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Perfluoroalkyl substances and fish consumption

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ABSTRACT

Background: Perfluoroalkyl substances (PFAS) are an emerging class of contaminants. Certain PFAS are regulated or voluntarily limited due to concern about environmental persistence and adverse health effects, including thyroid disease and dyslipidemia. The major source of PFAS exposure in the general population is thought to be consumption of seafood.

Objectives: In this analysis we examine PFAS levels and their determinants, as well as associations between PFAS levels and self-reported fish and shellfish consumption, using a representative sample of the U.S. population.

Methods: Data on PFAS levels and self-reported fish consumption over the past 30 days were collected from the 2007–2008, 2009–2010, 2011–2012, and 2013–2014 cycles of the National Health and Nutrition Examination Survey. Twelve different PFAS were measured in serum samples from participants. Ordinary least squares regression models were used to identify factors (demographic characteristics and fish consumption habits) associated with serum PFAS concentrations. Additional models were further adjusted for other potential exposures including military service and consumption of ready-to-eat and fast foods.

Results: Seven PFAS were detected in at least 30% of participants and were examined in subsequent analyses (PFDA, PFOA, PFOS, PFHxS, MPAH, PFNA, PFUA). The PFAS with the highest concentrations were PFOS, followed by PFOA, PFHxS and PFNA (medians of 8.3, 2.7, 1.5 and 1.0 ng/mL). Fish consumption was generally low, with a median of 1.2 fish meals and 0.14 shellfish meals, reported over the past 30 days. After adjusting for demographic characteristics, total fish consumption was associated with reduced MPAH, and with elevated PFDE, PFNA and PFuDA. Shellfish consumption was associated with elevations of all PFAS examined except MPAH. Certain specific fish and shellfish types were also associated with specific PFAS. Adjustment for additional exposure variables resulted in little to no change in effect estimates for seafood variables.

Conclusions: PFAS are emerging contaminants with widespread exposure, persistence, and potential for adverse health effects. In the general population, fish and shellfish consumption are associated with PFAS levels, which may indicate an avenue for education and outreach.

1. Introduction

Perfluoroalkyl substances (PFAS) are emerging chemical pollutants which have been used for a wide range of consumer products due to their non-stick/non-stain properties (ATSDR, 2009; Steenland et al., 2010). The primary non-occupational route of exposure to PFAS is through the diet, namely seafood from contaminated water bodies. PFAS levels in seafood vary by location, age and type of seafood, and other factors (EPA, 2009b). Human biomonitoring studies have demonstrated that exposure to PFAS is widespread (e.g. (CDC, 2015)) with the most common being perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and perfluorohexane sulfonate (PFHxS). However, in the United States (U.S.), PFOS and other PFAS with six or more carbon atoms were voluntarily phased out of production (reviewed in Buck et al. (2011)) and the U.S. Environmental Protection Agency (EPA) PFOA Stewardship Program was designed to reduce production and use of PFOA as well (EPA, 2009a). Despite these restrictions, PFAS continue to contaminate environmental media due to their persistence in the environment and in humans (Buck et al., 2011; Wang et al., 2013). Human exposure

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to PFAS is of concern because of the potential for adverse health effects observed in both animal (toxicology) and human (epidemiology) studies. For example, PFOA has been reported to be associated with thyroid disease (Melzer et al., 2010) and higher levels of cholesterol (Eriksen et al., 2013; Steenland et al., 2009) and uric acid (Gleason et al., 2015) in multiple human studies, and there is some evidence for an association between PFOA and elevation of liver enzymes (Gleason et al., 2015), and testicular and renal cancers (Benbrahim-Tallaa et al., 2014). While the evidence for health effects is not conclusive based on human epidemiology studies, investigation of exposure sources is still warranted.

Both in the U.S. and worldwide, fish are an increasingly important part of the human diet and offer many important nutritional benefits. Over the past few decades, fish consumption has increased by about 30% in the United States (Loke et al., 2012). Fish consumption may also be associated with health benefits; for example, epidemiologic studies suggest that increased fish consumption is associated with reduced risk of cardiovascular disease and coronary death, in part due to selenium and omega-three fatty acid content (He et al., 2004; Whelton et al., 2004). However, the presence of environmental contaminants such as PFAS in fish necessitates that risks and benefits both be considered when advising individuals about fish consumption (reviewed in Domingo (2016)). In the U.S. specifically, national fish tissue monitoring data have demonstrated widespread occurrence of many PFAS, with PFOS (median levels of 10.7 ng/g) being the most predominant, in the Great Lakes and in urban rivers across the country (Stahl et al., 2014). Although levels of certain PFAS are declining over time in the U.S. population, possibly reflecting limitation or elimination of certain exposure sources, levels of other PFAS are steady or increasing over time (CDC, 2015), pointing to the need to consider fish as an important ongoing source of exposure.

Associations between consumption of seafood and body burdens of PFAS have been observed in several studies across different countries. A cross-sectional study in Japan found significant associations between fish consumption (both raw and cooked) with increased PFOS serum concentrations (Yamaguchi et al., 2013). Similar observations were confirmed in studies conducted in Norway, where fish consumption is common in their traditional diets (Haug et al., 2010) (Hansen et al., 2016; Rylander et al., 2009, 2010). A study of fresh water anglers in Germany established a dose-response relationship between fish consumption and PFOS body burden (Holzer et al., 2011), and fresh water fish consumption was also found to be a significant contributor to PFAS body burden among anglers from a French metropolitan population (Denys et al., 2014). In the U.S., Egeghy and Lorber used a pharmacokinetic model to identify sources of PFOS exposure, and found that for the adult population the major source of exposure was indeed dietary; however, they noted the lack of occurrence data for the U.S. and indeed relied upon Canadian data for this purpose (Egeghy and Lorber, 2011). These concerns may be amplified for certain populations at increased risk for adverse health effects of PFAS exposure due to demographic characteristics or greater exposure via high fish consumption, including: pregnant women and women who are breast feeding, sport-anglers, subsistence anglers, and tribal communities.

PFAS concentrations and demographic characteristics in the U.S. general population have previously been studied using National Health and Nutrition survey (NHANES) data (Calafat et al., 2007; Kato et al., 2011). However, associations between specific seafood consumption and PFAS levels among the U.S. general population have not been explored and established. Due to their persistence in the environment and in the body, as well as the potential for adverse health effects due to exposure, it is important to monitor the levels of PFAS in the general population and in potentially vulnerable and susceptible subgroups. In this analysis we examine PFAS levels and associations with self-reported seafood consumption among a representative sample of the U.S. population.

2. Materials and methods

2.1. Study population

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional survey, designed to provide a representative sample of the US non-institutionalized civilian population (CDC, 2016). PFAS are measured in a random one-third subsample of NHANES participants 12 years of age and older. For this study, the four most recent NHANES cycles with PFAS information were combined: 2007/2008, 2009/2010, 2011/2012, and 2013/2014. Laboratory methods are described in detail in the NHANES documentation (CDC, 2014b); in brief, PFAS were measured in serum using solid phase extraction coupled to high performance liquid chromatography-turbo ion spray ionization-tandem mass spectrometry. As stated in the laboratory documentation, values below the limit of detection (LOD) are replaced with the value (LOD/√2). The list of PFAS analyzed is given in Table 1; PFAS which were not detected in at least 30% of samples (shaded in grey in Table 1) were not carried through further analyses. Due to inconsistency between PFAS acronyms used by NHANES and those generally accepted by the scientific community (Buck et al., 2011), chemical names, formulas, and acronyms are provided in Supplementary Table 1. Fish and shellfish consumption over the past 30 days was ascertained during the dietary interview (CDC, 2014c). Participants aged 12 years and older answered questions for themselves, and interviews were conducted in the participant's choice of either English or Spanish.

2.2. Statistical analysis

All data analysis was performed using SAS/STAT software version 9.4.[1] Ordinary least squares regression models were used to identify factors associated with PFAS serum levels; these factors included demographic characteristics as well as fish consumption. Demographic characteristics included: sex, age (years), body mass index (BMI), and race/ethnicity (Mexican American, Other Hispanic, Non-Hispanic white, Non-Hispanic Black, Other/multiracial). Fish and shellfish consumption were evaluated using self-reported meals over the past 30 days. This included total number of fish and shellfish meals consumed, as well as number of meals broken out by specific type of shellfish (clams, crabs, crayfish, lobsters, mussels, oysters, scallops, shrimp, other shellfish) and fish (breaded fish, tuna, bass, catfish, cod, flatfish, haddock, mackerel, perch, pike, pollock, porgy, salmon, sardines, sea bass, shark, swordfish, trout, walleye, and other fish). Additional models included family income and other suspected PFAS exposure sources, including history of military service and foreign-born versus U.S. born. The additional models included variables designed to capture potential non-seafood sources of PFAS exposure. PFAS have been used in firefighting substances, with subsequent detection at military (hence the inclusion of military service), firefighting and aviation sites (e.g., (Bhavsar et al., 2016; Hu et al., 2016)). The inclusion of country of birth is a proxy for differential exposure due to different sources and levels in non-U.S. countries.

Associations of demographic factors with PFAS levels and fish consumption were evaluated using Kruskal-Wallis tests. Each demographic factor evaluated was associated with at least one fish consumption parameter and one PFAS, and thus were included in multiple linear regression models as potential confounders. Due to non-normality of the data, PFAS levels were natural logarithm transformed. Effect estimates were exponentiated for easier interpretation of results, and represent proportional changes in the

[1] SAS/STAT software, Version 9.3 of the SAS System for Windows. Copyright © 2013 Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

Table 1
Distribution of PFAS measured in serum, given in μg/L. Shading indicates analytes detected in fewer than 30% of samples (n=7891).[a].

PFAS	Percent (SE) above the LOD	Median (SE)	25th (SE), 75th (SE) percentiles	95th percentile
2-(N-ethyl-PFOSA) acetate (EPAH)	5.1 (0.4)	--	--	--
Perfluorodecanoic acid (PFDE)	82.5 (1.1)	0.2 (0.01)	0.1 (0.01), 0.4 (0.02)	0.8 (0.03)
Perfluorooctanoic acid (PFOA)	99.8 (0.1)	2.7 (0.06)	1.8 (0.04), 4.3 (0.10)	7.5 (0.18)
Perfluorooctane sulfonate (PFOS)	99.8 (0.1)	8.3 (0.22)	4.7 (0.13), 13.9 (0.38)	30.6 (1.89)
Perfluorohexane sulfonic acid (PFHxS)	99.2 (0.1)	1.5 (0.03)	0.9 (0.03), 2.8 (0.08)	6.8 (0.46)
2-(N-methyl-PFOSA) acetate (MPAH)	63.1 (1.5)	0.2 (0.02)	0.1 (0.01), 0.3 (0.02)	1.0 (0.03)
Perfluorobutane sulfonic acid (PFBS)	0.9 (0.2)	--	--	--
Perfluoroheptanoic acid (PFHP)	15.1 (0.8)	--	--	--
Perfluorononanoic acid (PFNA)	99.4 (0.1)	1.0 (0.02)	0.7 (0.02), 1.5 (0.04)	2.9 (0.19)
Perfluorooctane sulfonamide (PFSA)	0.4 (0.1)	--	--	--
Perfluoroundecanoic acid (PFuDA)	49.6 (1.6)	0.1 (0.01)	0.1 (0.01), 0.2 (0.02)	0.6 (0.03)
Perfluorododecanoic acid (PFeDA)	7.4 (1.0)	--	--	--

[a] The LOD for each PFAS is as follows: PFOA – 0.10 for all cycles; PFOS – 0.20 for 2007–2012, 0.10 for 2013–2014; PFHxS – 0.10 for all cycles; EPAH – 0.20 for 2007–2008, 0.20 for 2009–2012, not measured in 2013–2014; MPAH – 0.20 for 2007–2008, 0.10 for 2009–2010 and 2013–2014, 0.09 for 2011–2012; PFDE – 0.20 for 2007–2008, 0.10 for 2009–2014; PFBS – 0.10 for all cycles; PFHP – 0.40 for 2007–2008, 0.10 for 2009–2014; PFNA – 0.08 for 2007–2012, not measured in 2013–2014; PFUA – 0.20 in 2007–2008, 0.10 in 2009–2014; PFDO – 0.20 for 2007–2008, 0.10 for 2009–2014. In 2013–2914, PFOA and PFOS were calculated as the sum of linear and branched isomers (each had the same LOD of 0.10)

geometric mean of PFAS concentrations in the exposure group compared to the reference group. For continuous fish or shellfish consumption, the estimates can be interpreted as a ratio of geometric mean PFAS for a 1 meal increase in fish or shellfish consumption (i.e. 2 vs 1 or 1 vs 0). All statistical analyses were adjusted for survey design and weighing variables.

3. Results

Across the 2007–2014 NHANES cycles, there were 7891 individuals aged 12 years or older with both seafood consumption information and with PFAS measurements. Participants were evenly distributed across NHANES cycles (24.8% in 2007–2008, 25.2% in

2009–2010, 24.2% in 2011–2012, 25.8% in 2013–2014), and by sex (48.6% male, 51.4% female). The majority of participants were between 18 and 59 years of age (68.7%), while 9.5% were aged 12–17 years, and 21.7% were ≥60 years of age. The majority of participants were non-Hispanic white (67.1%), followed by non-Hispanic Black (11.1%) and Mexican-American (9.3%). Other or multiracial race/ethnicity was reported by 6.7% of participants, and other Hispanic by 5.8%. Due to the small number of participants in non-white race/ethnicity categories, race/ethnicity was re-categorized as non-Hispanic white vs. other. Nearly one-third of participants fell in the overweight (31.9%) and in the obese (33.3%) categories of BMI, while 31.3% were in the normal weight range; 82 participants were missing BMI measurements.

Seven PFAS were detected in at least 30% of samples and were retained in subsequent analyses. The distributions of these PFAS are shown in Table 1. All PFAS significantly correlated with each other; unweighted Spearman correlation coefficients ranging from 0.16 (MPAH with PFUA) to 0.76 (PFDE with PFNA). The correlation between PFOS and PFOA (the two PFAS showing highest average concentrations) was 0.70.

Fish consumption was generally low, with a median of 1.2 fish meals (mean=3.0 [SE=0.08]) and a median of 0.14 shellfish meals (mean=1.8 [SE=0.08]) reported over the past 30 days. The most commonly reported types of seafood consumed included shrimp, tuna, salmon, 'other' fish and crab. Table 2 shows consumption information for both all fish and shellfish meals, as well as for specific types; the median and 25th and 75th percentile for number of meals is provided where there were at least 5% of participants reporting consumption over the past 30 days. Due to the low reported consumption for many types of fish and shellfish, only those types reported by at least 5% of participants were included in further analyses (clams, crabs, lobster, oysters, scallops, shrimp, tuna, catfish, cod, salmon). Breaded fish products and fish/shellfish of unknown or other type were not included in regression models due to the lack of specificity.

Associations between PFAS levels (after natural logarithm transformation) and demographic characteristics, seafood consumption and other exposure factors were examined individually using ordinary least squares regression models (data not shown). All PFAS levels decreased over time from 2007/2008 to 2013/2014. In general, PFAS levels were higher with decreasing BMI and with increasing age. Males had higher levels of all PFAS, while associations with race/ethnicity varied by specific PFAS. For example, non-Hispanic whites had higher levels of PFOA, PFHxS, and MPAH; while, non-Hispanic whites had lower levels of PFDE and PFuDA. Fish and shellfish consumption were somewhat higher in more recent years, although the increase was only significant for 2009/2010. For fish, consumption increased with older age, while the reverse was true for shellfish. There was no difference in consumption by sex for fish, but men had higher consumption of shellfish. There were no differences by race/ethnicity, but higher BMI was associated with lower fish consumption.

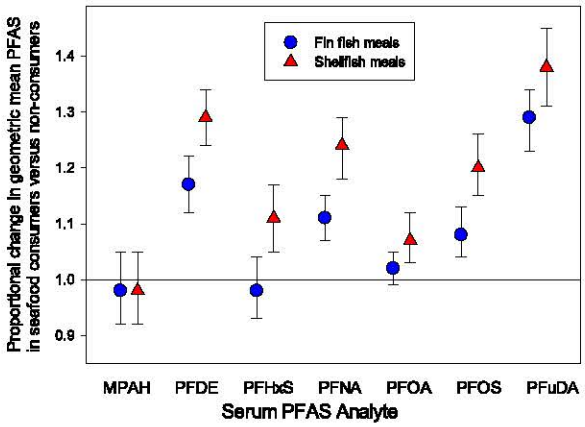

Fig. 1. Associations between seafood consumption in the last 30 days and PFAS concentrations, after adjusting for age, BMI, sex, race/ethnicity and survey cycle.

Each of the demographic factors examined was included as covariates in the final adjusted regression models to estimate the association between fish and shellfish consumption, and PFAS levels in serum; bivariate associations between demographic characteristics and PFAS remained unchanged. In the models including overall consumption, total number of fish and shellfish meals in the past 30 days was associated with each PFAS; fish meals were associated with higher PFDE, PFNA and PFuDA, and with lower MPAH. Shellfish meals were associated with higher levels of each PFAS except MPAH; these results are summarized in Fig. 1. Models treating fish and shellfish consumption as binary variables yielded largely similar results, with the exception that any fish consumption was associated with higher

Table 2
Distribution of fish and shellfish consumption over the past 30 days, for those who reported any consumption (n=6055).

Number of meals consumed over the past 30 days of:	Median (SE)	25th (SE), 75th (SE) percentiles	95th percentile (SE)
All fish and shellfish	3.6 (0.09)	1.5 (0.02), 7.1 (0.16)	17.2 (0.55)
All shellfish	1.7 (0.02)	1.0 (0.02), 3.5 (0.12)	9.6 (0.47)
All fish	2.5 (0.07)	1.1 (0.02), 4.9 (0.09)	11.6 (0.34)

Number of meals consumed over the past 30 days of:	Percent consuming any meals (SE)	Median (SE)	25th (SE), 75th (SE) percentiles
Clams	6.6 (0.5)	1.0 (0.07)	1.0 (0.07), 1.7 (0.07)
Crabs	12.2 (0.8)	1.0 (0.05)	1.0 (0.05), 1.6 (0.05)
Lobster	5.6 (0.4)	1.0 (0.08)	1.0 (0.08), 1.0 (0.08)
Oysters	5.4 (0.4)	1.0 (0.08)	1.0 (0.08), 1.4 (0.08)
Scallops	6.8 (0.5)	1.0 (0.06)	1.0 (0.06), 1.4 (0.06)
Shrimp	45.0 (0.9)	1.0 (0.02)	1.2 (0.02), 2.3 (0.06)
Breaded fish products	8.5 (0.4)	1.0 (0.04)	1.1 (0.04), 1.9 (0.04)
Tuna	30.3 (0.8)	1.6 (0.02)	1.0 (0.02), 2.8 (0.08)
Catfish	9.2 (1.0)	1.0 (0.04)	1.0 (0.04), 1.9 (0.04)
Cod	9.0 (0.6)	1.0 (0.05)	1.0 (0.05), 1.8 (0.05)
Salmon	25.7 (1.1)	1.4 (0.03)	1.0 (0.03), 2.6 (0.07)
Other fish	13.7 (0.6)	1.3 (0.03)	1.0 (0.03), 2.4 (0.08)
Fish, unknown type	5.6 (0.4)	1.0 (0.07)	1.0 (0.07), 2.1 (0.24)

There were n=1835 participants who did not report any fish or shellfish consumption in the past 30 days, who are omitted from this table. Fish and shellfish reported by less than 5% of participants included: crayfish, mussels, other shellfish, unknown shellfish, bass, flatfish, haddock, mackerel, perch, pike, Pollock, porgy, sardines, sea bass, shark, swordfish, trout, and walleye.

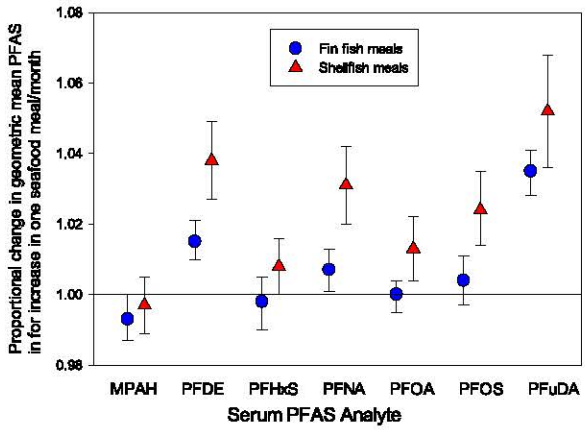

Fig. 2. Associations between any seafood consumption in the last 30 days and PFAS concentrations, after adjusting for age, BMI, sex, race/ethnicity and survey cycle.

PFOS in this set of models; these results are summarized in Fig. 2. Supplementary Table 2 shows the regression model results for overall fish and shellfish consumption.

Two sets of models are presented in Table 3; results are shown for models including individual types of fish and shellfish as either a continuous (number of meals) or binary (any consumption) over the past 30 days. The R^2 values for the models were similar when looking at a specific PFAS, and were generally in the range of 0.2–0.3. In general, more positive associations with PFAS were noted for binary than continuous predictors of shellfish. Any crab consumption was associated with increased levels of all PFAS except MPAH, while the number of crab meals was associated with increased PFDE, PFNA and PFuDA. Any clam consumption was associated with increased PFNA and PFuDA, but number of clam meals was not associated with any PFAS. Any consumption of oysters, scallops or shrimp was associated with increased PFDE, PFOS, PFNA and PFuDA; in addition, any scallop consumption was associated with increased PFOA, and any shrimp meals with increased PFHxS; no associations were seen for lobsters. When looking at number of meals for specific shellfish types, scallops and shrimp were associated with elevation in PFDE, PFOA, PFOS, PFNA, and PFuDA; no associations were seen for lobsters or oysters. Among specific fish types, tuna and salmon were associated with increased PFuDA, and catfish with increased PFDE, PFOS, MPAH, PFNA, and PFuDA when modeled as either binary or continuous variables. In contrast, cod was associated with increased PFuDA as a binary variable, but decreased PFOS and PFHxS.

A final set of regression models included overall fish and shellfish consumption, demographics and additional PFAS exposure routes (Supplementary Tables 3a, 3b). As shown in Supplementary Table 3a, these additional exposures were significantly associated with several PFAS, but adjustment did not substantially change the effect estimates for fish and shellfish consumption, with the exception of MPAH and PFNA, which did not remain significantly associated with total fish meals in the additionally adjusted models. However, when examining the effect of family income, there was evidence of potential effect modification. Consequently, product terms were introduced to account for potential interaction between family income and fish or shellfish consumption (Supplementary Table 3b). The interaction term was significant for PFDE, PFNA and PFUA, showing a stronger association between these PFAS and shellfish consumption when looking at higher income households. For PFOA, a similar effect was observed with fish consumption (stronger effect in higher income households).

4. Discussion

The primary source of PFAS for the general population is thought to be seafood consumption, but there have been few studies looking at PFAS levels in relation to diet, including specific items such as red meat, animal fats, and snacks (Halldorsson et al., 2008). Previous studies have also identified non-dietary pathways of PFAS exposure, including contaminated drinking water, household dust and outdoor and indoor air (Fromme et al., 2009). Most studies investigating this relationship have been based in Europe and may not be reflective of what is happening in the U.S. due to differing consumption habits, seafood sources and exposures routes. Further, many epidemiology

Table 3
Associations between PFAS levels in serum (after natural logarithm transformation) with fish and shellfish consumption over the past 30 days, adjusting for demographic covariates (n=7801).[a]

Parameter	PFDE	PFOA	PFOS	PFHxS	MPAH	PFNA	PFuDA
Including number of fish and shellfish meals by type in past 30 days, as continuous variables							
Clams	0.99 (0.95, 1.03)	1.01 (0.98, 1.03)	0.98 (0.94, 1.02)	0.98 (0.95, 1.02)	1.02 (0.97, 1.06)	1.01 (0.97, 1.05)	1.03 (0.98, 1.08)
Crabs	**1.05 (1.01, 1.09)***	1.03 (0.99, 1.06)	1.03 (0.98, 1.08)	1.02 (0.97, 1.07)	1.00 (0.97, 1.04)	**1.05 (1.00, 1.10)***	**1.09 (1.03, 1.15)***
Lobsters	1.02 (0.96, 1.10)	0.99 (0.92, 1.06)	0.95 (0.89, 1.02)	0.96 (0.89, 1.03)	0.94 (0.88, 1.01)	0.98 (0.92, 1.05)	1.02 (0.95, 1.10)
Oysters	1.03 (0.96, 1.10)	0.98 (0.93, 1.03)	1.03 (0.98, 1.09)	1.02 (0.99, 1.05)	1.00 (0.96, 1.04)	1.04 (0.98, 1.11)	1.02 (0.93, 1.11)
Scallops	**1.11 (1.07, 1.15)***	**1.07 (1.03, 1.13)***	**1.07 (1.03, 1.11)***	1.06 (1.00, 1.11)	0.97 (0.92, 1.02)	**1.09 (1.04, 1.14)***	**1.14 (1.09, 1.19)***
Shrimp	**1.05 (1.04, 1.07)***	**1.02 (1.00, 1.03)***	**1.04 (1.03, 1.06)***	1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	**1.04 (1.02, 1.05)***	**1.07 (1.05, 1.09)***
Tuna	1.01 (1.00, 1.02)	1.01 (1.00, 1.01)	1.01 (1.00, 1.01)	1.01 (1.00, 1.02)	1.00 (0.99, 1.01)	1.00 (1.00, 1.01)	**1.02 (1.01, 1.03)***
Catfish	**1.11 (1.06, 1.15)***	0.97 (0.94, 1.00)	**1.09 (1.04, 1.14)***	1.02 (0.97, 1.06)	**1.05 (1.00, 1.10)***	**1.06 (1.02, 1.10)***	**1.12 (1.07, 1.17)***
Cod	0.98 (0.96, 1.01)	0.99 (0.97, 1.01)	**0.97 (0.93, 1.00)***	**0.96 (0.93, 0.99)***	1.00 (0.97, 1.04)	0.98 (0.95, 1.00)	1.02 (1.00, 1.05)
Salmon	1.01 (0.99, 1.02)	1.00 (0.98, 1.01)	0.99 (0.97, 1.01)	0.98 (0.97, 1.00)	**0.98 (0.96, 1.00)***	1.00 (0.99, 1.02)	**1.05 (1.03, 1.06)***
Including any fish and shellfish meals by type in past 30 days, as binary variables							
Clams	1.07 (0.98, 1.17)	1.06 (0.99, 1.13)	1.01 (0.91, 1.12)	0.98 (0.88, 1.08)	1.13 (1.00, 1.28)	**1.12 (1.02, 1.23)***	**1.23 (1.11, 1.36)***
Crabs	**1.16 (1.08, 1.24)***	**1.11 (1.04, 1.19)***	**1.11 (1.02, 1.21)***	**1.10 (1.01, 1.20)***	1.05 (0.96, 1.14)	**1.17 (1.07, 1.27)***	**1.24 (1.12, 1.37)***
Lobsters	1.03 (0.94, 1.13)	0.97 (0.87, 1.07)	0.94 (0.85, 1.03)	0.94 (0.84, 1.04)	0.92 (0.83, 1.01)	0.96 (0.87, 1.06)	1.03 (0.92, 1.15)
Oysters	**1.21 (1.08, 1.35)***	1.01 (0.94, 1.08)	**1.16 (1.03, 1.30)***	1.08 (0.96, 1.21)	0.96 (0.85, 1.09)	**1.20 (1.08, 1.32)***	**1.23 (1.08, 1.41)***
Scallops	**1.19 (1.10, 1.29)***	**1.14 (1.04, 1.24)***	**1.10 (1.01, 1.20)***	1.10 (1.00, 1.21)	**0.89 (0.80, 0.99)**	**1.14 (1.05, 1.24)***	**1.31 (1.18, 1.44)***
Shrimp	**1.20 (1.15, 1.26)***	1.03 (1.00, 1.07)	**1.16 (1.11, 1.21)***	**1.06 (1.00, 1.11)***	0.97 (0.92, 1.02)	**1.15 (1.10, 1.20)***	**1.21 (1.16, 1.27)***
Tuna	1.00 (0.95, 1.04)	1.02 (0.98, 1.06)	0.99 (0.95, 1.04)	1.02 (0.97, 1.08)	0.95 (0.88, 1.01)	1.01 (0.97, 1.05)	**1.07 (1.02, 1.12)***
Catfish	**1.28 (1.15, 1.44)***	0.96 (0.90, 1.03)	**1.25 (1.13, 1.39)***	1.04 (0.94, 1.14)	**1.16 (1.06, 1.27)***	**1.16 (1.06, 1.27)***	**1.29 (1.15, 1.44)***
Cod	0.96 (0.89, 1.02)	0.97 (0.92, 1.03)	0.91 (0.81, 1.01)	**0.91 (0.84, 0.99)***	1.00 (0.90, 1.10)	0.96 (0.88, 1.04)	**1.07 (1.00, 1.15)***
Salmon	1.02 (0.98, 1.08)	0.99 (0.93, 1.04)	0.97 (0.90, 1.05)	0.94 (0.87, 1.02)	0.96 (0.89, 1.03)	1.00 (0.93, 1.07)	**1.12 (1.05, 1.18)***

[a] Each model included all fish and shellfish in table, age, BMI, sex, race/ethnicity and survey cycle. Estimates represent the proportional change in the geometric mean of serum PFAS for each 1 meal increase in fish/shellfish consumption for continuous measures of fish and shellfish, and the proportional change in the geometric mean of serum PFAS for fish consumers compared to non-consumers for binary fish and shellfish variables, adjusted for all other variables in the model.

* Bolded text indicates association is significant ($p < 0.05$).

studies focus on PFOA and PFOS, but other PFAS compounds (including shorter chain and replacement PFAS) may be of increasing importance due to changes in industrial usage patterns. In this NHANES study population, the highest PFAS concentrations were seen for PFOS followed by PFOA, PFNA and PFHxS; concentrations of the other PFAS studied were considerably lower and several were not detected in the majority of serum samples. We observed several significant associations between fish and shellfish consumption and serum PFAS levels in a sample of the general U.S. population after adjusting for demographic characteristics and other exposures. In general, consumption of both fish and shellfish were associated with increased levels of several PFAS, although associations varied by each PFAS and by specific types of fish and shellfish. We also observed that associations between PFAS and fish or shellfish consumption, were sometimes modified by income such that stronger associations were observed in higher income households. Similar findings have been observed previously (Nelson et al., 2012; Tyrrell et al., 2013), and are thought to be due to differential food purchasing and consumption patterns, as well as differences in other exposure sources (e.g., waterproofed fabrics) between individuals with higher or lower income levels.

Similar positive associations between shellfish and PFAS have been described in the literature. For example, a Norwegian study estimated that seafood may account for up to 93% of daily intake of certain PFAS (Haug et al., 2010). In the present analysis, we observed that shellfish were fairly consistently associated with increased concentrations of several PFAS; associations were also noted for fin fish, but these were generally weaker than shellfish effect estimates, with the notable exception of catfish meals. These findings agree with other studies that found a positive association between serum PFAS and fish consumption (Denys et al., 2014; Hansen et al., 2016; Haug et al., 2010; Holzer et al., 2011; Rylander et al., 2009, 2010; Yamaguchi et al., 2013). A cross-sectional study that examined the dietary patterns and plasma concentrations of PFOS among Norwegian women found that shellfish intake was particularly positively associated with PFOA (Rylander, 2010). Another Norwegian study found that fish liver and shrimps had a stronger influence on the increase in serum concentrations of PFAS than lean fish, even though all these food items were significantly associated with serum PFAS concentrations (Haug, 2010). Nevertheless, the majority of the literature observed a positive association of finfish or seafood (including finfish and shellfish) intake and PFAS, which varied by seafood type, including raw fish, freshwater fish, and fatty fish such as salmon, mackerel, wolfish, and herring (Yamaguchi et al., 2013; Denys et al., 2014; Holzer et al., 2011; Rylander et al., 2009, 2010). Literature on fish consumption and PFAS is more abundant in Europe than in the U.S.; differing contamination levels among fish and shellfish species might partially explain the variations across studies. Variability in PFAS levels in fish and shellfish may also occur depending on whether the source is wild or farmed; there is some literature to suggest differences in PFAS levels based on source (e.g., (Koponen et al., 2015) which found higher levels in wild versus farm-raised fish), but also reports of measureable PFAS levels in fishmeal and fish feed (Suominen et al., 2011). Further differences in observed PFAS levels in humans, could be due to varying fish consumption patterns and other sources of exposure may also differ between populations.

Human biomonitoring studies have shown that while levels of PFOS and PFOA may be stable or decreasing in recent years, levels of other PFAS are increasing (e.g., a Swedish study finding increased PFBS, PFHxS, PFNA and PFDA from 1996 to 2010 (Glynn et al., 2012); previous NHANES study finding increased PFNA and PFHxS (Kato et al., 2011)). Similarly, we observed a decrease in PFAS concentration when comparing more recent waves of NHANES to the 2007/2008 wave, with the greatest decreases seen for PFOS and PFOA (see Supplementary Table 4). This could be due in part to the phase-out of PFOS and PFOA. Though not the primary focus of this analysis, we did observe several associations between demographic characteristics and other exposure sources with PFAS levels. These findings were consistent with previously published analyses, including higher levels with increasing age, higher levels among males compared to females, BMI, and differences by race/ethnicity. Males were found to have higher levels of all PFAS, which was in line with other studies (Fromme et al., 2007; Harada et al., 2004; Kato et al., 2011; Olsen et al., 2004; Toms et al., 2009; Yamaguchi et al., 2013), suggesting the possibility of sex-related differences in exposure or elimination. Factors contributing to sex-specific differences include the effects of pregnancy, menstruation and breastfeeding (Haug et al., 2010; Monroy et al., 2008; Rylander et al., 2009; Yamaguchi et al., 2013). Positive association of age and PFAS levels were observed in earlier studies from different countries (Fromme et al., 2007; Ingelido et al., 2010), but not necessarily in US studies (Calafat et al., 2007; Kato et al., 2011; Olsen et al., 2004, 2003).

Limitations of this analysis included the use of 30-d dietary seafood intake, which may be less predictive than long term seafood consumption for PFAS, due to the long half-life of these contaminants (estimated to range from ~3 to 9 years for humans (EPA, 2009c)). Certain exposure media (including water, house dust and air) were not included in NHANES datasets and therefore not evaluated in this analysis. Strengths include the use of a multiple years of data from a large and nationally representative sample, consideration of multiple potential confounders, and examination of both overall fish and shellfish consumption as well as specific types commonly consumed by study participants.

In summary, we found that even though overall fish consumption levels were low among NHANES participants, fish and shellfish intake were both associated with elevated levels of multiple PFAS, with differences by specific type of fish or shellfish. Given the widespread potential for exposure to PFAS and concern over potential adverse health effects, it is important to continue to monitor PFAS levels in relation to dietary routes of exposure, which may indicate an avenue for education and outreach.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.envres.2016.12.032.

References

ATSDR, 2009. Draft Toxicological Profile for Perfluoroalkyls. U.S. Department of Health and Human Services. Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, GA. Available at: (http://www.atsdr.cdc.gov/toxprofiles/tp200.pdf).

Benbrahim-Tallaa, L., et al., 2014. Carcinogenicity of perfluorooctanoic acid, tetrafluoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone. Lancet Oncol. 15, 924–925.

Bhavsar, S.P., et al., 2016. High levels, partitioning and fish consumption based water guidelines of perfluoroalkyl acids downstream of a former firefighting training facility in Canada. Environ. Int. 94, 415–423.

Buck, R.C., et al., 2011. Perfluoroalkyl and polyfluoroalkyl substances in the environment: terminology, classification, and origins. Integr. Environ. Assess. Manag. 7, 513–541.

Calafat, A.M., et al., 2007. Polyfluoroalkyl chemicals in the U.S. population: data from the National Health and Nutrition Examination Survey (NHANES) 2003–2004 and comparisons with NHANES 1999–2000. Environ. Health Perspect. 115, 1596–1602.

CDC, 2014b. Laboratory Procedure Manual for Polyfluoroalkyl chemicals. Available at: (http://www.cdc.gov/nchs/data/nhanes/nhanes_11_12/PFC_G_met.pdf).

CDC, 2014c. NHANES MEC In-person Dietary Interviewers Procedures Manual. Available at: (http://www.cdc.gov/nchs/data/nhanes/nhanes_11_12/Dietary_MEC_In-Person_Interviewers_Manual.pdf).
CDC, 2015. Centers for Disease Control and Prevention. Fourth Report on Human Exposure to Environmental Chemicals, Updated Tables, (February 2015). Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. (http://www.cdc.gov/exposurereport/).
CDC, 2016. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Hyattsville, MD, 2007–2014.
Denys, S., et al., 2014. Is the fresh water fish consumption a significant determinant of the internal exposure to perfluoroalkylated substances (PFAS)? Toxicol. Lett. 231, 233–238.
Domingo, J.L., 2016. Nutrients and chemical pollutants in fish and shellfish. Balancing health benefits and risks of regular fish consumption. Crit. Rev. Food Sci. Nutr. 56, 979–988.
Egeghy, P.P., Lorber, M., 2011. An assessment of the exposure of Americans to perfluorooctane sulfonate: a comparison of estimated intake with values inferred from NHANES data. J. Expo. Sci. Environ. Epidemiol. 21, 150–168.
EPA, 2009a. 2010/2015 PFOA Stewardship Program. Available at: (http://epa.gov/oppt/pfoa/pubs/stewardship/index.html).
EPA, 2009b. State of the Great Lakes 2009. Prepared by Environment Canada and United States Environmental Protection Agency. Available at: (http://binational.net/wp-content/uploads/2014/11/En161-3-1-2009E.pdf)
EPA, 2009c. Long-Chain Perfluorinated Chemicals (PFCs) Action Plan. Available at: (http://www.epa.gov/opptintr/existingchemicals/pubs/pfcs_action_plan1230_09.pdf).
Eriksen, K.T., et al., 2013. Association between plasma PFOA and PFOS levels and total cholesterol in a middle-aged Danish population. PLoS One 8, e56969.
Fromme, H., et al., 2007. Exposure of an adult population to perfluorinated substances using duplicate diet portions and biomonitoring data. Environ. Sci. Technol. 41, 7928–7933.
Fromme, H., et al., 2009. Perfluorinated compounds – exposure assessment for the general population in Western countries. Int J. Hyg. Environ. Health 212, 239–270.
Gleason, J.A., et al., 2015. Associations of perfluorinated chemical serum concentrations and biomarkers of liver function and uric acid in the US population (NHANES), 2007–2010. Environ. Res. 136, 8–14.
Glynn, A., et al., 2012. Perfluorinated alkyl acids in blood serum from primiparous women in Sweden: serial sampling during pregnancy and nursing, and temporal trends 1996–2010. Environ. Sci. Technol. 46, 9071–9079.
Halldorsson, T.I., et al., 2008. Dietary predictors of perfluorinated chemicals: a study from the Danish National Birth Cohort. Environ. Sci. Technol. 42, 8971–8977.
Hansen, S., et al., 2016. Exposure to per- and polyfluoroalkyl substances through the consumption of fish from lakes affected by aqueous film-forming foam emissions – a combined epidemiological and exposure modeling approach. The SAMINOR 2 clinical study. Environ. Int. 94, 272–282.
Harada, K., et al., 2004. The influence of time, sex and geographic factors on levels of perfluorooctane sulfonate and perfluorooctanoate in human serum over the last 25 years. J. Occup. Health 46, 141–147.
Haug, L.S., et al., 2010. Diet and particularly seafood are major sources of perfluorinated compounds in humans. Environ. Int. 36, 772–778.
He, K., et al., 2004. Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation 109, 2705–2711.
Holzer, J., et al., 2011. Perfluorinated compounds in fish and blood of anglers at Lake Mohne, Sauerland area, Germany. Environ. Sci. Technol. 45, 8046–8052.
Hu, X.C., et al., 2016. Detection of Poly- and Perfluoroalkyl substances (PFASs) in U.S. drinking water linked to industrial. Environ. Sci. Technol. Lett. 3, 344–350.
Ingelido, A.M., et al., 2010. Perfluorooctanesulfonate and perfluorooctanoic acid exposures of the Italian general population. Chemosphere 80, 1125–1130.
Kato, K., et al., 2011. Trends in exposure to polyfluoroalkyl chemicals in the U.S. population: 1999–2008. Environ. Sci. Technol. 45, 8037–8045.
Koponen, J., et al., 2015. Perfluoroalkyl acids in various edible Baltic, freshwater, and farmed fish in Finland. Chemosphere 129, 186–191.
Loke, M., , et al.2012. An overview of seafood consumption and supply sources: Hawai'i versus U.S. Honolulu (HI): University of Hawaii. 9 p. (Economic Issues; EI-22). Available at: (http://www.fpir.noaa.gov/SFD/pdfs/seafood/EI-22.pdf).
Melzer, D., et al., 2010. Association between serum perfluorooctanoic acid (PFOA) and thyroid disease in the U.S. National Health and Nutrition Examination Survey. Environ. Health Perspect. 118, 686–692.
Monroy, R., et al., 2008. Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. Environ. Res. 108, 56–62.
Nelson, J.W., et al., 2012. Social disparities in exposures to bisphenol A and polyfluoroalkyl chemicals: a cross-sectional study within NHANES 2003–2006. Environ. Health 11, 10.
Olsen, G.W., et al., 2004. Serum concentrations of perfluorooctanesulfonate and other fluorochemicals in an elderly population from Seattle, Washington. Chemosphere 54, 1599–1611.
Olsen, G.W., et al., 2003. Perfluorooctanesulfonate and other fluorochemicals in the serum of American Red Cross adult blood donors. Environ. Health Perspect. 111, 1892–1901.
Rylander, C., et al., 2009. Dietary predictors and plasma concentrations of perfluorinated compounds in a coastal population from northern Norway. J. Environ. Public Health 2009, 268219.
Rylander, C., et al., 2010. Dietary patterns and plasma concentrations of perfluorinated compounds in 315 Norwegian women: the NOWAC Postgenome Study. Environ. Sci. Technol. 44, 5225–5232.
Stahl, L.L., et al., 2014. Perfluorinated compounds in fish from U.S. urban rivers and the Great Lakes. Sci. Total Environ. 499, 185–195.
Steenland, K., et al., 2010. Epidemiologic evidence on the health effects of perfluorooctanoic acid (PFOA). Environ. Health Perspect. 118, 1100–1108.
Steenland, K., et al., 2009. Association of perfluorooctanoic acid and perfluorooctane sulfonate with serum lipids among adults living near a chemical plant. Am. J. Epidemiol. 170, 1268–1278.
Suominen, K., et al., 2011. Occurrence of PCDD/F, PCB, PBDE, PFAS, and organotin compounds in fish meal, fish oil and fish feed. Chemosphere 85, 300–306.
Toms, L.M., et al., 2009. Polyfluoroalkyl chemicals in pooled blood serum from infants, children, and adults in Australia. Environ. Sci. Technol. 43, 4194–4199.
Tyrrell, J., et al., 2013. Associations between socioeconomic status and environmental toxicant concentrations in adults in the USA: NHANES 2001–2010. Environ. Int. 59, 328–335.
Wang, Z., et al., 2013. Fluorinated alternatives to long-chain perfluoroalkyl carboxylic acids (PFCAs), perfluoroalkane sulfonic acids (PFSAs) and their potential precursors. Environ. Int. 60, 242–248.
Whelton, S.P., et al., 2004. Meta-analysis of observational studies on fish intake and coronary heart disease. Am. J. Cardiol. 93, 1119–1123.
Yamaguchi, M., et al., 2013. Consumption of seafood, serum liver enzymes, and blood levels of PFOS and PFOA in the Japanese population. J. Occup. Health 55, 184–194.