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Associations between omega-3 poly-unsaturated fatty acids from fish consumption and severity of depressive symptoms: an analysis of the 2005–2008 National Health and Nutrition Examination Survey

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SUMMARY

Fish is the primary source of dietary omega-3 poly-unsaturated fatty acids EPA and DHA, which have been reported to reduce depressive symptoms in clinical trials. We assessed the association between fish consumption and depressive symptoms in a nationally representative sample of 10,480 adults from the 2005–2008 National Health and Nutrition Examination Survey. Depressive symptoms were classified by severity using the Patient Health Questionnaire. Fish meal consumption reported in 30-day food frequency questionnaires, and EPA+DHA intake computed from 24-hour dietary recalls were evaluated in relation to depressive symptoms using multivariable ordinal logistic regression. Consumption of breaded fish showed an increased risk of greater depressive symptom severity, while all fish, non-breaded fish, and shell fish were not associated. Any EPA+DHA intake was significantly associated with fewer depressive symptoms. Exposure-response analyses revealed no clear patterns for any intake measures. Inconsistent patterns of associations in our study may be partially explained by exposure misclassification.

INTRODUCTION

Fish is the primary dietary source of omega-3 poly-unsaturated fatty acids (n-3 PUFAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), essential nutrients which the

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human body does not appear to synthesize efficiently from precursor fatty acids including alpha-linolenic acid[1]. Thus, the US Government 2010 Dietary Guideline recommends that those in the general population "increase the amount and variety of seafood consumed by choosing seafood in place of some meat and poultry" and that women who are pregnant or breastfeeding "consume 8 to 12 ounces of seafood per week from a variety of seafood types" [2]. Indeed, research has demonstrated that these long chain fish-derived n-3 PUFAs, EPA and DHA, have many health benefits, including the promotion of cardiovascular and metabolic health and a reduced risk of cancer[3–8].

Recently, studies have also investigated the positive role of n-3 PUFAs on mental illness, especially depression which with a lifetime prevalence of at least 16% in United States adults[9] is an important public health concern. Depletions of n-3 PUFAs have been noted in depressed patients[10,11] and may be due to an interaction between dietary inadequacy and an underlying genetic abnormality[11]. Recent meta-analyses of double-blind, placebo-controlled, randomized clinical trials (RCTs) examining the effects of n-3 PUFA supplementation on depressive symptoms indicate that relatively low doses of EPA+DHA, and perhaps EPA alone, can reduce depressive symptoms for individuals with major depressive disorder (MDD)[12,13]. Individual study findings are mixed, however; EPA and DHA do not appear to be an effective preventive intervention, but do appear to have treatment benefits for those already depressed, especially when used as an adjuvant therapy to standard antidepressants[12,13]. Furthermore, findings from observational studies focusing on dietary intake rather than supplementation are less conclusive in regards to the relationship between fish intake and depressive symptoms. Although some studies have found a beneficial association between fish consumption and depression[14–16], others have not[15,17–20]. The apparent difference in findings between RCTs and observational studies may be due to strict inclusion and exclusion criteria in RCTs that create a tightly defined study population in an effort to reduce bias. However, it is well known that this approach may limit generalizability of study findings, hindering the broad application of such findings in clinical practice and to population-level recommendations. Therefore, it is important to further clarify the relationship between levels of dietary fish intake and depressive symptoms in broader population settings. Interestingly, although n-3 PUFAs are one of the most commonly studied dietary variables in relation to depressive symptoms worldwide, there have been no large observational studies conducted in the United States to date[21]. To address this research gap, we evaluated the association between fish consumption, EPA +DHA intake, and depressive symptom severity in a nationally representative sample of adults using the National Health and Nutrition Examination Survey (NHANES) from 2005 to 2008.

PATIENTS AND METHODS

Study population

NHANES is a national, population-based survey designed to assess the health and nutritional status of adults and children in the United States. It is comprised of an in-home interview, followed by a physical examination in a mobile examination unit and follow-up questionnaires for some participants. Details of the NHANES probability sampling strategy and data collection procedures have been extensively described[22,23]. Briefly, NHANES uses a complex multistage, stratified and clustered sampling design to generate a sample that represents the total US non-institutionalized civilian population when appropriate weights are used. Of the 10,480 adults 20 years and older who were interviewed for a mobile examination center exam in the 2005–2008 NHANES, 9,512 (90.8%) had complete data for depression symptoms collected. 221 subjects (2.3%) were removed due to missing data for any of the fish exposure variables. Finally, 15 subjects (0.2%) with missing data for one or more of the covariates of interest (gender, age, race, education level, marital status, smoking

history, general health status, antidepressant use, fish oil supplement use, and total energy intake) were excluded. Thus, the final sample consisted of 9,276 subjects with complete data.

Assessment of depressive symptoms

NHANES 2005–2008 utilized the nine-item Patient Health Questionnaire (PHQ-9) to screen for depressive symptoms. Based on DSM-IV diagnostic criteria, the PHQ-9 is a validated, self-report depression screener available in English and Spanish which can be scored to evaluate the severity of depressive symptoms[24–26]. This instrument has an estimated sensitivity and specificity of 88% to detect depression (score: 10+) compared to patient interviews with Mental Health professionals[25] and has been validated cross-culturally in English- and Spanish-speaking subjects[27,28]. The PHQ-9 is scored to generate a total depression score ranging from 0 – 27. We categorized this total score into a 3-level ordinal variable based on recommended cut-offs:[24] no to minimal depression (score: 0–4), mild depression (score: 5–9), and moderate to severe depression (score: 10+). In a sensitivity analysis, we compared our findings to those using an alternative depression classification scheme: no to minimal depression (score: 0–4), mild to moderate depression (score: 5–14), and moderately severe to severe depression (score: 15+).

Assessment of fish-derived n-3 PUFA intake

Dietary information was collected through both a food frequency questionnaire (FFQ) and two 24-hour dietary recalls (midnight to midnight)[23]. From this dietary information, we computed two primary exposure measures: FFQ-based fish consumption in the past 30 days and EPA+DHA estimates from 24-hour recall data. Both sets of exposure variables assess dietary EPA+DHA intake, as fish is the primary dietary source of these micronutrients[3].

The FFQ included a supplement which asked subjects to report specific types of fish and shellfish consumed in the past 30 days as well as the number of times each was eaten during that time period. The types of fish included: breaded fish products, tuna, bass, catfish, cod, flatfish, haddock, mackerel, perch, pike, pollock, porgy, salmon, sardines, sea bass, shark, swordfish, trout, walleye, and other. Types of shellfish included: clams, crabs, crayfish, lobster, mussels, oysters, scallops, shrimp, and other. Using the number of meals reported for each type of fish in the FFQ supplement, we computed the total number of meals within four fish groupings (all fish, non-breaded fish, breaded fish, and shellfish) to obtain continuous fish/shellfish meal variables. This continuous variable was then categorized into four levels: none, low, medium, and high fish consumption. Cut-off values for the low, medium and high levels were based on tertiles of the distribution of non-zero fish meals for each variable. A dichotomous (none vs. any) fish consumption variable was also created for each of the four fish intake measures.

Data from both 24-hour recalls were utilized to compute energy intake and the consumption of specific macro and micronutrients, including EPA and DHA. NHANES reported EPA and DHA in grams, and total energy intake in calories from the 24-hour dietary recalls. The first dietary recall was conducted in person with a trained interviewer during the MEC exam, and a follow-up recall was conducted over the telephone 3–10 days after the MEC exam. Instructions are provided orally in English and/or Spanish, and measurement aids are used to help subjects respond accurately to questions of food quantity. We computed average EPA +DHA intake estimates (EPA, DHA and their sum were highly correlated, therefore we considered only EPA+DHA intake), and total energy intake across the two recalls. Values for these variables were energy adjusted using the energy density method (g/1,000Kcal)[29]. Energy density-adjusted EPA+DHA from 24-hour recall was dichotomized into none vs.

any and categorized into a four-level variable using tertiles for participants with non-zero values as described above for the FFQ fish intake variables.

Covariates

The following covariates of interest were obtained from NHANES surveys due to their known relationships with depression[30,31]: age, gender, race (white, black, other), educational level (less than high school, high school graduate, greater than high school), marital status (married or living with partner, widowed, divorced or separated, never married), smoking status (never, former, current), overall health status (excellent, very good, good, fair, poor), and antidepressant use in the last 30 days (yes, no). Fish oil supplementation in the last 30 days (yes, no), and total energy intake (Kcal) were included because of their direct relationships to an individual's total EPA+DHA levels. Fish oil supplements were identified from the NHANES supplement file. Two of the authors (CAH and RCB) reviewed names and ingredients of all supplements in this file to identify all containing EPA or DHA. The identified EPA and/or DHA supplements were then matched to the individual level supplement usage file to create a dichotomous (yes, no) variable for supplement intake in the last 30 days. Similarly, all antidepressants in the prescription list file were matched to individual level prescription usage information to create a dichotomous (yes, no) variable for antidepressant use in the last 30 days; the NHANES prescription data indicates classes of medications, including antidepressants.

Statistical Analysis

Proportions and chi-square tests were used to examine the distribution of categorical fish intake measures and covariates across depression severity levels. Age in years and total energy intake (continuous variables) were compared across depression levels by computing means and standard errors. Crude odds ratios (OR) and 95% confidence intervals (CI) were computed for all covariates using ordinal logistic regression.

Subsequently, multiple ordinal logistic regression models were used to assess the relationship between FFQ and/or 24-hour recall measures of EPA+DHA intake and reported depressive symptoms. Two models were developed for each exposure category (dichotomous and categorical). All models controlled for age, race, gender, educational level, marital status, smoking and general health status, antidepressant use and fish oil supplementation in the last 30 days, and average total caloric intake from 24 hour dietary recall. We used a multivariable nutrient density model[29] in which total energy intake was included in the models for EPA+DHA from 24-hour recall as an independent variable despite the fact that the exposure was already energy adjusted in these models because total energy itself, if associated with depressive symptoms, can act as a confounder.

Sensitivity analyses were conducted to examine the alternative depressive symptom categorization above, and to evaluate the primary hypothesis in simplified models only adjusting for socio-demographic factors (age, gender, ethnicity, educational level, and marital status).

Descriptive analysis and ordinal logistic regression were conducted using SAS 9.2 (Cary, NC). Survey procedures (SURVEYMEANS, SURVEYFREQ, AND SURVEYLOGISTIC) with appropriate weights and domains were used to account for the complex survey design and probability weighting of NHANES. The proportionality assumption for ordinal logistic regression was confirmed graphically[32].

RESULTS

Of the 9,276 subjects with complete data, 6.8% and 14.8% were identified on the PHQ-9 as having moderate to severe depressive symptoms (score >10) and mild depressive symptoms (score 5–9), respectively. Table 1 summarizes the distribution of each covariate by depression level. All covariates examined, with the exception of total energy intake and age, were significantly related to depression in crude bivariate analyses (Table 1). Females, Blacks, subjects with less education, divorced or separated subjects, current smokers, subjects with poorer health status, subjects on antidepressants, and subjects not taking fish oil supplementation were more likely to experience depressive symptoms in this sample. In multivariable analysis, age, gender, education, marital status, smoking status, health status, and antidepressant use remained independent predictors of depression severity level (Table 1). Fish oil supplementation was not significantly associated with depression symptom severity in the multivariable model.

Unadjusted but not adjusted analyses show a small decreased risk of more depressive symptoms among individuals who report consuming all fish meals, non-breaded fish meals, and/or shellfish meals on the FFQ (Table 2). No clear trends emerge in categorical exposure-response analyses for these fish groupings. Reporting the consumption of any breaded fish on the FFQ showed an increased risk of greater depressive symptom severity in both crude (OR = 1.40, CI = 1.19–1.65) and multivariable analyses (OR = 1.34, CI = 1.07–1.67) (Table 2). The exposure-response relationship for categorized levels of breaded fish appeared inverse, with the highest OR of depressive symptoms in lowest exposed category and lowest OR of depressive symptoms in the highest exposed category.

Any EPA+DHA intake computed from 24-hour dietary recalls was significantly associated with a lower risk of depressive symptoms in both crude and multivariable analyses. After adjustment for all covariates, subjects who reported eating foods containing any EPA or DHA in the past 24 hours were 25% less likely to experience greater depressive symptoms than those who reported no EPA or DHA intake (CI: 0.59, 0.96). Nevertheless, no clear trends emerged in categorical exposure-response analyses for EPA+DHA intake from 24-hour recall.

Our findings were quite robust to variations in depression classification and simplified socio-demographic models in sensitivity analyses (data not shown). Odds ratio point estimates did not change by more than 7% in the alternative depression classification models. Although on a few occasions changes of up to 20% were observed, in the majority of the limited socio-demographic models, odds ratio point estimates did not change more than 12%. No changes in the direction or significance of the reported relationships between breaded fish from 30-day FFQ and EPA+DHA intake from 24-hour recall and depression were observed.

DISCUSSION AND CONCLUSIONS

The frequency of fish intake reported for a 30-day period using an FFQ dietary assessment was not consistently associated with depressive symptoms in this study. Furthermore, fish oil supplementation was not independently associated with depressive symptoms in our population-based sample. However, a beneficial role of fish-derived n-3 PUFAs cannot be excluded based on our findings from a 24-hour estimate of EPA+DHA intake via 24-hour dietary recall; any reported EPA or DHA intake in the past 24 hours was significantly, in crude and multivariable analyses, associated with a reduced prevalence of depressive symptoms by 25% although the lack of consistent exposure-response patterns reduces our confidence in this result.

It is scientifically plausible that EPA and/or DHA can improve or prevent depressive symptoms. In the human body, DHA and EPA, and many of their metabolites produced via a variety of biochemical pathways, have substantial anti-inflammatory and tissue protective effects in several tissues[33]. As DHA is very highly concentrated in the central nervous system and a vital nutrient in its optimum development[34], its deficiency disrupts serotonin, norepinephrine, and dopamine transmission across cellular membranes, neurotransmitters that contribute to the mood and cognitive dysfunction aspects of depression[10]. EPA, meanwhile, may play a more important role related to the somatic symptoms which affect up to 80% of individuals with major depression. At the cellular level, EPA can modulate proinflammatory reactions which induce symptoms of physical sickness[10]. The importance of these fatty acids in the human diet is underlined by the fact that their synthesis from other fatty acids, such as alpha-linolenic acid, has been shown to be quite poor[34]. This has important implications for central nervous system health at all ages.

EPA and DHA are known to be very safe dietary nutrients and supplements, even at high doses[35], and promote cardiovascular health[3] along with optimal brain development[4] as well as reduce insulin resistance[5]. They also improve the management of chronic inflammatory diseases[6,35]. Very importantly, when combined with prescription pharmaceuticals, fish oil is not associated with serious or very concerning drug-drug interactions[36]. When suggesting increased fish consumption to increase EPA and DHA intake, there are potential concerns related to pre- and postnatal mercury exposure and cognitive development in children, but recent research does not support these associations, even in populations that consume large amounts of fish[37]. Thus, fish consumption as well as supplementation with EPH + DHA should be widely recognized as safe, and beneficial to health.

Recent clinical trials indicate that EPA and DHA supplementation can reduce depressive symptoms for individuals with MDD, especially when used as an adjuvant therapy[12,13], but do not appear to be an effective preventive intervention in those without MDD. Likewise, our findings did not suggest that supplemental EPA and DHA were significantly associated with depressive symptom severity in the general US population. On the other hand, prior observational studies focusing on dietary intake rather than supplementation are less conclusive in regards to the relationship between fish intake and depressive symptoms[14–16]. Observational studies are instrumental to understanding this question, however, as national recommendations regarding dietary fish intake could have a large impact on depression at a population-level. Only one previous study has addressed this question[38]; Lucas et al did not find an association between n-3 PUFAs from fish and clinical depression in 54,632 women from the Nurses' Health Study, although they did find that α-linolenic acid (ALA), a plant-based n-3 PUFA, was inversely associated with depression risk in this population. We conducted a large, population-based study addressing this question in a nationally-representative sample of both men and women in the United States. Furthermore, we considered severity of depressive symptoms rather than a dichotomous clinical endpoint which allowed us to better evaluate dose-response patterns. Conducting this analysis with NHANES data opens up the possibility of repeating results with future cohorts, and comparing findings to those using blood sample biomarkers for EPA and DHA content as these variables may be added to NHANES data in the near future. Our findings were inconclusive, however, and may have been substantially affected by exposure misclassification.

Food frequency questionnaires and 24-hour dietary recall estimates for fatty acid intake have been shown to be correlated[38] and have been shown to correlate with biomarkers for fatty acids[38]. Despite this, both methods have strengths and weaknesses for measuring dietary EPA and DHA. FFQ is likely to be more representative of a person's usual diet compared to

nutrient computations from 24 hour dietary recalls as a single 24-hour recall only considers the food eaten over a given day. However, we were able to average two 24-hour recalls to improve this. The greatest benefit to dietary recalls is the fact that they take into account factors such as the specific type of fish, portion size, and cooking methods. These factors greatly influence the EPA and DHA content of a fish meal[39]. Dietary recall data should therefore more accurately reflect EPA+DHA intake during the time period reported. Thus, it is not surprising that in our study EPA+DHA correlated significantly, but weakly with all fish meals, non-breaded fish meals, and shellfish meals from 30-day FFQ data, and was uncorrelated with breaded fish meals from 30-day FFQ data in this study (data not shown). This pattern supports the validity of our classification system for FFQ-based fish intake as breaded fish meals are likely to be fried, and frying fish, as well as the type of fish most often fried, is associated with reduced EPA+DHA content[39]. At the same time, the low correlations between fish meals and EPA+DHA we observed indicates that reported fish meals in the past 30 days may not be a strong predictor of fish-derived dietary n-3 PUFA. Therefore, we believe EPA+DHA from a 24-hour recall is a more accurate predictor of dietary n-3 PUFAs in this study as findings from this analysis do support the a priori hypothesis that dietary omega-3 poly-unsaturated fatty acids reduce depressive symptoms. One further limitation to note for both FFQ and dietary recall is that both reflect relatively short-term fish intake, and do not help quantify more chronic (over years) intake which is may be important in the long-term development of depressive symptoms. This limitation is inherent to the cross-sectional design of NHANES, however, the dietary patterns of adults do not change dramatically over time. Since blood content of EPA and DHA is a very reliable measure of dietary intake, the addition of this metric to future studies will be very beneficial.

Interestingly, our FFQ findings suggest that breaded-fish meals significantly increase the risk of greater depressive symptoms, yet no consistent exposure-response pattern is observed for the categorical analysis. We would not expect breaded fish meals, which are often fried, to be an important source of dietary EPA and DHA and thus we would not expect consumption of such meals to protect against depressive symptom severity. The significantly increased risk is harder to explain, but breaded fish may simply be a proxy for consuming a higher fat, less healthful diet, which would help explain the association with greater depressive symptoms[40].

In conclusion, although our findings do not show consistent patterns across exposure classification methods, they do suggest that higher levels of dietary EPA+DHA may be associated with a reduced number of depressive symptoms. Future longitudinal studies are needed to directly link dietary intake of fish and biomarkers for fish-related n-3 PUFA with depressive symptoms.

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Table 1

Crude and Adjusted Relationships between Covariates and Depressive Symptom Severity

				Crude Analysis		Adjusted Analysis[1]	
Covariate	**No/Minimal Depression (0–4)** %	**Mild Depression (5–9)** %	**Moderate to Severe Depression (≥10)** %	**OR**	**95% CI**	**OR**	**95% CI**
Age[2]							
Continuous (years)[3]	46.8 ± 0.5	46.0 ± 0.7	46.0 ± 0.7	1.00	(0.99, 1.00)	0.98	(0.98, 0.99)
Gender							
Male	82.6	12.3	5.1	reference		reference	
Female	74.4	17.1	8.5	1.64	(1.50, 1.79)	1.55	(1.38, 1.74)
Race							
White	79.2	14.6	6.2	reference		reference	
Black	75.9	14.2	9.9	1.25	(1.03, 1.51)	1.00	(0.86, 1.17)
Other	76.5	15.9	7.6	1.18	(0.99, 1.39)	0.94	(0.78, 1.12)
Education							
< HS	69.7	19.0	11.3	reference		reference	
HS/GED	76.2	15.1	8.7	0.72	(0.62, 0.84)	0.89	(0.74, 1.07)
> HS	82.1	13.3	4.6	0.49	(0.42, 0.57)	0.78	(0.66, 0.91)
Marital Status							
Married/Living with Partner	81.2	13.3	5.5	reference		reference	
Widowed	74.1	20.1	5.8	1.46	(1.20, 1.78)	1.40	(1.11, 1.77)
Divorced/Separated	68.6	17.1	14.4	2.09	(1.75, 2.50)	1.65	(1.36, 1.99)
Never Married	76.2	17.0	6.8	1.34	(1.12, 1.59)	1.14	(0.97, 1.35)
Smoking Status							
Never	81.6	13.6	4.9	reference		reference	
Former	80.4	14.2	5.5	1.08	(0.92, 1.27)	1.10	(0.93, 1.31)
Current	69.2	18.1	12.6	2.05	(1.79, 2.34)	1.63	(1.36, 1.94)
Health Status							
Excellent	92.8	6.1	1.1	reference		reference	

				Crude Analysis		Adjusted Analysis[1]	
	No/Minimal Depression (0–4)	Mild Depression (5–9)	Moderate to Severe Depression (≥10)	OR	95% CI	OR	95% CI
Covariate	%	%	%				
Very Good	87.9	10.1	2.0	1.76	(1.25, 2.48)	1.69	(1.18, 2.43)
Good	77.3	16.4	6.4	3.83	(2.70, 5.44)	3.55	(2.47, 5.10)
Fair	55.8	26.8	17.4	10.71	(7.28, 15.75)	9.73	(6.52, 14.53)
Poor	24.1	28.8	47.1	47.51	(32.71, 69.00)	38.24	(25.80, 56.67)
Antidepressants							
No	81.2	13.3	5.4	reference		reference	
Yes	54.7	26.6	18.6	3.66	(3.20, 4.20)	3.04	(2.68, 3.45)
Fish Oil Supplements							
No	78.0	14.9	7.1	reference		reference	
Yes	82.4	13.9	3.7	0.74	(0.57, 0.96)	0.97	(0.72, 1.30)
Total Energy Intake (Kcal)[3]	2150.4 ± 14.3	2110.5 ± 38.5	1980.2 ± 43.9	1.00	(1.00, 1.00)	1.00	(1.00, 1.00)

[1] Adjusted values reported here are from multivariable models of depression and 4-level categorical all fish consumption in the last 30 days. Adjusted covariate ORs and 95% CI from the other multivariable models were very similar across categorical and dichotomous classifications of fish, shellfish, and EPA/DHA consumption.

[2] Age was assessed categorically in the crude analysis to assess for any non-linear trends, but as no clear trends emerged, this variable was entered continuously into the multivariable analyses.

[3] Mean ± standard deviation of age and total energy intake is reported by depression level.

Table 2

Crude and Adjusted Relationships between Fish Consumption and Depressive Symptom Severity

				Crude Analysis		Adjusted Analysis	
	No/Minimal Depression	Mild Depression	Moderate to Severe Depression	OR	95% CI	OR	95% CI
Exposure Classification	%	%	%				
All Fish Meals							
(30-day FFQ, # of meals)							
None (0)	76.0	16.2	7.7	reference		reference	
Low (1–2)	78.9	14.0	7.1	0.86	(0.76, 0.96)	0.98	(0.87, 1.11)
Medium (3–5)	80.0	14.1	5.9	0.79	(0.66, 0.95)	1.04	(0.84, 1.28)
High (6+)	78.5	14.9	6.5	0.87	(0.72, 1.04)	1.23	(1.03, 1.47)
Any (1+)	79.2	14.3	6.5	0.84	(0.74, 0.94)	1.06	(0.94, 1.19)
Non-Breaded Fish Meals							
(30-day FFQ, # of meals)							
None (0)	75.5	16.5	8.0	reference		reference	
Low (1–2)	79.3	13.8	6.9	0.81	(0.71, 0.92)	0.96	(0.84, 1.09)
Medium (3–5)	80.5	13.9	5.7	0.74	(0.63, 0.88)	0.99	(0.83, 1.19)
High (6+)	78.7	15.0	6.3	0.83	(0.68, 1.01)	1.19	(0.98, 1.45)
Any (1+)	79.5	14.1	6.4	0.79	(0.70, 0.90)	1.02	(0.90, 1.15)
Breaded Fish Meals							
(30-day FFQ, # of meals)							
None (0)	79.0	14.5	6.5	reference		reference	
Low (1)	71.1	20.7	8.3	1.50	(1.21, 1.86)	1.40	(1.07, 1.83)
Medium (2)	74.1	13.9	12.0	1.38	(0.95, 2.01)	1.32	(0.88, 1.98)
High (3+)	76.4	14.2	9.4	1.19	(0.89, 1.59)	1.21	(0.82, 1.78)
Any (1+)	73.0	17.4	9.6	1.40	(1.19, 1.65)	1.34	(1.07, 1.67)
Shellfish Meals							
(30-day FFQ, # of meals)							
None (0)	76.5	15.2	8.3	reference		reference	
Low (1)	79.2	14.0	6.8	0.85	(0.72, 1.01)	0.93	(0.80, 1.09)

				Crude Analysis		Adjusted Analysis	
	No/Minimal Depression	Mild Depression	Moderate to Severe Depression	OR	95% CI	OR	95% CI
Exposure Classification	%	%	%				
Medium (2–3)	79.5	16.1	4.4	0.81	(0.70, 0.94)	0.97	(0.83, 1.15)
High (4+)	81.1	12.9	6.0	0.75	(0.59, 0.96)	0.99	(0.77, 1.27)
Any (1+)	79.9	14.4	5.7	0.81	(0.70, 0.93)	0.96	(0.85, 1.10)
EPA + DHA							
(24-hour dietary recall, g/1,000 Kcal)							
None (0)	68.1	21.1	10.8	reference		reference	
Low (≤0.012)	77.7	14.8	7.5	0.62	(0.47, 0.81)	0.77	(0.60, 0.98)
Medium (>0.012 – ≤0.037)	78.5	14.9	6.6	0.59	(0.43, 0.79)	0.77	(0.59, 1.01)
High (>0.037)	80.9	13.5	5.6	0.50	(0.37, 0.68)	0.71	(0.55, 0.92)
Any (>0)	79.0	14.4	6.6	0.57	(0.43, 0.75)	0.75	(0.59, 0.96)

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