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n-3 Fatty Acids and Periodontitis in US Adults

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ABSTRACT

Background Periodontitis is a common, chronic inflammatory disease. Although n-3 fatty acids have anti-inflammatory properties, it is unclear whether n-3 fatty acids can treat or prevent periodontitis.

Method We studied 9,182 adults aged 20 years and older who participated in the National Health and Nutrition Examination Survey between 1999 and 2004. Periodontitis was assessed by dental exam and was defined as >4 mm pocket depth and >3 mm attachment loss in any one tooth. Intake of n-3 fatty acids was assessed by 24-hour dietary recall. We used multivariable logistic regression to estimate the associations between periodontitis and intakes of docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), and linolenic acid (LNA).

Results The weighted prevalence and 95% confidence interval (CI) of periodontitis was 8.2% (95% CI 7.0 to 9.4). Compared with the lowest tertiles, the adjusted odds ratios for periodontitis associated with the highest tertiles of dietary n-3 intake were 0.78 (95% CI 0.61 to 1.00; $P=0.009$) for DHA, 0.85 (95% CI 0.67 to 1.08; $P=0.10$) for EPA, and 0.86 (95% CI 0.60 to 1.23; $P=0.28$) for LNA. The associations were little changed by multivariable adjustment or exclusion of individuals reporting use of dietary supplements containing DHA, EPA, or LNA.

Conclusions In this nationally representative sample, higher dietary intakes of DHA and, to a lesser degree, EPA, were associated with lower prevalence of periodontitis. Interventional studies are needed to confirm the potential protective effects of n-3 fatty acids on periodontitis.

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Periodontitis is a common, chronic inflammatory disease caused by the accumulation of bacterial matrix at the gum line. It is characterized by gum tissue separation from the tooth, which forms a periodontal pocket and can lead to bone and tooth loss. Traditional therapies for periodontitis focus on targeting the bacterial infection, which may be the initiating event responsible for the ensuing inflammation and tissue destruction. More recent therapeutic strategies have targeted the host response to the bacterial infection, which may play a more crucial role in the pathogenesis of periodontitis and its associated systemic effects. In animal models, induced periodontitis induces fatty plaque buildup in blood vessels (1), which appears to be due to host inflammatory responses to the bacteria, rather than the bacteria (2).

Polyunsaturated fatty acids (PUFAs) are fatty acids with >1 carbon-carbon double bond, including n-3, n-6, and n-9 fatty acids. The n-3 fatty acids from marine sources, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and vegetable sources, such as linolenic acid (LNA), which includes alpha-linolenic acid (ALA) and a related n-6 fatty acid, gamma-linolenic acid (GLA), have all been shown to have anti-inflammatory properties (3-5). Indeed, topical application of bioactive products derived from n-3 fatty acids (including DHA and EPA) confer dramatic protection against inflammation-induced tissue and bone loss associated with periodontitis in experimental models (6).

In human beings, one trial randomized 30 subjects with periodontitis to receive 12 weeks systemic therapy of EPA, GLA, both EPA and GLA, or olive oil placebo (7). The study showed a significant decrease in probing depth in patients receiving GLA alone and a trend toward decreased probing depth in subjects receiving EPA alone. However, it is unknown if LNA or DHA intake is also inversely associated with periodontitis in human beings. Moreover, there are no large population studies of periodontitis and the PUFAs that are thought to have anti-inflammatory properties, such as DHA, EPA and LNA. This study aims to examine the association between these n-3 fatty acids and prevalence of periodontitis in a nationally representative sample of adults.

METHODS

Study Sample

This cross-sectional study used data from 9,182 adults aged 20 years and older who participated in the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2004. The survey provides information on the health and nutritional status of the US civilian, noninstitutionalized population by using a complex, stratified, multistage, probability-sampling design (8-10). NHANES includes both an initial in-home interview followed by an examination and personal interview at a mobile examination center for those who are eligible. A total of 31,126 individuals participated in the in-home interview. For this study, we excluded subjects younger than age 20 years (n=15,794), lacking periodontal exams or edentulous (n=4,118), lacking physical exams (n=1,119), having missing data from covariates of interest (n=426), not meeting minimal criteria for reliability of the dietary recall (n=314), lacking interpretable periodontal exams (n=98), or having incomplete periodontal exams (n=75), leaving 9,182 for analysis.

Periodontitis

Periodontitis was assessed during the periodontal exam by dentists trained in the survey examination protocol (11-13). Briefly, periodontal examinations during NHANES 1999-2000 were conducted in the midbuccal and mesiobuccal sites for each tooth in two randomly chosen quadrants, one maxillary and one mandibular, on the assumption that conditions in these two quadrants represent the mouth. Third molars were excluded because of their frequent extraction in young adulthood, so a maximum of 14 teeth and 28 sites per individual were examined. For the NHANES 2001-2002 and the NHANES 2003-2004, the periodontal examination was conducted in three sites, midbuccal, mesiobuccal and distobuccal for each tooth, although we only used the midbuccal and mesiobuccal sites to be consistent with the 1999-2000 examination. Periodontal measurements were rounded to the lowest whole millimeter and were made with a color-banded periodontal probe graduated at 2, 4, 6, 8, 10, and 12 mm. Detailed information on the NHANES dental examinations for the survey periods is available elsewhere (11-13).

Previous studies have used several combinations of clinical attachment loss and pocket depth to establish periodontitis case definitions (14-20). We defined periodontitis as ≥4 mm pocket depth and ≥3 mm attachment loss in any midfacial or mesial tooth, as in previous studies (14,16,20). For consistency across study cohorts, we used the two sites measured in NHANES 1999-2000, NHANES 2001-2002, and NHANES 2003-2004 to define periodontitis. We also validated the diagnosis by examining levels of circulating C-reactive protein (CRP) according to periodontitis status since elevated levels of CRP are known to be associated with periodontitis (21,22).

In post hoc analyses, we evaluated prevalence of moderate periodontitis, defined as 4 to 5 mm pocket depth and 3 to 4 mm attachment loss; and severe periodontitis, defined as >5 mm pocket depth and >4 mm attachment loss in any midfacial or mesial tooth.

Dietary Fatty Acids

Fatty acid intake in grams per day was assessed by a 24-hour dietary recall. From 1999 to 2001, dietary intake data were collected using the NHANES computer-assisted dietary interview system (CADI). The CADI is a multiple-pass recall method that provides instructions to interviewers for recording information about foods. Additional information about the CADI system is provided in the NHANES 1999-2000 Dietary Interviewers Procedures manual (8). From 2002-2004, data were collected using the US Department of Agriculture's dietary data collection instrument, the Automated Multiple Pass method (9,10), which was found to provide valid measures of group total energy and PUFA intake in 20 highly motivated premenopausal women using doubly labeled water total energy expenditure, the Block food-frequency questionnaire, the National Cancer Institute's Diet History Questionnaire, and 14-day dietary record (23). The variable for linolenic acid (18:3 octadecatrienoic acid, LNA) includes both ALA and GLA, which were not assessed separately in NHANES.

Supplemental Fatty Acids

Supplemental fatty acid intake was assessed by self-reported dietary supplement use. The interviewer entered the supplement's name and manufacturer into a computer database that contained information on individual ingredients. Trained nutritionists at the National Center for Health Statistics matched the product names to a known product when possible.

Other Covariates

We analyzed covariates that have been found to be related to periodontitis in previous studies, including age, race–ethnicity, socioeconomic status, physical activity, smoking status, diabetes mellitus, alcohol intake, body mass index (BMI), and pregnancy status (14-16,19,24). In secondary analyses, we included intake of various dietary factors based on possible relations with the exposure and outcome (17,25). We categorized age as 20 to 39, 40 to 59, 60 to 79 and ≥80 years. We assigned self-reported race-ethnicity as white, black, Mexican American, and other; the latter included non-Mexican American Hispanic and multiracial individuals. Annual income was categorized as <$20,000, $20,000 to $44,999, $45,000 to $74,999, ≥$75,000, and unreported. Education was assigned as less than high school, high school, or some college educa-

tion. Country of birth was self-reported and grouped as within the United States, Mexico, or other locations. Physical activity was assessed by questions regarding vigorous activity (ie, jogging or sports that cause a substantial increase in heart rate and heavy perspiration) and moderate activity (ie, brisk walking or dancing that cause a moderate increase in heart rate and perspiration) for at least 10 minutes during the past 30 days; we divided physical activity into three categories: sedentary (no moderate or vigorous activity), moderate activity alone, and vigorous activity. We categorized smoking as never, former, and current. Participants reported their general health, which we collapsed into excellent/very good, good/fair, and poor. Diabetes was defined as a self-report of a diagnosis of diabetes by a doctor or use of medication to lower blood sugar. We categorized alcohol intake into four groups: zero drinks/day, >0 to <2 drinks/day, 2 to 5 drinks/day, and >5 drinks/day. BMI was calculated from measured height (in meters) and weight (in kilograms) and categorized as <25, 25 to 29.9, and ≥30. Pregnancy status was ascertained from self-report or urine pregnancy tests. Dietary vitamin E (milligrams per day), vitamin C (milligrams per day), monounsaturated fatty acids (grams per day), saturated fat (grams per day), carbohydrates (grams per day), and linoleic acid (grams per day) were assessed using the same 24-hour dietary recall as described above. We dichotomized aspirin and/or non-steroidal anti-inflammatory drug (NSAID) use as regular ("daily or nearly every day"), chronic use ("greater than 21 days"), or non-use.

STATISTICAL ANALYSES

We calculated normality tests on the outcome variables and found CRP to be right skewed. We transformed the CRP data by taking the natural logarithm. We calculated descriptive statistics on the dietary intake of n-3 fatty acids and other characteristics. We compared the distributions of these characteristics between patients with and without periodontitis using χ^2 tests of independence. We calculated unadjusted odds ratios (ORs) for the relation between tertiles of each dietary n-3 fatty acid intake (first tertile referent) and prevalence of periodontitis in contingency tables. For multivariable analyses, we used two sequential logistic regression models. The first model adjusted for total energy intake (kilocalories per 24 hours), age (years), and sex. The second multivariable model additionally adjusted for general health status, race, smoking, diabetes mellitus, origin of birth, income, education, physical activity, pregnancy, BMI, alcohol intake, and intake of the other n-3 fatty acids of interest.

Sampling weights were used to generate weighted effect estimates, including ORs and 95% confidence intervals (CIs). We used SAS (version 9.1, 2002, SAS Institute, Cary, NC) and SAS-callable SUDAAN (version 9.0, 2007, SAS Institute, Research Triangle Park, NC) to analyze dietary recall data with appropriate 6-year weight assignment from years 1999 to 2004 (8-10).

Given suggestions of an interaction between n-3 and n-6 fatty acid intakes on inflammatory conditions (25), we tested for interaction with linoleic acid, a commonly consumed n-6 fatty acid. We also tested the number of teeth lost and regular, chronic aspirin and/or NSAID use as potential confounders. To adjust further for possible confounding, we constructed a dietary model in which linoleic acid (grams per day n-6 fatty acid), vitamin C (milligrams per day), and vitamin E (milligrams per day), and total intake of carbohydrate (grams per day), monounsaturated fats (grams per day) and saturated fats (grams per day) were forced into the model.

Due to the high correlations between EPA and DHA intake (26), one or the other was used in multivariable models; we also evaluated the association between combined EPA/DHA and periodontitis. To evaluate dose–response relationships, we introduced a centered quadratic term and evaluated intake in finer categories beyond tertiles chosen a priori. We also analyzed the association between tertiles (individually and first tertile vs second and third combined) dietary plus supplement n-3 fatty acid intake (for DHA, EPA, and LNA) and prevalence of periodontitis and performed an analysis restricted to nonsupplement users. In post hoc analyses, we evaluated the association of DHA intake with periodontitis severity. To evaluate whether observed associations of n-3 fatty acid intake and periodontitis had the expected systemic anti-inflammatory effects, we examined the association of n-3 fatty acids and logCRP in a multivariable linear model. Lastly, we evaluated the association between periodontitis severity and logCRP.

RESULTS

Of the 9,182 adults studied, a total of 1,024 had periodontitis. The weighted prevalence was 8.2% (95% CI 7.0 to 9.4). As Table 1 shows, periodontitis was most strongly associated with age, male sex, non-white race, lower socioeconomic status, smoking, and lower physical activity. As hypothesized, there was a positive association between presence of periodontitis and CRP (adjusted difference in logCRP 0.17±0.05; $P=0.002$).

The median dietary PUFA intakes among the 9,182 subjects were 1.274 g/day (interquartile range 0.77 to 1.98) for linolenic acid, 0.003 g/day (interquartile range 0.00 to 0.01) for EPA, and 0.020 g/day (interquartile range 0.00 to 0.06) for DHA. Spearman correlations between DHA and EPA, DHA and LNA and EPA and LNA were 0.86, 0.24, and 0.21, respectively (all $P<0.001$).

We found that higher dietary intake of DHA was associated with a lower odds of periodontitis (Table 2), with no statistical difference in effect between the second and third tertiles ($P=0.39$). Dietary EPA intake was more modestly associated with lower prevalence of periodontitis. We did not observe a statistically significant association between tertiles of LNA and periodontitis. For both DHA and EPA, there was little change in the ORs with multivariable adjustment. For LNA, a significant association in initial models were chiefly attributable to confounding by education, income, and race/ethnicity.

As the Figure shows, DHA and EPA were associated with lower logCRP in multivariable linear models. These associations were not significant in tests of heterogeneity but were significant in tests of linear trend. LNA was not associated with CRP levels in initial or multivariable models.

Only 145 subjects reported taking any dietary supplements containing DHA, EPA, ALA, or GLA.

The median dietary plus supplementary PUFA intakes among the 9,182 subjects were 1.276 g/day (interquartile range 0.77 to 1.99) for linolenic acid, 0.003 g/day (inter-

Table 1. Sample characteristics of US adults with and without periodontitis, based on data from the National Health and Nutrition Examination Survey between 1999-2004 (n=9,182)

	Periodontitis		No Periodontitis	
Characteristic	**n**	**%**	**n**	**%**
Age group (y)				
20-39	276	32	3,732	49
40-59	435	49	2,491	36
60-79	276	17	1,620	13
≥80	37	2	315	2
Sex				
Male	620	61	3,821	49
Female	404	39	4,337	51
Race/ethnicity				
Non-Hispanic white	295	52	4,168	73
Non-Hispanic black	291	21	1,399	10
Mexican American	333	12	1,932	8
Other	105	15	659	10
Annual income				
<$20,000	404	35	2,261	21
$20,000-$34,999	347	31	2,469	28
$35,000-$74.999	135	17	1,638	23
>$75,000	94	14	1,498	25
Refused to disclose	44	3	292	3
Education				
<High school	479	35	2,147	15
High school	225	26	1,950	25
Some college	320	39	4,061	60
Alcohol intake (drinks/d)				
0	385	32	2,703	28
>0-<2	180	17	1,899	23
2-5	330	38	2,914	41
>5	129	13	642	8
Smoking status				
Never	437	37	4,509	54
Former	266	23	1,940	23
Current	321	40	1,709	23
Body mass index				
<25	270	29	2,662	36
25-29.9	379	35	2,935	34
≥30	375	36	2,561	30
Activity level				
None	580	53	3,167	31
Moderate	226	24	2,358	30
Vigorous	218	23	2,633	39
Health status				
Excellent/very good	407	46	4,192	58
Good	348	33	2,529	29
Fair/poor	269	22	1,437	13
Diabetes				
No	899	90	7,604	95
Yes	125	10	554	5

quartile range 0.00 to 0.02) for EPA, and 0.021 g/day (interquartile range 0.00 to 0.06) for DHA. Similar associations in the second and third tertiles of n-3 fatty acid intake and periodontitis were found when using dietary plus supplemental DHA, EPA, or LNA (ALA plus GLA) intake or in analyses restricting to those who did not use supplements (Table 2). Similar associations in the second and third tertiles of combined EPA/DHA and periodontitis were found in multivariable models (median 0.74 [interquartile range 0.59 to 0.93] and 0.78 [interquartile range 0.61 to 1.02], respectively). There were no significant interactions between DHA, EPA, and LNA intake and linoleic acid ($P=0.16$, $P=0.14$, and $P=0.32$, respectively) with respect to prevalence of periodontitis.

Table 2. Tertiles of n-3 fatty acid intake and prevalence of periodontitis, based on data from the National Health and Nutrition Examination Survey between 1999-2004 (n=9,182)

	Tertile			
Variable	**1**	**2**	**3**	***P* value[a]**
Docosahexaenoic acid itake (g/d)	0	>0-<0.04	≥0.04	
Participants (n)	2,214	3,391	3,577	
Cases (n)	287	332	405	
	Odds ratio of periodontitis (95% confidence interval)			
Partial adjustment[b]	1.0	0.65 (0.52-0.82)	0.84 (0.66-1.06)	0.002
Multivariable[c]	1.0	0.70 (0.55-0.88)	0.78 (0.61-1.00)	0.009
Dietary model[d]	1.0	0.70 (0.56-0.88)	0.77 (0.61-0.98)	0.007
Diet plus supplement[e]	1.0	0.69 (0.55-0.87)	0.80 (0.62-1.02)	0.009
No supplements	1.0	0.70 (0.55-0.88)	0.76 (0.60-0.97)	0.009
Eicosapentaenoic acid intake (g/d)	0	>0-0.01	≥0.01	
Participants (n)	3,378	2,235	3,569	
Cases (n)	413	225	386	
	Odds ratio of periodontitis (95% confidence interval)			
Partial adjustment[b]	1.0	0.74 (0.58-0.95)	0.88 (0.70-1.11)	0.06
Multivariable[c]	1.0	0.78 (0.61-1.00)	0.85 (0.67-1.08)	0.10
Dietary model[d]	1.0	0.77 (0.61-0.99)	0.84 (0.66-1.07)	0.08
Diet plus supplement[e]	1.0	0.79 (0.64-0.99)	0.85 (0.66-1.10)	0.09
No supplements	1.0	0.79 (0.62-1.01)	0.84 (0.67-1.05)	0.09
Linolenic acid intake (g/d)	<0.91	0.91-1.67	>1.67	
Participants (n)	3,123	3,125	2,934	
Cases (n)	388	363	273	
	Odds ratio of periodontitis (95% confidence interval)			
Partial adjustment[b]	1.0	0.91 (0.69-1.21)	0.68 (0.48-0.95)	0.04
Multivariable[c]	1.0	1.08 (0.81-1.44)	0.86 (0.60-1.23)	0.28
Dietary model[d]	1.0	1.06 (0.79-1.41)	0.79 (0.51-1.22)	0.27
Diet plus supplement	1.0	1.12 (0.85-1.47)	0.84 (0.59-1.21)	0.15
No supplements	1.0	1.12 (0.85-1.48)	0.87 (0.61-1.24)	0.19

[a]Derived from tests of heterogeneity.
[b]Partial adjustment for age, sex, and total energy intake (kcal/d).
[c]Multivariable model: adjusted for age, sex, total energy intake (kcal/d), race/ethnicity, smoking, education, income, physical activity, pregnancy, self-reported health status, diabetes mellitus, body mass index, origin of birth, alcohol, and tertiles of other fatty acid intake.
[d]Adjusted for all multivariable model covariates as well as dietary carbohydrates, saturated fats, monounsaturated fats, and linoleic acid (a common dietary n-6 fatty acid).
[e]Adjusted for all multivariable model covariates.

In additional sensitivity analyses, we found no significant difference in the prevalence of periodontitis between the second and third tertiles of DHA, EPA, or LNA intake ($P=0.39$, $P=0.55$, and $P=0.11$, respectively). When categorized in quintiles, the inverse association of DHA and periodontitis appeared to be similar across Quintiles 2 through 5 (data not shown). Tests of quadratic trend for DHA, EPA, and LNA intake and periodontitis were $P=0.25$, $P=0.05$, and $P=0.17$, respectively. Additional adjustment for additional dietary factors slightly strengthened the observed associations (Table 2), chiefly due to partial negative confounding by carbohydrate intake. Adjustment for the number of teeth lost, linoleic acid (n-6 fatty acid) or regular, chronic aspirin and/or NSAID use did not change these associations.

In post hoc analyses, multivariable associations between tertile of DHA intake and prevalence of severe periodontitis were not significant ($P=0.33$). Finally, increasing periodontitis severity was associated with increased logCRP ($P<0.001$): 0.17±0.06 for moderate periodontitis and 0.26±0.11 for severe periodontitis.

DISCUSSION

Dietary DHA was associated with a lower prevalence of periodontitis in this nationally representative cross-sectional study of adults. This inverse association was not strengthened with higher intake beyond the second tertile nor with the addition of supplemental DHA, suggesting a threshold effect similar to what has been found in studies of fish intake for sudden cardiac death (27), where no further benefit is achieved beyond modest fish intake. In addition, dietary EPA had a more modest inverse association with periodontitis, whereas dietary LNA was not associated with periodontitis.

Both n-3 and n-6 fatty acids have been found to have anti-inflammatory effects through the production of nuclear transcription factors, enzymes, and cytokines in human cells (28). For example, Marion-Letellier and colleagues (28) found that DHA, EPA, GLA, and ALA increased levels of peroxisome proliferator-activated receptor-gamma (PPAR-γ) and reduced production of the pro-inflammatory cytokines interleukin-8 and interleu-

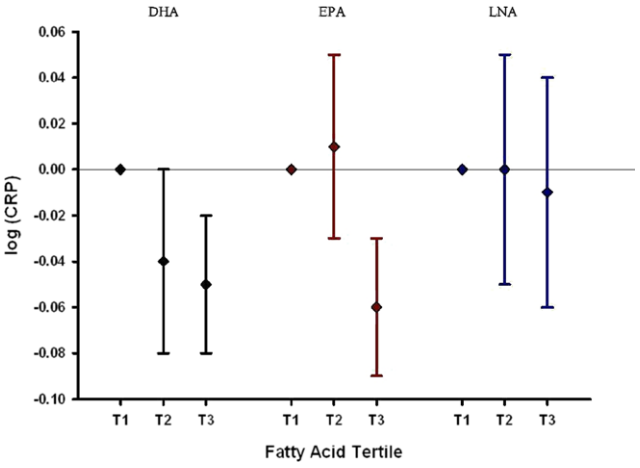

Figure. Multivariable linear association between tertile of polyunsaturated fatty acid intake and log C-reactive protein (CRP) (n=9,183). Multivariable model adjusted for age, sex, total energy intake (kcal/day), race/ethnicity, smoking, education, income, physical activity, pregnancy, self-reported health status, diabetes mellitus, body mass index, location of birth, alcohol, and tertiles of other fatty acid intake. T=tertile. DHA=docosahexaenoic acid. EPA=eicosapentaenoic acid. LNA=linolenic acid (alpha-linolenic acid and gamma-linolenic acid).

kin-6. The strongest anti-inflammatory effects tended to coincide with longer, more desaturated n-3 and n-6 carbon chains, effects that are consistent with our primary analysis. In addition, we found DHA and EPA to be associated with lower CRP in linear secondary analyses.

Furthermore, n-3 fatty acids have been found in animal models of periodontitis to be substrates for neutrophil production of resolvins and protectins, which appear central to the resolution of inflammation (29,30). Other animal studies have suggested n-3 fatty acids may have a protective effect on periodontitis by decreasing the host inflammatory responses to common asaccharolytic microbial pathogens, such as *Porphyromonas gingivalis*. This decreased inflammatory reaction may result in less tissue breakdown, rendering these microbes unable to sustain their protein-derived energy source (6,31).

Our findings expand upon the one human study of PUFAs for the treatment of periodontitis (7) by providing information on DHA intake in a large, generalizable sample of adults. The trial showed a significant decrease in probing depth (change in mean score −0.50) in patients receiving GLA alone and a trend toward decreased probing depth (change in mean score −0.41) in subjects receiving EPA alone. This trend toward reduced periodontitis prevalence with EPA is again consistent with our findings. However, our results also suggest that DHA (doses recommended by the American Heart Association of two servings per week of fatty fish such as salmon, mackerel, herring, or albacore tuna would be sufficient) may be as or more potent in influencing periodontitis.

We did not observe a statistically significant decrease in the prevalence of periodontitis with higher LNA (primarily ALA with minimal GLA) intake. However, this lack of association may be due to a relatively low median intake of LNA (1.27 g/day) compared to the GLA dose (3 g/day) found to be protective for periodontitis in the previously mentioned trial (7).

Limitations of our study include the cross-sectional design, which permits the detection of associations but not a temporal relationship nor causation. It is also possible that tooth loss due to periodontitis could have affected diets. However, we excluded edentulous subjects and found no change in associations when adjusting the analyses for tooth loss. Participants of the NHANES who did not have a periodontal exam reported older age, higher income, greater alcohol consumption, and less tobacco use. Nonetheless, NHANES is likely the most representative study of periodontitis currently conducted. Individuals' dietary intakes vary from day to day, so a 24-hour dietary recall does not necessarily provide an ideal estimate of an individual's long-term average or "usual" daily intake. However, dietary recalls tend to provide highly reliable estimates of recent intake, and the mean of a group's recent intake yields a reasonable estimate of the mean of the group's usual nutrient intake if the dietary recalls are collected on all days of the week and seasons of the year, as is the case with NHANES. As a result, the mean nutrient intakes reported here for groups (ie, tertiles) approximate their mean usual nutrient intakes. Also, NHANES provides no quantitative assessment of sugar or other refined carbohydrates, which may bias our results toward the null given the negative confounding observed with total carbohydrate intake in the model.

Lastly, ALA and GLA are combined into one variable, linolenic acid, which could represent opposing effects on chronic inflammation since ALA is an n-3 fatty acid, whereas GLA is an n-6 fatty acid (25). However, the great majority of dietary LNA intake is from ALA (32,33). Moreover, as noted above, GLA has been found to have anti-inflammatory effects in vitro (28) and a protective effect on periodontitis in one randomized controlled trial (7). Moreover, we found no effect modification or confounding by a much more common dietary source of n-6, linoleic acid.

Strengths of our study include the large and representative sample of civilian, noninstitutionalized US adults. Also, detailed periodontal assessments were conducted with a number of quality control procedures, including calibration of dentists before and triannually throughout the survey and periodic replications of dental exams by dental experts to monitor consistancy of examinations. Finally, detailed information on potentially confounding covariates was available in a systematic manner.

CONCLUSIONS

We found that n-3 fatty acid intake, particularly DHA and EPA, are inversely associated with periodontitis in the US population. To date, the treatment of periodontitis has primarily involved mechanical cleaning and local antibiotic application. Thus, a dietary therapy, if effective, might be a less expensive and safer method for the prevention and treatment of periodontitis. Given the evidence indicating a role for n-3 fatty acids in other chronic inflammatory conditions (27,34-38), it is possible that treating periodontitis with n-3 fatty acids could have the added benefit of preventing other chronic diseases associated with inflammation, including ischemic cerebrovas-

cular disease (39), as well. Both of these questions warrant further investigation in prospective cohort and randomized clinical trials.

STATEMENT OF POTENTIAL CONFLICT OF INTEREST: Dr Mukamal is the principal investigator on an ongoing study funded by Harvard Medical School for which Beth Israel Deaconess Medical Center received a donation of DHA and placebo capsules from Martek Corporation. Drs Phillips, Davis, and Naqvi are co-investigators on that trial. Martek provided no other resources or funds and has no role in the conduct or analysis of that study.

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