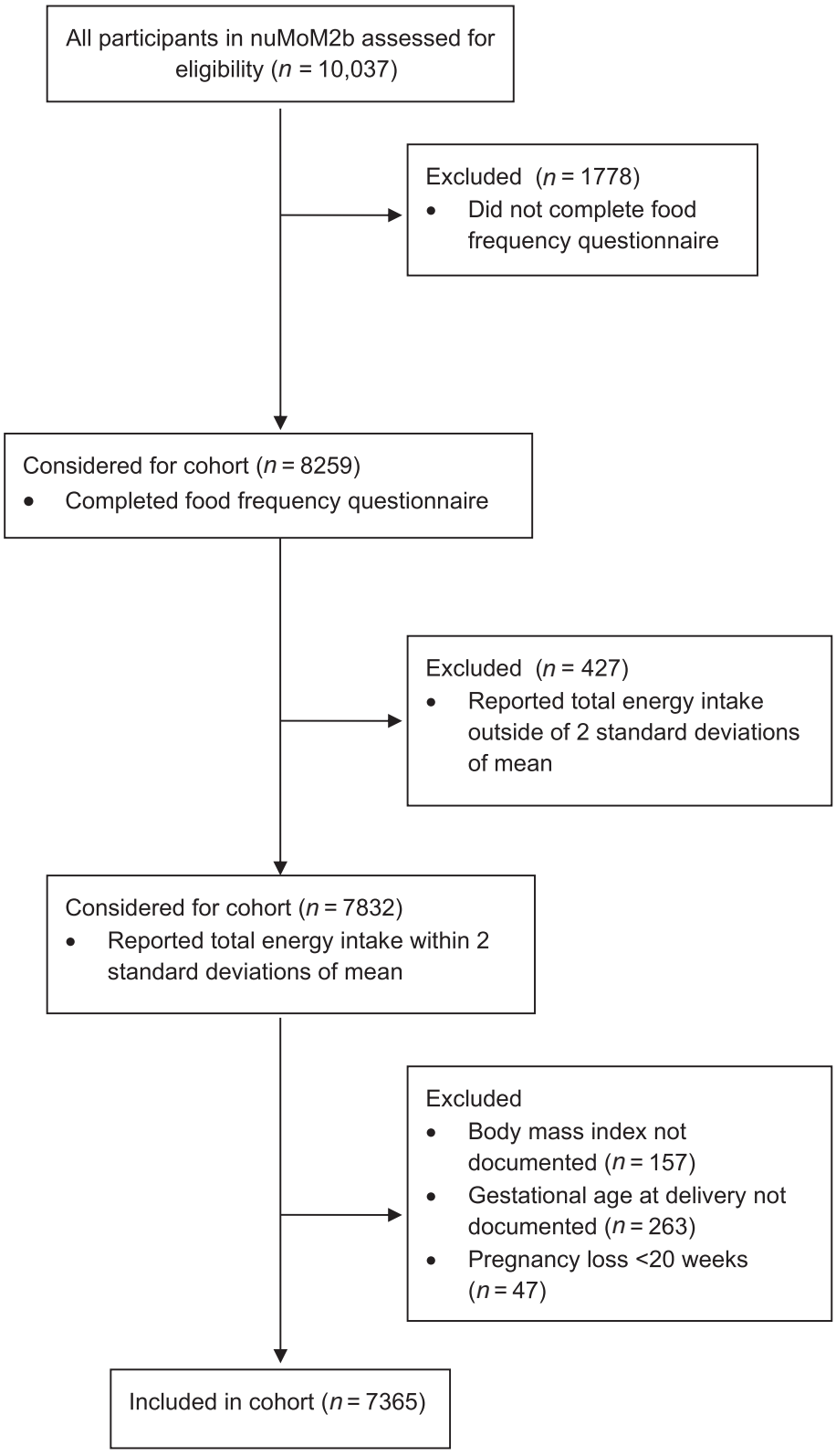

FIGURE 1 Flow diagram of participant eligibility and final inclusion.

TABLE 1 Characteristics of participating women[1]

Maternal demographic	Term delivery ($n = 6762$)	Preterm delivery ($n = 603$)
Gestational age at delivery, wk	39.0 (39.0, 40.0)	35.0 (32.0, 36.0)
BMI category		
Underweight	273 (4.0)	24 (4.0)
Normal	3884 (57.4)	298 (49.4)
Overweight	1419 (21.0)	138 (22.9)
Obese	1186 (17.5)	143 (23.7)
Race[2]		
White	4831 (71.4)	391 (64.8)
Black	662 (9.8)	93 (15.4)
Other/multiple	1266 (18.7)	119 (19.7)
Completed education		
Less than high school	381 (5.6)	46 (7.6)
High school or some college	1838 (27.2)	200 (33.2)
Associate/technical or Bachelor's	2784 (41.2)	226 (37.5)
Master's/doctoral	1759 (26.0)	131 (21.7)
Marital status		
Single, never married	2176 (32.2)	232 (38.5)
Married	4514 (66.8)	357 (59.2)
Widowed/divorced/separated	72 (1.1)	14 (2.3)
Total family income[3]		
<$50,000	1693 (29.4)	165 (27.4)
$50,000–$100,000	1795 (31.2)	147 (24.4)
$100,000–$150,000	1105 (19.2)	85 (14.1)
>$150,000	1167 (20.2)	78 (12.9)
Health insurance provider[4]		
Any government insurance	1523 (22.5)	177 (29.4)
Commercial	4928 (72.9)	401 (66.5)
Other (military, personal, other)	277 (4.1)	22 (3.6)
Smoker[5]		
Never smoker	3973 (58.8)	335 (55.6)
Smoker, not in last month	2476 (36.6)	225 (37.3)
Smoker, yes in last month	308 (4.6)	39 (6.5)
Alcohol use in the preceding month[6]		
Yes	274 (4.1)	22 (3.6)
No	5419 (80.1)	492 (81.6)
Physical activity during the past 4 wk,[7] times/wk	2.00 (0.00, 4.00)	2.00 (0.00, 4.00)
Diabetes prior to pregnancy, recently requiring medication[8]	41 (0.6)	18 (3.0)
Hypertension prior to pregnancy, recently requiring medication[9]	50 (0.7)	11 (1.8)

[1] Values are medians (IQRs) or *n* (%) within the column where percentages include women with missing data.
[2] Missing $n = 3$.
[3] Missing $n = 1130$.
[4] Missing $n = 37$.
[5] Missing $n = 9$.
[6] Missing $n = 1158$.
[7] Missing $n = 79$.
[8] Missing $n = 177$.
[9] Missing $n = 176$.

Seafood intake, in particular fatty fish, provides the highest sources of recommended n–3 PUFAs, and women who included any fish in their diet had overall higher diet quality as measured by AHEI-2010 scores. The fish most frequently consumed were salmon and tuna, which supply substantial amounts of the n–3 fatty acids. Nevertheless, other fish that are sources of n–3 fatty acids, including herring, mackerel, and sardines, were not a common part of diets, perhaps representing an opportunity for enhanced nutrition education (6).

While some prenatal vitamins contain n–3 supplements, the reported use of these types of prenatal vitamins was not common among women in the nuMoM2b cohort, consistent with NHANES data (33). This lack of supplementation contrasts markedly with that found in Norwegian women, two-thirds of whom reported taking n–3 PUFA supplements in addition to dietary sources (4). There is interest in supplementation as it has reportedly been associated with reduced frequency of PTB in some, but not all, clinical trials (9, 11). The doses used in these clinical trials may not be achievable through food sources (10). Nevertheless, dietary sources and whole foods remain an ideal intervention due to their contributions to increased intake of other essential nutrients, including vitamin D, selenium, and protein in fish (34).

TABLE 2 Distinctions in energy and nutrient intake among nulliparous women based on preterm birth status in unadjusted models[1]

	All women ($n = 7365$)	Term birth ($n = 6762$)	Preterm birth ($n = 603$)	OR (95% CI)	*P*	FDR-corrected *P* value
Energy intake, kcal	1503.2[2] (1165.1, 1914.0)	1502.0 (1165.5, 1914.2)	1523.7 (1161.8, 1908.0)	1.00 (0.984–1.013)	0.84	0.88
% of calories as fat	34.6 ± 5.9[3]	34.6 ± 5.8	34.7 ± 6.2	1.00 (0.988–1.016)	0.81	0.88
% of calories as protein	14.9 ± 2.8	14.9 ± 2.8	14.9 ± 2.8	1.00 (0.971–1.030)	0.99	0.99
% of calories as carbohydrate	49.9 ± 7.5	49.9 ± 7.5	50.4 ± 7.8	1.01 (0.997–1.019)	0.16	0.39
Total fat, g	57.5 (43.1, 74.9)	57.4 (43.1, 74.8)	58.3 (42.0, 75.7)	1.00 (0.994–1.002)	0.31	0.51
				1.00 (1.000–1.000)[4]	0.04[4]	0.22[4]
Polyunsaturated fat, g	11.9 (8.8, 15.96)	11.9 (8.8, 15.96)	11.8 (8.8, 15.96)	1.00 (0.989–1.019)	0.60	0.79
Monounsaturated fat, g	22.6 (16.7, 29.5)	22.6 (16.7, 29.5)	22.5 (16.1, 30.0)	0.99 (0.984–1.003)	0.16	0.39
				1.00 (1.000–1.001)[4]	0.04[4]	0.22[4]
Saturated fat, g	18.1 (13.3, 24.3)	18.1 (13.3, 24.3)	18.5 (13.1, 24.6)	1.00 (0.992–1.011)	0.79	0.88
Average daily n–6 PUFAs, g	10.0 (7.4, 13.4)	10.0 (7.4, 13.4)	10.1 (7.4, 13.5)	1.00 (0.987–1.022)	0.62	0.79
Average daily n–3 PUFAs, g	1.17 (0.86, 1.61)	1.17 (0.86, 1.61)	1.18 (0.84, 1.60)	1.05 (0.931–1.191)	0.41	0.63
Linoleic acid (18:2n–6), g	9.96 (7.4, 13.3)	9.96 (7.4, 13.3)	10.1 (7.3, 13.5)	1.00 (0.987–1.022)	0.61	0.79
α-Linolenic acid (18:3n–3), g	1.05 (0.77, 1.44)	1.05 (0.77, 1.44)	1.06 (0.78, 1.47)	1.09 (0.948–1.243)	0.24	0.47
Stearidonic acid (18:4n–3), g	0.004 (0.001, 0.01)	0.004 (0.001, 0.01)	0.004 (0.001, 0.009)	0.94 (0.879–0.994)	0.03	0.21
Arachidonic acid (20:4n–6), g	0.077 (0.052, 0.111)	0.077 (0.052, 0.111)	0.078 (0.052, 0.113)	2.46 (0.496–12.216)	0.27	0.48
EPA (20:5n–3), g	0.024 (0.009, 0.055)	0.025 (0.009, 0.056)	0.023 (0.008, 0.049)	0.95 (0.889–1.01)	0.10	0.37
Docosapentaenoic acid (22:5n–3), g	0.009 (0.004, 0.016)	0.009 (0.004, 0.016)	0.008 (0.004, 0.016)	0.95 (0.879–1.025)	0.18	0.40
DHA (22:6n–3), g	0.046 (0.022, 0.09)	0.046 (0.022, 0.091)	0.044 (0.019, 0.082)	0.95 (0.874–1.023)	0.16	0.39
Combined intake of EPA and DHA, g	0.07 (0.032, 0.145)	0.071 (0.032, 0.146)	0.065 (0.028, 0.130)	0.94 (0.876–1.017)	0.13	0.39
Total protein, g	55.1 (42.1, 72.0)	55.1 (42.1, 71.96)	54.2 (41.9, 72.3)	1.00 (0.996–1.003)	0.84	0.88
Total carbohydrate, g	185.1 (141.9, 240.8)	184.7 (141.9, 240.4)	189.5 (141.8, 242.7)	1.00 (0.999–1.001)	0.85	0.88
AHEI-2010 total score	55.6 ± 12.5	55.7 ± 12.5	54.3 ± 12.4	0.99 (0.984–0.998)	<0.01	0.12
Alcoholic drinks score	5.0 (2.5, 5.0)	5.0 (2.5, 5.0)	5.0 (2.5, 5.0)	0.98 (0.950–1.004)	0.07	0.29
EPA and DHA intake score	2.8 (1.3, 5.8)	2.8 (1.3, 5.8)	2.6 (1.1, 5.2)	0.98 (0.951–1.005)	0.10	0.37
Fruit score	3.3 (1.7, 6.3)	3.3 (1.7, 6.3)	2.9 (1.7, 5.9)	0.98 (0.953–1.01)	0.20	0.42
Nuts and legumes score	4.3 (2.2, 8.2)	4.4 (2.2, 8.3)	4.2 (2.0, 7.7)	0.98 (0.957–1.008)	0.15	0.39
Polyunsaturated fat score	6.3 (5.2, 7.7)	6.3 (5.2, 7.7)	6.4 (5.2, 7.9)	1.02 (0.976–1.068)	0.37	0.59
Red meats servings score	6.9 (4.8, 8.3)	6.9 (4.9, 8.3)	6.7 (4.5, 8.3)	0.98 (0.951–1.012)	0.25	0.48
Sodium intake score	6.8 (4.1, 9.1)	6.8 (4.1, 9.1)	6.9 (4.1, 9.1)	1.00 (0.976–1.028)	0.91	0.93
Sugary beverages score	1.3 (0.0, 6.9)	1.4 (0.0, 6.9)	0.0 (0.0, 6.9)	0.98 (0.962–1.006)	0.15	0.39
trans Fat percent score	8.3 (7.6, 8.96)	8.3 (7.6, 8.96)	8.3 (7.6, 8.95)	0.99 (0.920–1.064)	0.76	0.88
Vegetable score	4.2 (2.6, 6.7)	5.0 (2.5, 5.0)	3.96 (2.4, 6.5)	0.96 (0.932–0.993)	0.01	0.16
Whole-grains score	1.7 (0.9, 2.8)	2.8 (1.3, 5.8)	1.6 (0.8, 2.7)	0.97 (0.919–1.03)	0.28	0.48

[1]AHEI-2010, Alternate Healthy Eating Index 2010; FDR, false discovery rate.
[2]Value reported in this format are medians (IQRs).
[3]Value reported in this format are means ± SDs.
[4]Based on best fit, dietary factors were evaluated as linear terms except for those noted with this footnote, indicating the dietary factor was evaluated as a quadratic term.

TABLE 3 Associations between fish intake and n–3 PUFA supplement use and preterm delivery status in unadjusted and adjusted models as well as interactions with BMI category[1]

	All women ($n = 7365$)	Delivered full-term infant ($n = 6762$)	Delivered preterm infant ($n = 603$)	Unadjusted OR (95% CI)	P[2]	Adjusted OR (95% CI)[3]	P[4]	FDR-corrected P value for adjusted OR
Fried fish	2945 (39.99)[5]	2683 (39.7)	262 (43.4)	1.17 (0.987–1.382)	0.0702			
Underweight BMI						0.36 (0.128–1.000)	0.05[6]	0.13[7]
Normal BMI						0.98 (0.761–1.262)	0.88[6]	0.93[7]
Overweight BMI						1.15 (0.798–1.649)	0.46[6]	0.57[7]
Obese BMI						1.47 (1.024–2.114)	0.04[6]	0.53[7]
Tuna	4791 (65.1)	4393 (65.0)	398 (66.0)	1.05 (0.878–1.248)	0.6087	1.08 (0.899–1.297)	0.41	0.53[7]
Salmon	4214 (57.2)	3900 (57.7)	314 (52.1)	0.80 (0.675–0.942)	0.0078			
Underweight BMI						0.44 (0.185–1.05)	0.06[6]	0.15[7]
Normal BMI						0.72 (0.56–0.926)	0.01[6]	0.08[7]
Overweight BMI						1.31 (0.905–1.892)	0.15[6]	0.25[7]
Obese BMI						1.06 (0.740–1.517)	0.75[6]	0.82[7]
Halibut	1638 (22.2)	1526 (22.6)	112 (18.6)	0.78 (0.633–0.969)	0.0242	0.93 (0.740–1.167)	0.53	0.60[7]
Trout	754 (10.2)	708 (10.5)	46 (7.6)	0.71 (0.518–0.964)	0.0284	0.77 (0.555–1.063)	0.11	0.21
Mackerel	298 (4.1)	280 (4.1)	18 (3.0)	0.71 (0.439–1.156)	0.1704	0.77 (0.473–1.264)	0.31	0.41
Herring	204 (2.8)	183 (2.7)	21 (3.5)	1.30 (0.820–2.054)	0.2664	1.61 (1.006–2.579)	<0.05	0.12
Sardines	502 (6.8)	464 (6.9)	38 (6.3)	0.91 (0.649–1.285)	0.6012	0.97 (0.682–1.390)	0.88	0.93
Whitefish[8]	3319 (45.1)	3055 (45.2)	264 (43.8)	0.94 (0.799–1.118)	0.5086			
Underweight BMI						0.50 (0.191–1.325)	0.17[6]	0.26[7]
Normal BMI						0.81 (0.627–1.040)	0.09[6]	0.19[7]
Overweight BMI						1.57 (1.094–2.262)	0.01[6]	0.09[7]
Obese BMI						1.12 (0.783–1.616)	0.53[6]	0.60[7]
Shellfish	4929 (66.9)	4543 (67.2)	386 (64.0)	0.87 (0.730–1.034)	0.113			
Underweight BMI						0.57 (0.239–1.343)	0.20[6]	0.29[7]
Normal BMI						0.66 (0.515–0.852)	<0.01[6]	0.043[7]
Overweight BMI						1.30 (0.872–1.940)	0.20[6]	0.29[7]
Obese BMI						1.355 (0.925–1.984)	0.12[6]	0.22[7]
Quantity of n–3 PUFA intake from supplements[9]								
None	6094 (82.7)	5589 (82.7)	505 (83.7)	Reference	0.7619	Reference	0.94	0.96
≤50 mg	269 (3.7)	245 (3.6)	24 (4.0)	1.08 (0.71–1.67)		1.146 (0.730, 1.798)		
>50 mg to 143 mg	229 (3.1)	212 (3.1)	17 (2.8)	0.89 (0.54–1.47)		0.963 (0.571, 1.623)		
>143 mg to 357 mg	202 (2.7)	190 (2.8)	12 (2.0)	0.7 (0.39–1.26)		0.839 (0.462, 1.523)		
>357 mg to 500 mg	571 (7.8)	526 (7.8)	45 (7.5)	0.95 (0.7–1.30)		1.026 (0.734, 1.434)		

[1] FDR, false discovery rate.
[2] P value is for unadjusted logistic regression; applying false discovery rate correction resulted in P values >0.1 for all shown (results not shown)
[3] Adjusting for maternal education, race, physical activity, marital status, household income, smoking, primary health insurance provider, alcohol use, gestational weight gain, diabetes, and hypertension prior to pregnancy recently requiring medication and including interaction terms between BMI and variable of interest where specified.
[4] P value is for adjusted logistic regression.
[5] Values in this format are n (%).
[6] Interaction terms significant, $P < 0.05$.
[7] Interaction terms not significant, $P > 0.05$.
[8] Includes cod, sole, flounder, catfish, perch, or haddock.
[9] Comparing 0 mg to any amount, up to 500 mg/d; n–3 supplementation includes any of α-linolenic acid, EPA, or DHA.

TABLE 4 Distinctions in dietary intake and AHEI-2010 score according to BMI category[1]

Energy and nutrient intake	Underweight ($n = 297$)	Normal ($n = 4182$)	Overweight ($n = 1557$)	Obese ($n = 1329$)	*P*	FDR-corrected *P* value
AHEI-2010 score	54.056 ± 13.026	57.355 ± 12.819	54.53 ± 11.67	51.444 ± 11.146	<0.01	<0.01
Energy intake, kcal	1620.4 (1175.8, 2056.8)	1476.0 (1165.1, 1866.9)	1516.7 (1162.9, 1923.5)	1582.2 (1168.5, 2043.4)	<0.01	<0.01
% of calories as fat	34.8 ± 5.8	34.4 ± 5.8	34.6 ± 5.7	35.2 ± 6.0	<0.01	<0.01
% of calories as protein	14.5 ± 2.8	15.0 ± 2.8	14.8 ± 2.8	14.7 ± 3.0	<0.01	<0.01
% of calories as carbohydrate	50.8 n ± 7.6	49.9 ± 7.4	49.9 ± 7.5	50.0 ± 7.7	0.19	0.21
Total fat, g	59.19 (43.85, 82.36)	56.045 (42.66, 72.4)	57.95 (43.3, 74.34)	60.83 (44.31, 81.44)	<0.01	<0.01
Polyunsaturated fat, g	12.64 (9.390, 17.370)	11.695 (8.74, 15.5)	11.98 (8.9, 15.76)	12.48 (8.95, 17.050)	<0.01	<0.01
Monounsaturated fat, g	23.72 (16.920, 32.180)	22.275 (16.54, 28.81)	22.61 (16.99, 29.28)	23.93 (16.86, 31.89)	<0.01	<0.01
Saturated fat, g	18.52 (13.05, 27.88)	17.61 (13.03, 23.3)	18.280 (13.34, 24.21)	19.4 (14.0, 26.46)	<0.01	<0.01
Average daily n–6 PUFAs, g	10.5 (7.92, 14.8)	9.810 (7.32, 13.02)	10.08 (7.45, 13.46)	10.55 (7.54, 14.57)	<0.01	<0.01
Average daily n–3 PUFAs, g	1.25 (0.886, 1.87)	1.140 (0.848, 1.56)	1.19 (0.851, 1.6)	1.23 (0.888, 1.72)	<0.01	<0.01
Linoleic acid (18:2n–6), g	10.48 (7.89, 14.68)	9.750 (7.29, 12.97)	10.02 (7.41, 13.38)	10.52 (7.5, 14.51)	<0.01	<0.01
α-Linolenic acid (18:3n–3), g	1.15 (0.817, 1.66)	1.010 (0.756, 1.38)	1.06 (0.775, 1.44)	1.12 (0.808, 1.56)	<0.01	<0.01
Stearidonic acid (18:4n–3), g	0.004 (0.001, 0.009)	0.004 (0.001, 0.01)	0.003 (0.001, 0.009)	0.003 (0.001, 0.007)	<0.01	<0.01
Arachidonic acid (20:4n-6), g	0.079 (0.049, 0.108)	0.075 (0.051, 0.108)	0.078 (0.053, 0.111)	0.083 (0.059, 0.125)	<0.01	<0.01
EPA (22:5n–3), g	0.026 (0.009, 0.050)	0.026 (0.009, 0.058)	0.022 (0.009, 0.053)	0.02 (0.008, 0.047)	<0.01	<0.01
Docosapentaenoic acid (22:5n–3), g	0.008 (0.005, 0.015)	0.009 (0.004, 0.017)	0.008 (0.004, 0.016)	0.008 (0.004, 0.016)	0.01	0.01
DHA (22:6n–3), g	0.044 (0.023, 0.085)	0.048 (0.023, 0.095)	0.043 (0.022, 0.084)	0.042 (0.02, 0.078)	<0.01	<0.01
Combined intake of EPA and DHA, g	0.07 (0.032, 0.136)	0.075 (0.033, 0.153)	0.066 (0.031, 0.136)	0.061 (0.03, 0.125)	<0.01	<0.01
Total protein, g	57.56 (42.33, 75.01)	54.710 (42.03, 70.6)	55.16 (42.32, 71.94)	56.48 (42.09, 75.47)	0.04	0.04
Total carbohydrate, g	199.95 (150.86, 260.19)	181.52 (141.59, 232.57)	184.2 (140.78, 239.46)	196.75 (142.36, 260.9)	<0.01	<0.01
Any fish intake or n–3 PUFA supplementation, *n* (%)						
Fried fish	116 (39.1)	1554 (37.2)	660 (42.4)	615 (46.3)	<0.01	<0.01
Tuna	191 (64.3)	2747 (65.7)	1008 (64.7)	845 (63.6)	0.54	0.54
Salmon	185 (62.3)	2577 (61.6)	835 (53.6)	617 (46.4)	<0.01	<0.01
Halibut	72 (24.2)	1102 (26.4)	310 (19.9)	154 (11.6)	<0.01	<0.01
Trout	38 (12.8)	508 (12.1)	124 (8.0)	84 (6.3)	<0.01	<0.01
Mackerel	18 (6.1)	185 (4.4)	60 (3.9)	35 (2.6)	<0.01	0.01
Herring	12 (4.0)	122 (2.9)	42 (2.7)	28 (2.1)	0.23	0.24
Sardines	33 (11.1)	309 (7.4)	102 (6.6)	58 (4.4)	<0.01	<0.01
Whitefish[2]	124 (41.8)	1968 (47.1)	680 (43.7)	547 (41.2)	<0.01	<0.01
Shellfish	191 (64.3)	2855 (68.3)	1051 (67.5)	832 (62.6)	<0.01	<0.01
Received any portion of their average daily n–3 PUFA intake from supplements[3]	54 (18.2)	786 (18.8)	253 (16.2)	178 (13.4)	<0.01	<0.01

[1] Values are means ± SD or medians (IQR) unless otherwise indicated. AHEI-2010, Alternate Healthy Eating Index 2010; FDR, false discovery rate.
[2] Includes cod, sole, flounder, catfish, perch, or haddock.
[3] n–3 supplements include any of α-linolenic acid, EPA, or DHA.

TABLE 5 Associations between energy and fat intake and AHEI-2010 scores and preterm birth status in adjusted models[1]

	OR (95% CI)[2]	*P*	*P* value for interaction terms	FDR-corrected *P* value	FDR-corrected *P* value for interaction terms
Energy intake, kcal	1.00 (1.000–1.000)	0.076		0.17	
Percentage of calories as fat					
Underweight	0.90 (0.827–0.969)	0.006	<0.01	0.08	0.07
Normal	0.99 (0.967–1.008)	0.24		0.34	
Overweight	1.01 (0.980–1.043)	0.49		0.58	
Obese	1.03 (0.999–1.059)	0.056		0.13	
Percentage of calories as protein	1.02 (0.987–1.050)	0.26		0.36	
Percentage of calories as carbohydrate					
Underweight	1.07 (1.009–1.133)	0.023	0.03	0.09	0.10
Normal	1.02 (1.000–1.033)	0.056		0.13	
Overweight	1.00 (0.972–1.019)	0.69		0.77	
Obese	0.99 (0.964–1.010)	0.26		0.37	
Total fat, g	1.00 (0.993–1.000)	0.085		0.17	
	1.00 (1.000–1.000)[3]	0.36[3]		0.48[2]	
Polyunsaturated fat, g					
Underweight	0.90 (0.825–0.983)	0.019	0.02	0.09	0.09
Normal	0.98 (0.959–1.004)	0.108		0.21	
Overweight	1.02 (0.993–1.055)	0.125		0.22	
Obese	1.00 (0.974–1.029)	0.935		0.96	
Monounsaturated fat, g	0.99 (0.980–1.000)	0.047		0.12	
	1.00 (1.000–1.001)[3]	0.30[3]		0.41[2]	
Saturated fat, g	0.99 (0.983–1.002)	0.14		0.24	
Average daily n–6 PUFAs, g					
Underweight	0.88 (0.796–0.978)	0.017	0.02	0.09	0.09
Normal	0.98 (0.951–1.003)	0.085		0.17	
Overweight	1.02 (0.989–1.061)	0.181		0.28	
Obese	1.00 (0.968–1.032)	0.972		0.98	
Average daily n–3 PUFAs, g					
Underweight	0.35 (0.156–0.783)	0.011	<0.01	0.08	0.08
Normal	0.85 (0.691–1.044)	0.121		0.22	
Overweight	1.16 (0.944–1.435)	0.156		0.25	
Obese	1.09 (0.863–1.383)	0.462		0.57	
Linoleic acid (18:2n–6), g					
Underweight	0.88 (0.797–0.979)	0.018	0.02	0.09	0.09
Normal	0.98 (0.950–1.003)	0.086		0.17	
Overweight	1.02 (0.989–1.061)	0.181		0.28	
Obese	1.00 (0.968–1.032)	0.984		0.98	
α-Linolenic acid (18:3n–3), g					
Underweight	0.34 (0.144–0.821)	0.016	0.02	0.09	0.09
Normal	0.87 (0.697–1.087)	0.221		0.32	
Overweight	1.20 (0.915–1.577)	0.187		0.29	
Obese	1.10 (0.854–1.423)	0.454		0.57	
Stearidonic acid (18:4n–3), g					
Underweight	0.72 (0.532–0.969)	0.03	0.03	0.10	0.10
Normal	0.87 (0.796–0.954)	0.003		0.05	
Overweight	1.15 (0.999–1.323)	0.051		0.13	
Obese	1.05 (0.910–1.201)	0.527		0.60	
Arachidonic acid (20:4n–6), g	0.58 (0.105–3.237)	0.54		0.61	
EPA (20:5n–3), g					
Underweight	0.70 (0.507–0.979)	0.037	<0.01	0.11	0.04
Normal	0.87 (0.796–0.956)	0.003		0.06	
Overweight	1.19 (1.025–1.379)	0.023		0.09	
Obese	1.06 (0.918–1.224)	0.427		0.54	
Docosapentaenoic acid (22:5n–3), g					
Underweight	0.69 (0.488–0.987)	0.042	<0.01	0.12	0.07
Normal	0.88 (0.788–0.973)	0.014		0.09	
Overweight	1.18 (0.977–1.415)	0.086		0.17	
Obese	1.07 (0.893–1.275)	0.476		0.58	

(*Continued*)

TABLE 5 (*Continued*)

	OR (95% CI)[2]	*P*	*P* value for interaction terms	FDR-corrected *P* value	FDR-corrected *P* value for interaction terms
DHA (22:6n–3), g					
Underweight	0.67 (0.453–0.986)	0.042	<0.01	0.12	0.05
Normal	0.87 (0.778–0.971)	0.013		0.09	
Overweight	1.21 (1.009–1.457)	0.04		0.12	
Obese	1.06 (0.887–1.268)	0.518		0.60	
Combined intake of EPA and DHA, g					
Underweight	0.67 (0.457–0.977)	0.038	<0.01	0.11	0.04
Normal	0.87 (0.779–0.961)	0.007		0.07	
Overweight	1.21 (1.018–1.438)	0.03		0.10	
Obese	1.06 (0.897–1.255)	0.49		0.58	
Total protein, g	1.00 (0.995–1.002)	0.32		0.43	
Total carbohydrate, g	1.00 (0.998–1.000)	0.14		0.24	
AHEI-2010 total score					
Underweight	1.02 (0.992–1.058)	0.137	<0.01	0.23	0.04
Normal	0.99 (0.978–0.999)	0.029		0.10	
Overweight	1.02 (1.005–1.037)	0.008		0.08	
Obese	1.01 (0.991–1.024)	0.401		0.52	
AHEI-2010 Alcoholic drinks score	0.98 (0.953–1.011)	0.22		0.33	
AHEI-2010 EPA and DHA intake score			<0.01		0.08
Underweight	0.87 (0.733–1.034)	0.114	<0.01	0.21	0.07
Normal	0.95 (0.913–0.992)	0.018		0.09	
Overweight	1.06 (1.005–1.125)	0.034		0.11	
Obese	1.01 (0.946–1.068)	0.864		0.92	
AHEI-2010 Fruit score					
Underweight	1.08 (0.943–1.240)	0.264	0.03	0.36	0.10
Normal	0.96 (0.918–1.002)	0.062		0.14	
Overweight	1.06 (0.996–1.125)	0.069		0.15	
Obese	1.02 (0.963–1.088)	0.459		0.57	
AHEI-2010 Nuts and legumes score	1.00 (0.975–1.030)	0.9		0.94	
AHEI-2010 Polyunsaturated fat score					
Underweight	0.79 (0.620–1.008)	0.059	0.04	0.14	0.12
Normal	0.99 (0.922–1.052)	0.657		0.74	
Overweight	1.08 (0.977–1.188)	0.136		0.23	
Obese	1.08 (0.987–1.186)	0.093		0.19	
AHEI-2010 Red meats servings score	1.01 (0.979–1.047)	0.48		0.58	
AHEI-2010 Sodium intake score	1.02 (0.990–1.044)	0.23		0.34	
AHEI-2010 Sugary beverages score	1.01 (0.980–1.031)	0.70		0.78	
AHEI-2010 *trans* Fat percent score	1.06 (0.983–1.153)	0.13		0.22	
AHEI-2010 Vegetable score	0.98 (0.948–1.015)	0.26		0.37	
AHEI-2010 Whole-grains score	0.99 (0.936–1.054)	0.82		0.89	

[1]AHEI-2010, Alternate Healthy Eating Index 2010; FDR, false discovery rate.
[2]Adjusting for maternal education, race, physical activity, marital status, smoking, primary health insurance provider, and maternal indication for delivery including hypertensive disorders of pregnancy. If interaction term nominally significant ($P < 0.05$), all 4 BMI categories are listed for that variable.
[3]Based on best fit in unadjusted models, dietary factors were evaluated as linear terms except for odds ratios noted with this footnote, indicating the dietary factor was evaluated as a quadratic term.

Although the associations of both SDA and DPA with PTB were no longer statistically significant after FDR correction, the associations that we did find in the adjusted models prior to correction have not been reported and suggest avenues for future investigation. The combined intake of SDA and DPA represents approximately 10% of the total n–3 PUFA intake in this study. SDA and DPA are intermediaries in the endogenous biosynthetic steps that convert ALA to EPA and DHA (35, 36). High concentrations of DPA are found in fish, including salmon, Atlantic mackerel, Pacific herring, and other fish (37). While insufficient information exists to fully inform dietary recommendations regarding pregnancy, specific attention to these n–3 PUFAs in addition to EPA and DHA may be warranted.

In addition, notable differences in dietary patterns were observed among women of different BMI categories. Specifically, among those who were underweight, self-reported nutrient intakes revealed relatively higher total PUFA and combined EPA+DHA intakes compared with that in overweight and obese women. Yet, when accounting for total energy intake (fat intake per 1000 kcal), underweight women still reported higher total PUFAs, yet women with normal weight reported the highest intake of combined EPA+DHA. While underweight women in

the nuMoM2b cohort had higher AHEI-2010 scores than obese women, diet quality was still lower than in women with normal weight. Our findings are consistent with other nationally representative cohorts; prepregnancy BMI inversely correlated with the total AHEI score in US women in the Infant Feeding Practices Study II (38). In our analysis, prior to FDR correction, multiple n–3 PUFAs were associated with reduced risk of PTB for underweight and normal categories, yet were associated with increased risk for those in the overweight category. In US women with prior PTB who had participated in a randomized trial of n–3 PUFA supplementation to reduce subsequent PTB, when accounting for study group assignment fish intake reduced the risk of PTB for normal-weight women yet increased the risk for obese women (14). Distinctions of fatty versus lean fish were not included in that investigation. Altogether, we affirm that evaluations of dietary effects on pregnancy outcomes should assess for variable responses based on maternal BMI.

Limitations imposed by the number of exposures tested are evident from the contrasting findings when FDR corrections are applied. A study powered for a primary analysis of targeted dietary fat exposures and PTB is warranted. Although prepregnancy BMI was self-reported in nuMoM2b, validity between self-report and documented medical records is relatively strong (39, 40). There is inherent bias common among all self-reported dietary recall instruments, but serial administration of FFQs can reproducibly evaluate PUFA intake (41), although multiple 24-h recalls are considered the gold standard (42). Among nonpregnant adults, measuring intake of minimally consumed fatty acids can be limited by FFQ assessment (41), but among Australian pregnant women, FFQ assessment correlated well with blood concentrations of EPA and DHA (43). The FFQ utilized for nuMoM2b was specifically enhanced to evaluate PUFA intake, yet still differs from diet assessments used by others, affecting comparison of data across studies. Also, PTB may very well have also been influenced by nutrients measured by the FFQ yet not analyzed in this study. Findings in this study suggest that future research could benefit from detailed and quantified diet assessment as well as the incorporation of biomarkers to objectively quantify and compare women's PUFA status (44).

In conclusion, while intake of dietary n–3 PUFAs preconception remains considerably lower than recommended for US women and differs by BMI categories, intake of EPA+DHA specifically is associated with PTB. This suggests that preventive strategies should encourage diverse intakes of fish and seafood among women of reproductive age to substantially increase EPA, DHA, and other n–3 PUFA intake as well as overall dietary quality, and further focused investigation regarding the association of PUFAs with PTB should be undertaken. Further attention to maternal weight and BMI status preconception is also warranted. Future research aimed at discerning pregnancy outcomes in US populations should include women from diverse backgrounds with varying sources and intakes of n–3 PUFAs, including women who meet dietary recommendations.

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