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Dietary Patterns and PFAS Plasma Concentrations in Childhood: Project Viva, USA

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Abstract

Background: Diet is thought to account for most adult human exposure to per- and polyfluoroalkyl substances (PFAS). Children are particularly vulnerable to adverse health effects

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of PFAS and may have different eating habits than adults. However, studies of dietary patterns and PFAS in children are limited.

Methods: We studied 548 Boston-area children with food frequency questionnaire data (89 food items) in early childhood (median age 3.3 years) and plasma concentrations of 6 PFAS quantified in mid-childhood (median age 7.7 years). We used univariate linear regression to examine associations between each food item and PFAS, accounting for multiple comparisons. We next used reduced rank regression (RRR) to estimate overall percent variation in PFAS explained by diet and identify dietary patterns most correlated with PFAS. All models were adjusted for race/ethnicity, maternal education, and household income.

Results: In univariate analyses, 2-(N-methyl-perfluorooctane sulfonamide) acetate (MeFOSAA) plasma concentrations were 17.8% (95% CI: 7.2, 29.5) and 17.0% (95% CI: 6.4, 28.7) higher per SD increment in intake of ice cream and soda, respectively. RRR identified 6 dietary patterns that together explained 18% variation in the plasma concentrations of the 6 PFAS, of which 50% was explained by a dietary pattern consisting of primarily packaged foods (including ice cream and soda) and fish. Children with higher intake of the packaged foods and fish dietary pattern had higher plasma concentrations of all PFAS, particularly MeFOSAA and PFOS.

Conclusions: Our analysis examined food intake in association with several PFAS in children and identified dietary determinants that may be sources of PFAS exposure or reflect correlated lifestyle or toxicokinetic factors. Further investigation may help inform measures to modify childhood PFAS exposure.

Keywords

perfluoroalkyl substances; dietary pattern; diet; reduced rank regression; childhood

Introduction

Exposure to per- and polyfluoroalkyl substances (PFAS), a group of persistent and ubiquitous surfactant chemicals, has been associated with adverse health outcomes in adults and children, including high cholesterol, thyroid disease, and immune dysfunction (Rappazzo et al. 2017; Sunderland et al. 2019). Identifying specific pathways of human exposure to PFAS is a critical first step to minimize exposure.

Although PFAS exposure sources vary depending on the specific population, diet is estimated to be a major source of PFAS exposure in adults, with a smaller contribution from other routes such as water, carpeting and apparel, or dust (Haug et al. 2011; Tittlemier et al. 2007). Because of their water and grease-repellant properties, PFAS are used in food utensils and packaging (Lindstrom et al. 2011; Schaider et al. 2017; Wang et al. 2017) and may migrate into foods from packaging (Begley et al. 2005) or during preparation (Susmann et al. 2019). In addition, some PFAS can accumulate in fish and animal products (Carlsson et al. 2016; Christensen et al. 2017; Tittlemier et al. 2007; Vestergren et al. 2013), possibly as a result of contaminated aquatic habitats and biomagnification within food webs (Fair et al. 2019) or through contaminated biosolids applied to crops used as animal feed (Venkatesan and Halden 2013).

Prior studies have measured PFAS concentrations in foods and found PFAS in fish, meat, fats, fast food, and dairy (Gebbink et al. 2015). In addition, a few studies have observed that people with higher intake of fish as well as fast food, pizza, restaurant food, and microwavable popcorn have higher plasma concentrations of certain PFAS (Averina et al. 2018; Hu et al. 2018; Papadopoulou et al. 2019; Susmann et al. 2019).

The majority of prior studies have tested only foods without consideration of dietary patterns. Studies of dietary patterns are important because they account for correlations and interactions between foods and may identify foods previously unrecognized as potential sources of PFAS. Limited investigation of dietary patterns and PFAS plasma concentrations in adults found that individuals who consumed a high-fat meat (Lin et al. 2020) or Mediterranean (Sjogren et al. 2016) dietary pattern had higher PFAS plasma concentrations. However, to our knowledge, there have been no studies of dietary patterns and PFAS plasma concentrations in children in the United States, who may have different eating habits than adults (Wu et al. 2015) and may be more vulnerable to health effects of PFAS (Rappazzo et al. 2017).

In this analysis, we use data from a large, relatively high socioeconomic status Boston-area cohort. We used reduced rank regression (RRR), a modern statistical dimension reduction method in nutritional epidemiology, to identify foods and dietary patterns in early childhood (median 3.3 years of age) that were associated with PFAS plasma concentrations measured in mid-childhood (median 7.7 years of age; 2007-2010).

Methods

Study population and design

We conducted a prospective analysis of data from Project Viva, an ongoing longitudinal cohort study of 2128 mother-child pairs recruited prenatally between 1999 and 2002 from Atrius Harvard Vanguard Medical Associates, a multi-specialty group practice in the greater Boston area (Oken et al. 2015). We obtained parent-reported dietary data from children (N=1271) from the initial cohort during their early childhood research visit (age range 2.8 – 6.2 years; median 3.1 years). Of these, 559 had PFAS concentrations measured in plasma in mid-childhood (age range 6.7 – 10.5 years; median 7.7 years), collected between 2007-2010. An advantage of our PFAS plasma collection in mid-childhood in the context of this analysis is that although breastfeeding is known to be a dietary source of PFAS exposure, by mid-childhood, breastfeeding duration has minimal impact on PFAS plasma concentrations, as we have previously shown (Harris et al. 2017). The present analysis included 548 participants who had covariate information, in addition to dietary data and PFAS plasma concentrations. Among children who attended both early and mid-childhood visits, those included in the present study (compared to those excluded) were more likely to be Black, or from households with total annual income less than $70,000 (see Table S1).

All mothers provided written informed consent for their child’s participation, and the institutional review boards of participating institutions approved this analysis. The involvement of the Centers for Disease Control and Prevention (CDC) laboratory did not constitute engagement in human subjects research.

Dietary assessment

We obtained parent report of dietary intake in early childhood using the Harvard Service Food Frequency Questionnaire (FFQ), which asked about typical weekly intake of 89 food items over the past month (Blum et al. 1999). This FFQ has been validated with 24-hour dietary recalls in other cohorts of similarly aged children (Blum et al. 1999) but not with nutritional biomarkers. We rescaled responses to servings per day by calculating numeric means corresponding to each FFQ category (e.g., 2-4 times/week was coded as 3 times/week or 0.43 servings/day). We excluded participants who were missing weekly intake data for six or more food items. Otherwise, we considered missing values to be zero servings per day, as recommended (Willett 2013).

We obtained parent report of dietary intake in mid-childhood using a PrimeScreen, an abbreviated dietary assessment which asked about weekly intake of 18 food groups/items (Rifas-Shiman et al. 2001). We rescaled PrimeScreen responses to servings per day as described above.

Plasma PFAS concentrations

We measured several PFAS in plasma collected in mid-childhood as previously described (Cluett et al. 2019; Harris et al. 2017). Staff at the CDC (Atlanta, GA) quantified PFAS using online solid-phase extraction with isotope dilution high performance liquid chromatography mass spectrometry as described in detail before (Kato et al. 2011). The analytical method was the same used to quantify PFAS concentrations in the 2013–2014 Health and Nutrition Examination Survey (NHANES) cycle (Centers for Disease Control and Prevention 2016). Low and high-concentration quality control materials, prepared from a calf serum pool, were analyzed with study samples, analytical standards, and reagent and matrix blanks to ensure accuracy and precision of the data; the laboratory also successfully participated in external quality assessment schemes (Centers for Disease Control and Prevention 2016). Repeated measurements of serum quality control pools, reflecting both inter- and intraday variation, had coefficients of variation for the PFAS in this study between 4% to 11%; the limit of detection (LOD) was 0.1 ng/mL for all PFAS (Centers for Disease Control and Prevention 2016). We replaced values below the LOD with the LOD/√2 (Centers for Disease Control and Prevention 2019; Lubin et al. 2004). We summed the concentrations of linear and branched isomers of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) to obtain total PFOA and total PFOS, respectively. We decided *a priori* to consider only PFAS with detectable concentrations in greater than 60% of samples for the current analysis (Centers for Disease Control and Prevention 2019). The PFAS that met this threshold were total PFOA, total PFOS, perfluorodecanoate (PFDA), perfluorohexane sulfonate (PFHxS), 2-(N-methyl-perfluorooctane sulfonamide) acetate (MeFOSAA), and perfluorononanoate (PFNA).

Covariates

We obtained participant sociodemographic information including child race/ethnicity (White, Black, Hispanic, Asian, other), maternal education (with or without college degree), and annual household income (< $40k, $40k- $70k, >$70k) from questionnaires at enrollment and in early childhood.

Statistical Analysis

The Project Viva cohort collected dietary data in both early and mid-childhood and measured PFAS plasma concentrations in participants in mid-childhood. PFAS have a 3-8 year biological half-life (Gebbink et al. 2015; Li et al. 2018), so PFAS concentrations in mid-childhood are likely to have been impacted by diet over the preceding 3-8 years, encompassing both our early and mid-childhood data collection points. We made the *a priori* decision to focus our primary analyses on early childhood dietary intake because the PrimeScreen we administered in mid-childhood was a limited 18-item dietary assessment that would not allow us to comprehensively evaluate specific food items or dietary patterns associated with PFAS concentrations. We examined the contemporaneous association between dietary intake as measured on the PrimeScreen and PFAS plasma concentrations in mid-childhood in secondary analyses.

In our primary analyses, we first used linear regression to separately examine associations of intake (servings per day) of each of the foods on the early childhood FFQ with plasma concentrations of each of the PFAS in mid-childhood. We ln-transformed PFAS plasma concentrations to meet model assumptions, and for ease of interpretation, exponentiated regression coefficients to report results as a percent change [% change = (exp(beta) − 1) × 100] in PFAS plasma concentration per standard deviation (SD) increment in food intake (Barrera-Gomez and Basagana 2015). We ran models unadjusted and adjusted for socioeconomic status measures (child race/ethnicity, maternal education, and annual household income). We accounted for multiple comparisons using Benjamini-Hochberg false discovery rate (FDR) correction (Benjamini and Hochberg 1995) at a level of 0.1 within each set of 89 tests for each PFAS.

Next, we performed RRR, an *a posteriori* dimension reduction method, to identify early childhood dietary patterns that explained the most variation in PFAS plasma concentrations. Similar to principal component analysis (PCA), RRR identified dietary patterns that were linear functions of the food items and were uncorrelated. However, RRR was advantageous to PCA in the present analysis because it identified dietary patterns that explained the most variability in the outcome (PFAS plasma concentrations) rather than identifying dietary patterns based on ways in which the predictors (food items) clustered (Hoffmann et al. 2004). RRR was additionally advantageous because we were able to enter plasma concentrations of all PFAS together as a matrix in the model, which allowed us to identify dietary patterns that explained the most variation in the overall mixture of PFAS, rather than just one PFAS at a time.

We started with an unadjusted RRR analysis, as has been done previously (Hoffmann et al. 2004; Tabung et al. 2016). From this analysis, we obtained 6 unique dietary patterns that explained variability in PFAS plasma concentrations. For each participant, we obtained factor scores (i.e., “dietary pattern scores”) that described the strength of a participant’s adherence to each dietary pattern, with higher scores representing greater adherence to the pattern. We also obtained model loadings (i.e., correlation coefficients between each food item and dietary pattern score) which described the strength and directionality of how intake of each food item loaded onto each dietary pattern.

We next examined participant characteristics by quartiles of the dietary pattern 1 score (i.e., the dietary pattern that explained the most variation in PFAS plasma concentrations). The dietary pattern 1 score tracked strongly with race/ethnicity, maternal education, and household income, likely because PFAS plasma concentrations are closely linked to socioeconomic status (Harris et al. 2017). For example, 84% of participants in the highest quartile of the dietary pattern 1 score were college educated versus 52% in the lowest quartile. The score was not closely linked to other variables (e.g., child age and sex, data not shown). The RRR analysis did not directly permit us to incorporate confounding variables. Thus, to minimize the extent to which the dietary patterns we identified simply reflected socioeconomic status, we used the residual method of adjustment (Willett et al. 1997) to adjust for socioeconomic status, as has been done in prior RRR analyses (Tabung et al. 2016). We regressed plasma concentrations of each of the six PFAS on the socioeconomic status variables of interest (race/ethnicity, maternal education, and household income) in six separate linear regression models, and used the residuals obtained in this step as dependent variables in the covariate-adjusted RRR analysis that we present here.

To present the RRR results, first we show which foods loaded most strongly (i.e., absolute model loadings in the top 25^{th} percentile) onto each dietary pattern. Next, we used linear regression models to quantify the association between the dietary pattern score for each dietary pattern and plasma concentrations of each PFAS. We ln-transformed plasma concentrations of PFAS to meet model assumptions. For ease of interpretation, we exponentiated regression coefficients and report results as a percent change [% change = (exp(beta) − 1) × 100] in PFAS plasma concentration per standard deviation (SD) increment in dietary pattern score.

In secondary analyses, we used linear regression to separately examine unadjusted and covariate-adjusted associations of intake (servings per day) of each of the food groups/items on the PrimeScreen administered in mid-childhood with plasma concentrations of each of the PFAS in mid-childhood, and results as a percent change in PFAS plasma concentration per SD increment in food intake, as described above. Further, we accounted for multiple comparisons using Benjamini-Hochberg false discovery rate (FDR) correction (Benjamini and Hochberg 1995) at a level of 0.1 within each set of 18 tests for each PFAS.

For the RRR analysis, we ran the PROC PLS procedure using SAS Enterprise Guide version 7.15 (SAS Institute Inc. Cary, NC, USA). We used R version 3.5.1 (R Core Team 2018) for all other analyses and visualizations.

Results

Study population

Participants included in our analyses were [median (IQR)] 3.1 (0.2) years of age at the dietary assessment in early childhood, and [median (IQR)] 7.7 (0.8) years of age at the dietary assessment and blood draw for PFAS plasma concentrations in mid-childhood. Forty-seven percent of children were female, 64% were white, and 69% of their mothers were college graduates at the time of cohort enrollment (Table 1).

Most PFAS considered in our study (except PFDA and MeFOSAA) were detectable in the plasma of >99% of Project Viva participants. PFAS plasma concentrations in Project Viva were similar to those reported in U.S. children in the National Health and Nutrition Examination Survey (NHANES) during the same period, from 2007-2008 (Centers for Disease Control and Prevention 2019). In our Project Viva analysis, the highest PFAS plasma concentrations were of PFOA [median (IQR) 4.5 (2.9) ng/mL] and PFOS [median (IQR) 6.5 (5.8) ng/mL]. PFAS plasma concentrations were generally moderately correlated (Spearman's $\rho = 0.004\text{-}0.71$), with the strongest correlation between PFOS and PFOA ($\rho = 0.71$) (see Table S2).

Food items in early childhood and PFAS plasma concentrations in mid-childhood

In covariate-adjusted analyses of individual food items and each PFAS, we found that only two food items were associated with PFAS plasma concentrations after accounting for multiple comparisons. Plasma concentrations of MeFOSAA were 17.8% (95% CI: 7.2, 29.5) higher per SD increment in intake of ice cream and 17.0% (95% CI: 6.4, 28.7) higher per SD increment in intake of soda. Other food items were not associated with PFAS plasma concentrations. In Table S3, we show associations between select food items (i.e., those that loaded most strongly onto dietary pattern 1, identified by our RRR analysis) and plasma PFAS concentrations.

Dietary patterns in early childhood and PFAS plasma concentrations in mid-childhood

The covariate-adjusted RRR analysis identified six uncorrelated dietary patterns that together explained 18% variation in PFAS plasma concentrations. Of the 18% total explained variation, 50% was explained by dietary pattern 1, 31% was explained by dietary patterns 2 and 3, and only 19% was explained by dietary patterns 4-6. Consequently, we do not describe the final three dietary patterns (4, 5, and 6) in detail here.

Children who adhered to dietary pattern 1 (frequently packaged foods and fish) had higher intake of fish (other than fried fish or canned tuna) and foods that are frequently packaged, such as ice cream, lettuce, salad dressing, candy, butter, white rice, and soda (Figure 1). Some items in dietary pattern 1 that are not always packaged (e.g., lettuce and tomatoes) were correlated with packaged items (e.g., salad dressing) (see Figure S1). Children who adhered strongly to dietary pattern 1 had higher plasma concentrations of all 6 PFAS, particularly MeFOSAA and PFOS. For each SD increment in dietary pattern 1 score, plasma concentrations of MeFOSAA and PFOS were 34.5% (95% CI: 22.5, 47.6) and 27.9% (95% CI: 21.0, 35.1) higher respectively (Table 2). Children with dietary pattern scores in the highest quartile of dietary pattern 1 were more likely to have mothers who were older and college-educated (Table 1).

Children who adhered to dietary pattern 2 (high vegetables and canned tuna) had high intake of vegetables (i.e., squash, sweet potatoes and yam, broccoli, carrots) and canned tuna and lower intake of meat (i.e., pork, ham, beef, bacon, and cold cuts) (see Figure S2). Children who adhered most strongly to dietary pattern 2 had higher plasma concentrations of PFHxS and PFOS and lower plasma concentrations of PFDA and PFNA, but associations with PFAS plasma concentrations were not as strong as for dietary pattern 1. For each SD increment in

dietary pattern 2 score, PFHxS was 24.6% higher (95% CI: 15.5, 34.4), PFOS was 6.7% higher (95% CI: 0.7, 13.2), PFDA was 11.8% lower (95% CI: −16.3, −7.0), and PFNA was 9.1% lower (95% CI: −14.1, −3.8) (Table 2).

Children who adhered to dietary pattern 3 (high meat and low vegetables) had high intake of animal products (e.g., pork, beef, cold cuts, and poultry) and low intake of vegetables (e.g., broccoli, carrots, and spinach), beans, fruits, and nuts and starches (see Figure S3). Children who adhered most strongly to dietary pattern 3 had higher plasma concentrations of PFNA and PFHxS and lower plasma concentrations of MeFOSAA. For each SD increment in dietary pattern 3 score, PFNA was 15.9% higher (95% CI: 9.6, 22.6), PFHxS was 7.6% higher (95% CI: −0.4, 16.3), and MeFOSAA was 14.1% lower (95% CI: −21.9, −5.4) (Table 2).

Secondary analysis: Dietary intake and PFAS plasma concentrations in mid-childhood

In our covariate-adjusted analyses of the associations between dietary intake in mid-childhood and each PFAS, PFNA was 7.9% (−12.9, −2.6) lower per SD increment in the intake of low-fat milk. Associations between other food groups/items and other PFAS were null, after accounting for multiple comparisons (Table S4), although greater consumption of vegetables was non-significantly associated with lower concentrations of several PFAS and greater consumption of meat and fish were non-significantly associated with higher concentrations of several PFAS.

Discussion

In our analysis of a large, prospective Boston-area cohort, we found that children with greater intake of ice cream and soda had higher plasma concentrations of MeFOSAA. We also found that a dietary pattern comprised of fish, as well as ice cream, soda, and other frequently packaged foods such as candy and salad dressing was associated with higher plasma concentrations of all 6 PFAS, particularly MeFOSAA and PFOS. The two other dietary patterns that we identified, comprised largely of vegetables, meat, and poultry, had weaker associations with only some PFAS, with inconsistent directionality. The dietary factors that we identified may be sources of PFAS exposure or reflect correlated lifestyle or toxicokinetic factors.

Our findings build upon existing studies that have tested for PFAS in food and extend the limited epidemiologic literature investigating dietary predictors of PFAS plasma concentrations in children. Our results also expand current understanding of sources of PFAS exposure in children, which may be different from sources previously documented in adults. We identified greater intake of soda and ice cream (and greater adherence to a dietary pattern that included high intake of soda and ice cream) to be positively associated with higher PFAS concentrations in children. Consistent with our findings, a large adolescent cohort in Norway also identified intake of sugary drinks to be associated with higher PFAS plasma concentrations (Averina et al. 2018). Soda may be contaminated with PFAS from tap water used in its preparation or from production equipment during processing (Eschauzier et al. 2013). We are not aware of prior studies that have identified PFAS in ice cream, but other high-fat dairy products have been found to contain PFAS (Vestergren et al. 2013; Wu et al.

2015) which may be introduced during the industrial phase separation of cream from milk, during the churning processes, or through packaging (Still et al. 2013).

In our analysis, we were unable to determine whether soda and ice cream were direct sources of PFAS exposure or whether intake of these items might have been a proxy for other sources of PFAS exposure. Intake of soda and ice cream were correlated with each other in our cohort (see Figure S1), and children who had high soda and ice cream intake may have had high intake of other packaged foods such as microwave popcorn which has been associated with greater PFAS plasma concentrations (Park et al. 2019; Susmann et al. 2019) but was not quantified in our FFQ.

Soda and ice cream intake may also be associated with certain toxicokinetic or lifestyle factors that are, in turn, associated with greater PFAS plasma concentrations. For example, children with greater soda and ice cream intake are more likely to be obese (Malik et al. 2006) and obese children have been shown to have lower glomerular filtration rate (Correia-Costa et al. 2015) which has been associated with higher PFAS plasma concentrations (Verner et al. 2015). Also, young children whose diets contain high intake of soda and ice cream may be particularly sedentary and may spend more time indoors, putting them in frequent contact with upholstered or carpeted areas that have been independently linked to greater exposure to MeFOSAA, PFOS, and PFHxS (Harris et al. 2017; Wu et al. 2020).

High intake of fish was included in both of the top two dietary patterns we found to be associated with PFAS plasma concentrations. While not all studies of children have observed an association between fish intake and PFAS serum concentrations (Jain 2018; Wu et al. 2015), high intake of fish was associated with higher PFAS plasma concentrations in children in Norway (Averina et al. 2018), the Faroe Islands (Hu et al. 2018), and across Europe (Papadopoulou et al. 2019). Fish consumption has also been shown to be a major source of exposure to PFAS for several adult populations worldwide (Carlsson et al. 2016; Christensen et al. 2017; Haug et al. 2011; Lin et al. 2020; Tittlemier et al. 2007). This is presumably related to bioaccumulation of PFAS in fish from contaminated aquatic habitats and biomagnification within food webs (Fair et al. 2019). Thus, although fish are considered beneficial to health because they are good sources of protein, micronutrients, and heart-healthy omega-3 fatty acids (Kris-Etherton et al. 2002; Mozaffarian and Rimm 2006), fish consumption may increase exposure to environmental chemicals such as PFAS. The FFQ in Project Viva asked separately about intake of canned tuna, fried fish, and other fish but did not otherwise specify fish species. Additional research to understand which specific fish species are more likely to contain PFAS would help to improve recommendations to consumers.

We also found high-fat dairy products, including butter and cheese, to be prominent components of the dietary pattern (i.e., frequently packaged foods and fish) most closely linked to greater PFAS plasma concentrations. A study of children and adults in California found that consumption of butter/margarine was associated with higher serum concentrations of PFAS (Wu et al. 2015). Interestingly, in our study, the dietary pattern most strongly linked to PFAS plasma concentrations included high intake of butter and low intake of margarine. This is likely explained by the strong negative correlation we observed

between the two food intakes (see Figure S2), possibly reflecting lifestyle choices whereby participants' diets included either butter or margarine, but not both.

In our dietary pattern analysis, we also found lettuce, spinach, and salad dressing to be major components of the dietary pattern most closely linked to greater PFAS plasma concentrations. PFAS have been previously identified in samples of fresh leafy vegetables (Ghisi et al. 2019), packaged lettuce (Jogsten et al. 2009), and other vegetables such as potatoes (Herzke et al. 2013; Noorlander et al. 2011), which may uptake PFAS from contaminated biosolids or irrigation used in agriculture (Venkatesan and Halden 2013), or from packaging. However, there is mixed evidence describing the associations of vegetable intake and PFAS plasma concentrations, with some prior studies reporting inverse or no associations of vegetable intake and PFAS plasma concentrations (Halldorsson et al. 2008; Lin et al. 2020; Tian et al. 2018).

Additionally in our cohort, intake of salad dressing was closely correlated with intake of lettuce and spinach (see Figure S1), raising the possibility that one or more of these items appeared in dietary pattern 1 due to correlated intake frequency, and not as an independent source of PFAS exposure. We also found candy, tomato juice/sauce/salsa, and white rice to be prominent components of the dietary pattern most closely linked to greater PFAS plasma concentrations. Thus, our findings raise the potential for these items to contain PFAS, and further studies are needed to directly investigate PFAS levels independently in each of these foods.

In addition to identifying potential foods that may be contaminated with PFAS, our analysis extends current literature by examining food intake in association with several unique PFAS chemicals. Of those, we identified plasma concentrations of MeFOSAA and PFOS to be most strongly linked to diet, although MeFOSAA plasma concentration had relatively low variability. In addition, the associations of diet and MeFOSAA may more accurately reflect lifestyle choices that are correlated with greater PFAS exposure rather than exposure from specific foods themselves as MeFOSAA is an oxidation product of N-methyl perfluorooctanesulfonamidoethanol, used primarily in surface treatment applications (e.g., carpets, textiles) (Olsen et al. 2003), and may be a marker of time spent indoors.

In the case of PFOS, our findings are consistent with the fact that N-ethyl perfluorooctane sulfonamidoethaol (N-EtFOSE), a parent compound for EtFOSAA and PFOS, is known to have been used in some food packaging around the time of this study (Hu et al. 2018; Olsen et al. 2003; Shoeib et al. 2005). We found plasma concentrations of PFOS to be higher in children who adhered to dietary pattern 1 (frequently packaged foods and fish), which largely included packaged food items commonly found in grocery or convenience stores that may be distinct from food-contact materials (e.g., popcorn bags, takeout containers, and paper cups) previously identified as potential sources of PFAS (Hu et al. 2018; Olsen et al. 2003; Shoeib et al. 2005). Our findings are consistent with and add to prior analyses of adults and children in the USA (Hu et al. 2018; Susmann et al. 2019), and across multiple demographics in the Faroe Islands (Hu et al. 2018). These studies found higher plasma concentrations of MeFOSAA (as well as PFOS, EtFOSAA, and PFHxS) in individuals from

both populations who reported greater consumption of a variety of packaged foods, likely resulting from a combination of consumer-product and dietary exposures.

Notable in our study is that children who adhered more strongly to dietary pattern 2 (i.e., high vegetables and canned tuna), had lower plasma concentrations of PFDA and PFNA, consistent with studies that have shown lower PFAS body burden in adults and children who have greater vegetable intake (Halldorsson et al. 2008; Lin et al. 2020). This finding may be explained in part by the fiber-enhanced excretion of PFAS, PFNA in particular (Dzierlenga et al. 2021). Greater adherence to dietary pattern 2, which included high intake of canned tuna, was also associated with higher concentrations of PFHxS, in alignment with findings from the US/Faroe Islands study (Hu et al. 2018) and with Averina et al. (2018), who reported that adolescents with more frequent intake of canned food had higher plasma concentrations of PFHxS.

Children in our study with greater adherence to dietary pattern 3 (high meat and low vegetables) had higher PFNA and lower MeFOSAA plasma concentrations, consistent with serum PFAS profiles observed in adults with a high meat dietary pattern (Lin et al. 2020). Additional research would help to elucidate whether meat is a source of PFNA or if greater meat intake is correlated with lifestyle behaviors that increase PFNA or decrease MeFOSAA exposure.

We found diet to explain only 18% of the variability in PFAS plasma concentrations in children, whereas exposure modeling studies in adults estimate diet to account for over half of all PFAS exposure (Haug et al. 2011; Tittlemier et al. 2007). The relatively low variability may partly reflect the fact that the FFQ does not include information on food packaging and does not specifically quantify intake of foods such as popcorn and fast food. Furthermore, based on the 3-8 year biological half-life of PFAS (Gebbink et al. 2015; Li et al. 2018) we expect plasma concentrations to primarily reflect cumulative exposures over the 3-8 years prior. However, our FFQ was administered at only one point in time, on average 4 years before PFAS were measured, which may partly explain its relatively low explanatory power. We found no consistent, significant contemporaneous associations between dietary as measured by the abbreviated dietary assessment in mid-childhood and PFAS plasma concentrations. This may have been because food group categories were broad (e.g., whole milk or high-fat dairy), effectively masking any associations between a given food item (e.g., ice cream) within that category and PFAS plasma concentrations. Future analyses may be able to identify dietary patterns that capture greater variability in PFAS by examining more granular contemporaneous dietary data with information on food packaging and by directly measuring PFAS in food items (i.e., paired food/plasma PFAS concentrations).

An additional limitation of our study was that we did not have information on water consumption and we were unable to account for PFAS contamination of water used for drinking, or food preparation or processing. Although generalizability is a limitation of our study because Project Viva is primarily made up of white children of moderately high SES, PFAS plasma concentrations among children in Project Viva are comparable to young participants from contemporaneous NHANES cycles, and may thus be generalizable to similar populations.

A major strength of the present study is our evaluation of a large number of food items as well as dietary patterns associated with PFAS plasma concentrations, which has not been undertaken previously in U.S. children. Another strength of our study is that we adjust for socioeconomic status measures, which are tightly linked to both diet and PFAS plasma concentrations. Similar FFQs are used by many cohorts to evaluate dietary intake, and if our findings can be replicated, the RRR factor score may be able to be used as a marker of PFAS exposure from diet. To the extent that the factor score may be associated with health outcomes, it could also be used as a marker of confounding by diet in PFAS-health outcome analyses.

In conclusion, our analysis evaluates dietary patterns associated with increased PFAS plasma concentrations among Boston-area children. We observed that children with greater intake of packaged foods, especially ice cream and soda, and fish had higher concentrations of select PFAS, particularly MeFOSAA. Identifying and reducing childhood exposures to PFAS may help minimize potential adverse health effects.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights:

- Children with a diet of frequently packaged foods and fish had higher PFAS
- Ice cream and soda were key components of the packaged foods and fish diet
- Findings may reflect novel PFAS sources or correlated lifestyle/toxicokinetic factors

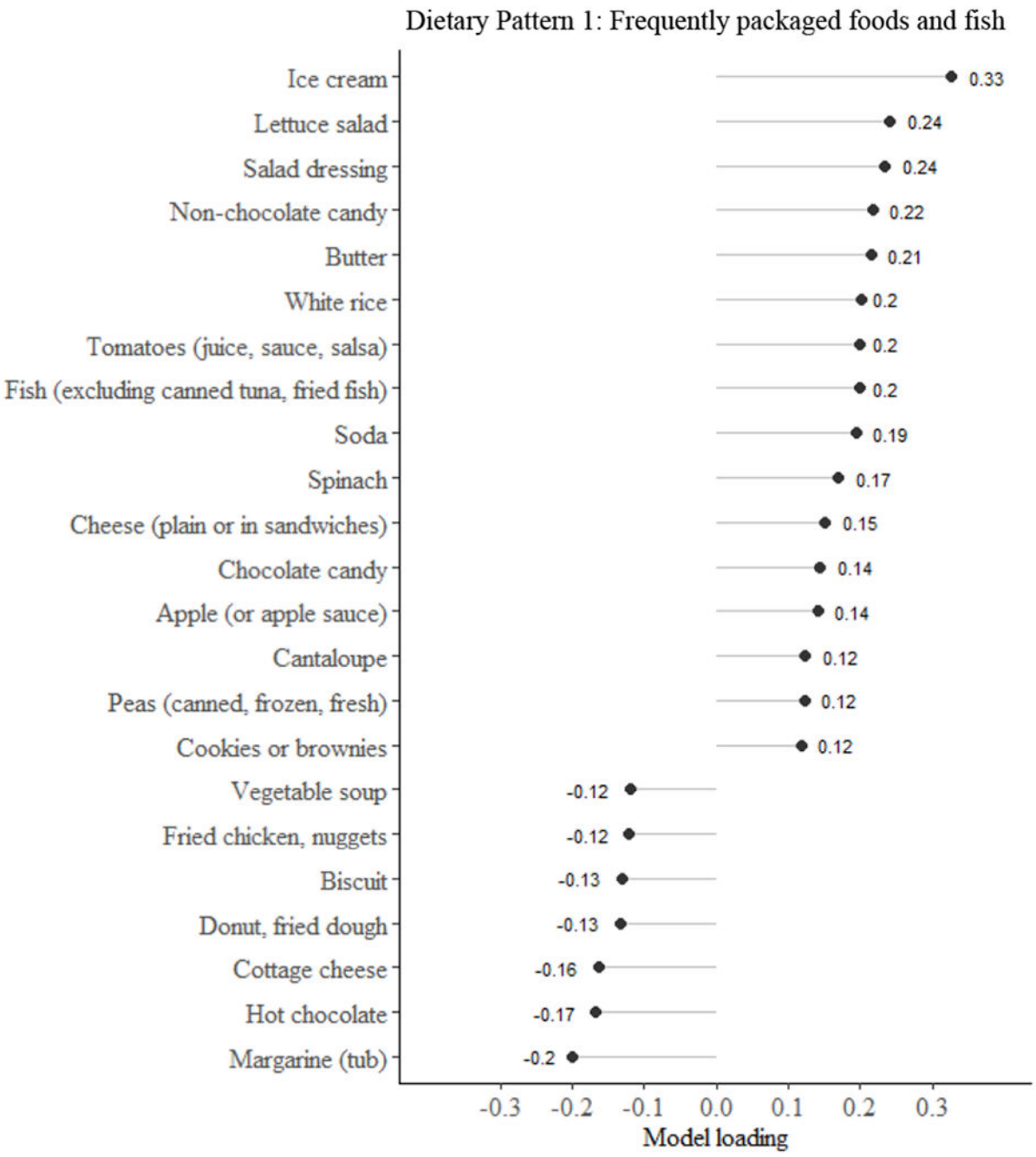

Figure 1.

Food items with highest loadings onto dietary pattern 1 (frequently packaged foods and fish)[a, b]

Abbreviation: PFAS – Per- and polyfluoroalkyl substances

[a] Dietary pattern that explained the most variation in PFAS plasma concentrations in the reduced rank regression analysis

[b] Food items with absolute model loadings in the top 25th percentile are shown

Table 1.

Characteristics of 548 participants from Project Viva, overall and by quartiles of the dietary pattern 1 (frequently packaged foods and fish) score[a] assessed in early childhood

		Dietary pattern 1 score, quartiles[b]			
	Overall N = 548	**Q1 N = 137**	**Q2 N = 137**	**Q3 N = 137**	**Q4 N = 137**
	Median (IQR) or N (%)				
Child characteristics					
Age at dietary assessment (years)	3.1 (0.2)	3.1 (0.2)	3.1 (0.2)	3.1 (0.2)	3.1 (0.2)
Female, N (%)	258 (47)	61 (45)	62 (45)	64 (47)	71 (52)
Race/ethnicity, N (%)					
White	349 (64)	88 (64)	85 (62)	91 (66)	85 (62)
Black	99 (18)	27 (20)	28 (20)	23 (17)	21 (15)
Hispanic	22 (4)	4 (2.9)	4 (2.9)	7 (5.1)	7 (5.1)
Asian	12 (2)	2 (1.5)	3 (2.2)	1 (0.7)	6 (4.4)
Other	66 (12)	16 (12)	17 (12)	15 (11)	18 (13)
Age at PFAS assessment (years)	7.7 (0.8)	7.6 (0.9)	7.7 (0.8)	7.7 (0.8)	7.7 (0.8)
Maternal characteristics					
Age at initial enrollment (years)	32.8 (6.7)	31.7 (7.0)	32.5 (8.1)	33.0 (5.5)	33.6 (5.6)
College graduate, N (%)	378 (69)	84 (61)	89 (65)	105 (77)	100 (73)
Household income, N (%)					
< $40,000/year	87 (16)	22 (16)	25 (18)	22 (16)	18 (13)
$40,000 - $70,000/year	117 (21)	31 (23)	33 (24)	18 (13)	35 (26)
>$70,000/year	344 (63)	84 (61)	79 (58)	97 (71)	84 (61)

Abbreviations: PFAS – Per- and polyfluoroalkyl substance; Q1 – First/lowest quartile; IQR – Interquartile range; PFOS – Perfluorooctane sulfonate; PFOA – Perfluorooctanoate; PFDA – Perfluorodecanoate; PFHxS – Perfluorohexane sulfonate; MeFOSAA – 2-(N-methyl-perfluorooctane sulfonamido) acetate; PFNA – Perfluorononanoate

[a]Factor score corresponding to the dietary pattern that explained the most variation in PFAS plasma concentrations in the reduced rank regression analysis. This score represents the strength of a participant's adherence to dietary pattern 1 (frequently packaged foods and fish), with higher scores representing greater adherence

[b]Quartile minimum and maximum values: Q1 [−2.53,−0.43], Q2 (−0.43,−0.069], Q3 (−0.069, 0.46], Q4 (0.46, 2.6]

Table 2.

Percent change in plasma PFAS concentrations per standard deviation increment in dietary pattern[a] scores obtained from reduced rank regression analysis

	PFOA	PFOS	PFDA	MeFOSAA	PFHxS	PFNA
	% change (95% CI)					
Dietary pattern 1	20.5 (15.4, 25.9)	27.9 (21.0, 35.1)	24.7 (18.6, 31.1)	34.5 (22.5, 47.6)	22.7 (13.7, 32.4)	18.2 (11.8, 24.9)
Dietary pattern 2	−2.1 (−6.6, 2.6)	6.7 (0.7, 13.2)	−11.8 (−16.3, −7.0)	6.3 (−3.5, 17.0)	24.6 (15.5, 34.4)	−9.1 (−14.1, −3.8)
Dietary pattern 3	1.1 (−3.5, 5.9)	1.4 (−4.4, 7.5)	1.8 (−3.5, 7.4)	−14.1 (−21.9, −5.4)	7.6 (−0.4, 16.3)	15.9 (9.6, 22.6)

Abbreviations: PFAS – Per- and polyfluoroalkyl substances; PFOA – Perfluorooctanoate; PFOS – Perfluorooctane sulfonate; PFDA – Perfluorodecanoate; PFHxS – Perfluorohexane sulfonate; MeFOSAA – 2-(N-methyl-perfluorooctane sulfonamido) acetate; PFNA – Perfluorononanoate

[a]Dietary pattern 1: frequently packaged foods and fish; dietary pattern 2: high vegetables and canned tuna; dietary pattern 3: high meat and low vegetables