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Shifting Global Exposures to Poly- and Perfluoroalkyl Substances (PFASs) Evident in Longitudinal Birth Cohorts from a Seafood Consuming Population

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Abstract

Rapid declines in legacy poly- and perfluoroalkyl substances (PFASs) have been reported in human populations globally following changes in production since 2000. However, changes in exposure sources are not well understood. Here, we report serum concentrations of 19 PFASs (19 PFAS) measured in children between 1993 and 2012 from a North Atlantic fishing community (Faroe Islands). Median 19 PFAS concentrations in children (ages 5 to 13 years) peaked in 2000 (47.7 ng mL⁻¹) and declined significantly by 14.4% yr⁻¹ until 2012. Principal component analysis (PCA) identified two groups of PFASs that likely reflect exposures from diverse consumer products and a third group that consisted of perfluorocarboxylic acids (PFCAs) with nine or more carbons (C₉). These C₉ PFASs are strongly associated with mercury in children's hair, a well-established proxy for seafood consumption, especially perfluoroundecanoic acid (PFUnDA, $r = 0.72$). Toxicokinetic modeling shows PFAS exposures from seafood have become increasingly important (53% of perfluorooctane sulfonate: PFOS in 2012), despite a decline in whale consumption in recent years. We infer that even in a major seafood consuming population, declines in legacy PFAS exposure after 2000 were achieved by the rapid phase out of PFOS and its precursors in consumer products. These results emphasize the importance of better understanding exposures to replacement PFASs in these sources.

Graphical Abstract:

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Supporting Information

Additional tables containing summary statistics on all measurements, toxicokinetic model parameters, regression results, and PCA analysis.

Introduction

Poly- and perfluoroalkyl substances (PFASs) are a family of synthetic persistent organic pollutants consisting of over 3000 individual compounds.¹ Human exposure to PFASs has been associated with many adverse health effects including immune suppression, metabolic disruption, cancer, and impaired renal function.^{2, 3} Young children are especially vulnerable to PFAS exposures, and relatively few biomonitoring studies have focused on this demographic.⁴ Exposure sources for PFASs are diverse and include dust, consumer products, drinking water, and aquatic biota (seafood).^{5–8} Understanding their relative importance is critical for explaining temporal trends in human populations and mitigating future risks. In non-occupational settings, some of the highest PFAS serum concentrations have been reported in Inuit men from Greenland who frequently consume seafood.⁹ Here we quantify the changing contribution of seafood consumption to PFAS exposures in children from a North Atlantic fishing community (Faroe Islands).

A main global manufacturer of PFASs, 3M, voluntarily discontinued production of the parent chemical to one of the most prevalent legacy compounds, perfluorooctane sulfonate (PFOS), and its precursors around the year 2000.^{10, 11} The use of PFOS and its precursors in products such as food packaging, outdoor gear, dental floss, new carpet, and furniture coatings was thus phased out by 2002 and replaced with mainly new PFASs.¹ PFOS and other perfluoroalkyl acids (PFAAs), the class of compounds that historically make up the largest contribution of measured PFASs, do not degrade in the environment and have long lifetimes in the ocean and other aquatic systems.^{11–13} This can lead to a temporal lag between declining releases from industrial and consumer sources and exposures from seafood.

Many populations have reported rapid declines (8–12% year⁻¹) in concentrations of legacy PFASs measured in human serum since 2002.^{14–17} Such large decreases are much more rapid than the persistence of PFOS in the environment.^{13, 18} In other seafood consuming populations, a plateau or steady increase in recent years of certain PFASs has been reported.^{19, 20} Variability in exposure sources across populations are likely responsible for these different trajectories.

Prospective birth cohorts were established in the Faroe Islands in the mid-1980s to study health outcomes associated with exposures to environmental toxicants.²¹ Faroese individuals are mainly of Irish and Nordic origin and have similar lifestyles and access to products as

other European countries. A wide-range of PFAS exposures have been measured in this population and some individuals consume North Atlantic pilot whale (*Globicephala melas*) as part of their traditional diet.^{22, 23} As apex predators, pilot whales are sentinels for marine pollution and can thus provide insight into seafood exposures attributable to changing PFAS concentrations in the North Atlantic Ocean.^{13, 24} Past work indicates that PFAS concentrations in drinking water in the Faroes are below detection.²⁵

The main objective of this study is to better understand how PFAS exposures of children from populations that frequently consume seafood have been affected by changes in the use and release of legacy PFASs around the year 2000. We measured concentrations of 19 PFASs in the serum of Faroese children between the ages of 5 and 13 from three birth cohorts between 1993 and 2012. We used dietary survey information and repeated hair mercury (Hg) measurements to reconstruct changes in seafood consumption over time. We combined statistical and toxicokinetic modeling to characterize the effects of age and growth dilution on serum PFAS concentrations and quantify exposures from seafood consumption over time. We use this analysis to infer the relative importance of different PFAS exposure sources before and after the phase-out in production of the parent chemical to PFOS and its precursors.

Methods

Sample selection

We randomly selected 51 children from each of three Faroese birth cohorts (Cohorts 1, 3 and 5) consisting of between 494 and 1022 total individuals for repeated measurements of concentrations of 19 PFASs in serum between 1993 and 2012 (Figure 1). Samples from children at similar ages (5–7 or 13–14 years) were collected over different years for comparison. We analyzed archived serum from individuals in Cohort 1 (born in 1986) collected in 1993 (age 7) and 2000 (age 14). For Cohort 3 (born 1997–1998), we analyzed archived serum collected from children in 2002 (age 5), 2004 (age 7), and 2011 (age 13). For cohort 5 (born in 2007), we analyzed serum from children in 2012 (age 5). Additional details of these birth cohorts can be found elsewhere.²¹

Pilot whales are a large seafood source of PFASs in the Faroe Islands. In previous work, we reported concentrations of PFASs in whale muscle between 1987 and 2013.²⁴ The composition of PFASs in pilot whales is similar to other seafood with the exception of elevated levels of the PFOS precursor, perfluorooctane sulfonamide (FOSA).²⁴ Pilot whales lack the enzyme necessary for metabolism of FOSA, which is converted to PFOS in humans and thus appears similar to other seafood exposure sources.^{26, 27}

Information on seafood consumption for all children was obtained from dietary questionnaires administered to mothers. Prior studies have shown that recall bias can affect the reliability of such surveys, and that total Hg in human hair provides a useful proxy for seafood consumption.^{28, 29} Seafood is the only source of methylmercury exposure for most individuals in Western countries outside occupational settings.^{30, 31} We thus use hair Hg concentrations previously measured in Faroese children as an additional indicator for seafood consumption.²¹ Written and informed consent was obtained from all mothers. The

study protocol was reviewed and approved by the Faroese ethics review committee and the institutional review board at the Harvard T.H. Chan School of Public Health.

Analysis of PFASs in serum

Serum samples were analyzed for 19 PFASs using high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS), as described in Grandjean et al.³² The perfluoroalkyl sulfonic acids (PFASs) measured include: perfluorobutanesulfonic acid (PFBS, four carbon chain length: C-4), perfluorohexanesulfonic acid (PFHxS: C-6), perfluoroheptanesulfonic acid (PFHpS: C-7), branched and linear PFOS (brPFOS, nPFOS: C-8), perfluorodecanesulfonic acid (PFDS: C-10). The perfluoroalkyl carboxylic acids (PFCAs) measured include: perfluorohexanoic acid (PFHxA: C-6), perfluoroheptanoic acid (PFHpA: C-7), perfluorooctanoic acid (PFOA: C-8), perfluorononanoic acid (PFNA: C-9), perfluorodecanoic acid (PFDA: C-10), perfluoroundecanoic acid (PFUnDA: C-11), perfluorododecanoic acid (PFDoA: C-12). The neutral precursors measured include: branched and linear FOSA (brFOSA, nFOSA: C-8), N-methyl perfluorooctane sulfonamidoacetic acid (MeFOSAA: C-8), and N-ethylperfluorooctane sulfonamidoacetic acid (EtFOSAA: C-8). Detection limits (DLs) for each compound are provided in the Supporting Information (SI) Table S1.

Serum was separated from blood by spinning at 2000 g for 10 min after allowing to clot for approximately 30 minutes. All samples were stored at -80°C until analysis. A 150 μL serum sample was pipetted into a 2 mL centrifuge tube and spiked with isotopically-labeled PFAS mixture as an internal standard for quantification (30 μL , 50 ng mL^{-1} for PFOS and 20 ng mL^{-1} for other PFASs, Wellington Laboratories, Canada). The sample was diluted with 120 μL of methanol and whirl mixed. Calibration solutions were prepared in serum from newborn calves (Biological Industries, Israel) because it matches the matrix of human serum. Calibration solutions spanned a concentration range from 0.050 to 100 ng PFASs mL^{-1} serum for all analytes. Both calibration solutions and samples were centrifuged at 21,000 g for 20 minutes. The supernatant, constituting approximately 160 μL , was transferred to a polypropylene autosampler vial. Formic acid (400 μL , 0.1 M) was added and the solution, mixed on a whirl mixer, and placed in the autosampler for injection into the chromatographic system consisting of a Thermo Scientific EQuan MAX system connected to a TSQ Quantum Ultra tandem mass spectrometer (Thermo Fisher Scientific, San Jose, CA, USA).

PFASs were extracted by online-solid phase extraction and the chromatographic separation was performed using a Betasil C8 column 50 mm $\times$ 2.1 mm (3 μm particles) (Thermo Fisher Scientific, San Jose, CA, USA). Each batch of samples was analyzed with procedural blanks, quality control samples, and a calibration curve. Detection limits (DLs) ranged from 0.03 to 0.1 ng mL^{-1} (Table S1). Within-batch and between-batch coefficient of variations for samples run in duplicate were lower than 8.9% and 12.9%, respectively, for all analytes.

Statistical analysis

All statistical analyses were performed in R version 3.3.3. Seven compounds (PFBS, PFDS, PFBA, PFPeA, PFHxA, PFDoA, FOSA) were infrequently detected. Detection frequencies

for the remaining 10 compounds were all greater than 75% over the study period (Table S1). For samples that contained compounds below the detection-limit (DL), non-detects were replaced by $DL/\sqrt{2}$.

Repeated measurements in a single child can lead to correlations that violate assumptions of independence in a traditional regression model. We thus used a marginal regression model for each compound when testing for significant trends as implemented by the R package, *geepack*. We log transformed all concentration and assumed an auto-regressive covariance matrix, which allows for correlation between repeated measurements within individuals to decrease exponentially in time. We included covariates to control for age and weight. We also included hair Hg concentrations as an additional covariate to control for the variability in total seafood consumption across individuals. As an additional control for the effects of age we performed a stratified analysis using standard linear regressions on children at ages 5 years and 13–14 years.

In our prior work, we found that composition of PFASs in human sera can provide useful information on dominant exposure sources.³³ We used principal component analysis (PCA) on serum PFAS concentrations measured in children to identify characteristic groupings of different PFASs. These groupings reflect PFASs that co-occur in the exposure matrix and provide insight into how predominant sources have changed over time. We used PCA coupled with varimax rotation in the R package, *psych*³⁴ to analyze the covariance matrix of the PFAS concentration profiles. An eigenvalue greater than one was used to determine the number of principal components.

Toxicokinetic model

Single compartment toxicokinetic models for PFOS and PFNA have been shown to accurately reproduce concentrations measured in human serum.^{35, 36} We developed a toxicokinetic model for PFOS, PFNA and FOSA to diagnose factors contributing to temporal changes in PFAS exposures from seafood for individual children. Reliable toxicokinetic parameters have not been established for other PFASs that showed a strong relationship to seafood consumption. Toxicokinetic modeling allows us to control for varying ages, elimination rates, body weights, seafood consumption rates, and PFAS concentrations in pilot whale tissue. We modeled PFOS, PFNA and FOSA in Faroese children based on first-order elimination rates measured in retired fluorochemical factory workers (PFOS = 4.87 years),³⁷ and urinary clearance rates (PFNA = 4.63 years).^{38, 39} We used a distribution volume of 230 mL kg⁻¹ for PFOS and 170 mL kg⁻¹ for PFNA.^{35, 38} Absorption efficiencies for PFOS, FOSA, and PFNA were all parameterized as 0.91, based on previous work.^{40–42} Temporal changes in PFAS concentrations in pilot whales were based on measurements reported in Dassuncao et al.²⁴ We assumed that 31% of absorbed FOSA is immediately converted to PFOS in humans, which has been established as a likely lower bound in prior work.⁴³

We estimated the contribution of pilot whale consumption to overall PFAS burden by comparing modeled exposures at each time period to total measured serum concentrations. For PFOS, we also modeled exposures due to biotransformation of ingested FOSA in pilot whale meat. We quantified seafood consumption magnitudes on an individual level using

measured hair Hg concentrations as a proxy for seafood ingestion and a well-established one-compartment model for methylmercury developed by the United States Environmental Protection Agency (US EPA).⁴⁴ Blood to hair partitioning, assimilation efficiencies and other parameters were modeled following the US EPA's reference dose calculation for methylmercury.⁴⁴ We obtained blood volume from allometric equations for children.⁴⁵ Concentrations of methylmercury in whale meat were based on repeated measurements (mean: $1.3 \mu\text{g g}^{-1}$) that showed no statistically significant changes over the past three decades.⁴⁶ Dietary survey data indicate children begin eating whale meat at 18 months of age, which we use in our model. A complete description of all model equations and parameters is provided in Table S2.

Results

Serum PFAS composition in children

The sum of 19 PFASs ($\Sigma 19$ PFAS) measured in the serum of children (ages 5 to 13) in the most recent years (2011–2012) was lower than all prior years (1993–2005) (Figure 2A). Peak serum concentrations of $\Sigma 19$ PFAS were measured in 2000 (median 47.7 ng mL^{-1}) and fell to a low of 8.7 ng mL^{-1} by 2012, an average decline of 14.4% per year. This decline can be primarily attributed to large decreases in the legacy PFASs, PFOS and PFOA in serum (Figure 2B, Table S1).

Across all years, PFOS accounted for the largest fraction (54% - 74%) of the Σ PFASs in serum, followed by PFOA (11–24%). Contributions to $\Sigma 19$ PFAS exposure in children from PFCA with nine or more carbon atoms ($\text{C} \geq 9$) increased over time (Figure 2A). For example, PFNA increased from 2% of $\Sigma 19$ PFAS in 1993 to 10% in 2012. The other 11 PFASs accounted for 5% of the $\Sigma 19$ PFAS across all years. Linear PFOS isomers ranged between a low of 51% in 2000 and a high of 66% in 2011 (Table S1). Linear isomers made up 73% of serum FOSA in 1993, the only year with a high (100%) detection frequency. While FOSA was only detected in 31% of children in 2011, all of those children had almost exclusively linear isomers present (>98%). Medians, interquartile ranges, and detection frequencies for all measured compounds are presented in Table S1.

Effects of variability in age, seafood consumption and body mass

Results of regression modeling (Table 1) reveal age is a significant covariate for serum concentrations of three compounds (PFOS, PFUnDA, MeFOSAA). Both PFOS and PFUnDA have long half-lives in the human body³⁸ and thus accumulate more in the 13-year old children compared to those at five years of age. Regression coefficients suggest that for each year of age, serum concentrations increased by 15% for PFOS and 22% for PFUnDA.

Serum concentrations of the PFOS precursor, MeFOSAA, were significantly higher in children at age 5 compared to age 13 (Table 1). In 2012, MeFOSAA was frequently detected in 78% of children at age 5 but only 2% of those at age 13 (Figure 2B, Table S1). This difference may indicate an exposure source to MeFOSAA in children age 5 that is not present for children age 14.

Log-linear regression modeling results showed seafood consumption, as indicated by hair Hg concentrations, is significantly correlated with serum concentrations of PFHpS, PFOS, and the C 9 PFCAs (Table 1). For each doubling of hair Hg, we found an 11% to 27% increase in serum PFAS. This is consistent with the high levels of PFOS and C 9 PFCAs reported in pilot whales from the Faroe Islands.²⁴

Body mass of children was negatively associated with the serum concentrations of PFHxS, PFOS, and PFOA (Table 1). For each 10% increase in weight, declines in these PFASs ranged between 3.3–4.9%, likely indicating the effects of growth dilution.

Temporal trends of PFASs in children's serum

After controlling for age, weight, and seafood consumption (hair-Hg), most PFASs declined significantly between 2000 to 2012 based on log-linear marginal regression models. Exceptions included PFDS (not significant) and PFDA (increase of 0.9% yr⁻¹, $p=0.05$) (Table 1). As an additional test for the influence of age on temporal trends, we conducted a stratified regression analysis for children at ages 5 years and 13–14 years. Results reveal that the annual declines in serum PFAS concentrations are similar to the corrected log-linear marginal regression model when isolating each age category (Table S3, Table S4).

The two most prevalent compounds in children's serum prior to 2000, PFOS and PFOA, declined more rapidly (13–14% yr⁻¹) than other PFCAs and PFASs after controlling for age, weight and seafood consumption (Table 1). Changes in serum concentrations for longer chain PFASs that are more abundant in seafood such as PFNA and PFDA were relatively smaller, ranging from a significant increase of 0.9 % yr⁻¹ to a decrease of 1.1 % yr⁻¹ between 2000 and 2012. Exposures to PFUnDA decreased by 5.7% yr⁻¹ after controlling for covariates.

Among all PFASs detected, the short-lived precursor compounds (EtFOSAA, MeFOSAA, and FOSA) declined most rapidly in serum (by up to 28% yr⁻¹) between 2000 and 2012 (Figure 2B and Table 1). These precursor compounds are known to biotransform *in vivo* and therefore only represent short-term exposures.^{47, 48} The detection frequency of these compounds also declined over time from 100% in 1993 to as low as 2–6% in the most recent years, consistent with a reduction in exposures (Table S1).

Temporal clustering of PFASs

Principal component analysis reveals three distinct groupings of the PFASs measured in this study that explain 70% of the variability in serum concentrations in children (Figure 3A). The first component explains 31% of the variability and includes legacy PFASs and their precursors (PFOS, FOSA, PFHpS, and EtFOSAA with loadings of 0.81–0.85) and to a lesser extent PFHxS (0.47). The second component explains 21% of the variability in serum PFAS composition and includes C 9 PFCAs (loadings: PFNA=0.81, PFDA=0.96, PFUnDA=0.76). The third component explains 18% of the variability in serum PFAS concentrations and consists of PFHpA, PFOA, and MeFOSAA.

Along the first and third components, distinct clusters are apparent based on measurement years (Figure 3B). Movement of the clusters over time reflects a shift in exposures away

from the first component representing the legacy PFASs and their precursors. Loadings increased along the third component from 1993 until a peak in 2003, followed by a decrease through 2012. Spread of the data points along the first and third components shown in Figure 3 reflects variability in exposure profiles across children. A decrease in this variability is evident over time, suggesting a reduction in the number of exposure sources as represented by PFASs in the first and third components (Figure 3B).

Unlike components one and three, the second component consisting of C 9 PFASs does not show distinct clustering by year. Instead, clustering is dominated by whether or not a child reported consuming pilot whale (Figure 4A). Children who showed elevated loadings for both components one and two (first quadrant) identified as eating pilot whales. Supporting this finding, we find strong correlations between the C 9 PFCA that comprise the second component, particularly PFUnDA, and hair Hg levels ($r = 0.72$, Figure 4B). These observations suggest that the second component is driven by PFAS exposures from pilot whale and other seafood consumption.

Modeled contributions of pilot whale to children's PFAS exposure

Repeated measurements of hair Hg in children indicate a decline in whale meat consumption over time among Faroese children (Table S1). Children who identified as eating pilot whale had higher levels of Hg in hair compared to those who did not across all years (Figure 5A). For both groups, hair Hg levels decreased over time indicating a decline in overall seafood consumption. Among children who reported consuming pilot whale, median hair Hg levels declined by 82% between 1993 (5.7 ng g^{-1}) and 2012 (0.98 ng g^{-1}). Additionally, the number of children who were identified as eating pilot whale decreased across the cohorts (Table S1).

Figure 5B shows the decrease in modeled pilot whale consumption by children at different ages based on measured concentrations of Hg in their hair and toxicokinetic modeling (Figure 5A). Among pilot whale consumers, modeled consumption by children at age 7 years declined from $0.28 \text{ g kg}^{-1} \text{ day}^{-1}$ in 1993 to $0.08 \text{ g kg}^{-1} \text{ day}^{-1}$ in 2013. Modeled consumption rates for children who did not report consuming whale meat were much smaller and remained unchanged over time. Hg exposures for individuals who did not report consuming pilot whale are likely from other seafood and/or unreported intermittent pilot whale consumption.

Exposures to PFOS from pilot whale decreased over time for all ages, while PFNA exposure remained steady (age 5, 1991–2012) or increased (age 14, 2000–2012) (Figures 5C and 5D). These results emphasize that increasing levels of PFNA in pilot whale muscle²⁴ have been counteracted by decreasing consumption, stabilizing PFNA exposures (Figure 2B). Without these decreases in whale consumption, PFNA exposures would have increased over time in Faroese children.

Despite high rates of seafood consumption, non-seafood sources of PFASs dominated the exposure profiles for all Faroese children between 1993 and 2012. Figure 5E shows the median contribution of pilot whale to overall PFOS exposure in pilot whale consumers increased from 18% in 2000 (Cohort 1, age 13) to 53% in 2011 (Cohort 5, age 14).

Biotransformation of the neutral precursor to PFOS, FOSA, from pilot whale tissue contributed between 45% (2012) and 72% (2005) of the modeled PFOS in serum. Model results (Figure 5F) show pilot whale consumption accounted for a steady fraction of PFNA exposure (11%) for children age 5 and 24–28% for children age 13–14 over this period.

Discussion

Even in this remote population of frequent seafood consumers, rapid declines in the 19 PFASs measured in children's serum between 1993 and 2012 reported here parallel those reported in other parts of the world. Similar declines have been reported in children from the U.S. east coast,⁴⁹ women from the U.S. west coast,¹⁷ Swedish primiparous women,⁵⁰ the general Australian population,¹⁶ and Norwegian Men.⁵¹ These findings emphasize the global benefits for human exposure of the phase out in production of PFOS around the year 2000 and the PFOA stewardship initiatives in the United States and European Union around 2006. Despite large declines in PFOS and PFOA, the entire suite of 19 legacy PFASs was still detectable in children from the Faroe Islands in 2012.

Both statistical analysis and toxicokinetic modeling confirm that the observed decline in 19 PFAS from Faroese children was not driven by changes in seafood consumption or shifting temporal concentrations in pilot whale meat (Table 1, Figure 5). Dassuncao et al.²⁴ found increasing levels of long-chained PFCAs in pilot whales from the Faroe Islands over the same time period as serum collected from children in this study. Hair Hg concentrations and toxicokinetic modeling reveal whale meat consumption among Faroese children aged 7 dropped by 71% between 1993 and 2012. However, the fraction of PFAS exposure from seafood increased (PFOS) or remained steady (PFNA) over the study period, indicating that other exposure sources were responsible for the measured decline in serum PFAS levels in children.

This inference is supported empirically by the findings of our statistical analyses (Table 1, Figure 4). No discernable temporal patterns are apparent in the second component of the PCA, consisting of C 9 PFCAs, but we observed distinct clustering based on whether or not a child was identified as a pilot whale consumer. C 9 PFCAs have increased bioaccumulation potential and have been associated with seafood consumption in several previous studies.^{7, 52} Additionally, each C 9 PFCA was significantly associated with hair-Hg levels in regression modeling (Table 1). In particular, PFUnDA is highly correlated with hair Hg ($r = 0.72$) and thus may be the best tracer of seafood consumption (Figure 4B). This would explain why the highest levels of PFUnDA (and other C 9 PFCAs) measured in serum that are reported in the literature are from high seafood consuming populations in Asia.⁵³ Similarly, Hu et al. (2018) noted that reported frequency of fish and shellfish consumption was positively associated with an increase in PFNA in the U.S. National Health and Nutrition Examination Survey (NHANES) for 2005–06 and a cohort of pregnant women in Vancouver, Canada. Positive associations between seafood consumption and serum concentrations of other C 9 PFASs, including PFUnDA, have also been reported for NHANES data between 2007 and 2014.⁷

In prior work, we found a substantial change in the composition of PFASs in pilot whales from 1986 to 2013 driven mainly by a large decrease in FOSA.²⁴ Serum data from Faroese children show a temporal decline in the detection frequency of FOSA from 100% in 1993 to 6–31% in recent years. In the most recent years, all children with detectable FOSA were identified as pilot whale consumers by their mothers. Furthermore, the FOSA in all of these children was almost exclusively made up of linear isomers (>98%), which is similar to the isomer composition found in pilot whales.²⁴ This demonstrates that pilot whale acts as an ongoing exposure source for FOSA despite the phase-out in production of its parent chemical in North America and illustrates the lag-time associated with environmental exposure sources.

The composition of PFASs in children's sera combined with results of toxicokinetic modeling point to the increasing importance of seafood as a source of exposure to legacy PFASs for Faroese children. There are no known manufacturing sources of PFASs in the Faroe Islands and previous work reported that concentrations in drinking water from 2011/2012 are below detection.²⁵

Rapid observed declines in serum PFAS concentrations in Faroese children following the global production shifts that occurred around the year 2000 are consistent with rapid changes in PFAS exposures from short-lived consumer products used in the indoor environment. Evidence for this can be seen in the temporal shifts in the first and third component of the PCA shown in Figure 3. The first component contains PFOS, FOSA, PFHpS, and EtFOSAA, which are all based on perfluorooctane sulfonyl fluoride (POSF) chemistries that were phased-out by 3M in 2000.¹¹ PFOS and PFHpS were marketed under the label Fluorad™, which was used in a variety of products including fire-extinguishing foams, as surfactants in various industrial processes, coatings, carpet cleaners, and insecticides.⁴³ EtFOSAA is an intermediate degradation product of volatile PFOS precursors, including phosphate esters of EtFOSE.^{54, 55} These were the building blocks of ScotchBan™, used in food contact paper.⁴³ Other studies have reported that between 2002 and 2008, concentrations of EtFOSE in indoor air and dust of Canadian homes declined by 93% and 89%, respectively.^{56, 57}

Rapid temporal changes in serum PFAS composition of Faroese children are also captured by shifts in the third component of the PCA shown in Figure 3. The third component includes PFHpA, PFOA and MeFOSAA. PFHpA is found as a common impurity in PFOA-based products, and both compounds can result from degradation of fluorotelomer alcohols and other precursors used in various consumer products.¹ The 2006 PFOA stewardship program initiated the phase-out of PFOA and longer chained PFCAs by 2015. We see a decline in PFHpA and PFOA begin during this period indicating a quick removal of exposure sources consistent with that of consumer products. We do not see a similar decline in C₉ PFCAs, which were also phased-out, because of the much longer time-scales of response for the marine environment. Unlike the C₉ PFCAs, PFOA and PFHpA do not bioaccumulate to such a degree and are present in very low levels in pilot whales.^{24, 58}

MeFOSAA is an intermediate degradation product of the volatile PFOS precursor, MeFOSE, a primary ingredient in Scotchgard™ used in textile and carpet treatments.⁴³ We therefore

hypothesize that elevated levels of MeFOSAA in Faroese children at age 5 compared to age 13 reflect higher exposure from hand-to-mouth contact from Scotchgard™ treated carpets (Table 1, Table S1, Figure 2B). The Faroese children at age 5 measured here were sampled in 2005, which is around the same time as a major shift in the exposures to the legacy PFCAs in component 3 (PFOA and PFHpA) that were driven by changes in production. We thus postulate that similar temporal trajectories in MeFOSAA, PFOA, and PFHpA occur for different reasons and results in their common grouping in component 3 of the PCA. Specifically, the grouping of MeFOSAA into component 3 reflects an age-effect associated with carpet contact that persists despite the earlier shifts in production of the other consumer related compounds based on POSF chemistries from component 1.

Using our integrated approach for evaluating changing PFAS profiles in serum, we find that seafood intake did not drive rapid observed declines in 19 PFAS levels in Faroese children between 1993 and 2012 but remained a substantial source of exposure. Multivariate statistical analyses on 19 PFAS concentrations in serum from Faroese children show consistent decreases in PFASs targeted by the regulatory phase-out of PFOS and related products after 2000 as well as the later decline in PFCAs targeted by the PFOA stewardship program. Our findings suggest that product phase-outs have successfully lowered exposures to legacy PFASs in this population confirming recent modeling efforts for the American and Australian populations.⁵⁹

Despite the decline in some legacy PFASs measured in this study, many new PFASs have been introduced to the market as replacement compounds following the phase out in POSF production.¹ Data characterizing the chemical structures of these new PFASs as well as chemical standards required to facilitate detection are limited. Therefore, total fluorine (TF) and extractable organic fluorine (EOF) measurements are needed to provide additional insight into trends in overall exposures to PFASs.⁶⁰ For example, serum measurements from China in 2004 showed that legacy PFASs only accounted for 30–70% of EOF. Similarly, detectable PFASs accounted for approximately 30% of EOF measured in dolphin and porpoise livers in Hong Kong.⁶¹

Although seafood has historically been a relatively small fraction of exposure, the marine environment takes much longer to respond to changes in PFAS production than consumer products manufacturing.¹³ Seafood-consuming populations may thus continue to be exposed to legacy PFASs that have already been associated with adverse health outcomes for the foreseeable future. This study demonstrates the usefulness of an integrative toxicokinetic approach for investigating how changes in the use and release of different PFASs have affected exposures of children from populations that frequently consume seafood.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Wang Z; DeWitt JC; Higgins CP; Cousins IT, A Never-Ending Story of Per- and Polyfluoroalkyl Substances (PFASs)? *Environ Sci Technol* 2017, 51, (5), 2508–2518. [PubMed: 28224793]
2. Rappazzo KM; Coffman E; Hines EP, Exposure to Perfluorinated Alkyl Substances and Health Outcomes in Children: A Systematic Review of the Epidemiologic Literature. *Int J Environ Res Public Health* 2017, 14, (7), 691–712.
3. ATSDR Toxicological Profile for Perfluoroalkyls; Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services, Public Health Service: Atlanta, GA, 2015.
4. Winkens K; Vestergren R; Berger U; Cousins IT, Early life exposure to per- and polyfluoroalkyl substances (PFASs): A critical review. *Emerging Contaminants* 2017, 3, (2), 55–68.
5. Vestergren R; Berger U; Glynn A; Cousins IT, Dietary exposure to perfluoroalkyl acids for the Swedish population in 1999, 2005 and 2010. *Environ Int* 2012, 49, 120–7. [PubMed: 23018201]
6. Hu XC; Andrews DQ; Lindstrom AB; Bruton TA; Schaider LA; Grandjean P; Lohmann R; Carignan CC; Blum A; Balan SA; Higgins CP; Sunderland EM, Detection of Poly- and Perfluoroalkyl Substances (PFASs) in U.S. Drinking Water Linked to Industrial Sites, Military Fire Training Areas, and Wastewater Treatment Plants. *Environ Sci Technol Lett* 2016, 3, (10), 344–350. [PubMed: 27752509]
7. Christensen KY; Raymond M; Blackowicz M; Liu Y; Thompson BA; Anderson HA; Turyk M, Perfluoroalkyl substances and fish consumption. *Environ Res* 2017, 154, 145–151. [PubMed: 28073048]
8. Schaider LA; Balan SA; Blum A; Andrews DQ; Strynar MJ; Dickinson ME; Lunderberg DM; Lang JR; Peaslee GF, Fluorinated Compounds in U.S. Fast Food Packaging. *Environmental Science & Technology Letters* 2017, 4, (3), 105–111. [PubMed: 30148183]
9. Lindh CH; Rylander L; Toft G; Axmon A; Rignell-Hydbom A; Giwercman A; Pedersen HS; Goalczyk K; Ludwicki JK; Zvezday V; Vermeulen R; Lenters V; Heederik D; Bonde JP; Jonsson BA, Blood serum concentrations of perfluorinated compounds in men from Greenlandic Inuit and European populations. *Chemosphere* 2012, 88, (11), 1269–75. [PubMed: 22494529]
10. Armitage JM; Schenker U; Sceringer M; Martin JW; Macleod M; Cousins IT, Modeling the Global Fate and Transport of Perfluorooctane Sulfonate (PFOS) and Precursor Compounds in Relation to Temporal Trends in Wildlife Exposure. *Environ Sci Technol* 2009, 43, 9274–9280. [PubMed: 20000520]
11. Wang Z; Boucher JM; Scheringer M; Cousins IT; Hungerbuhler K, Toward a Comprehensive Global Emission Inventory of C4-C10 Perfluoroalkanesulfonic Acids (PFASs) and Related Precursors: Focus on the Life Cycle of C8-Based Products and Ongoing Industrial Transition. *Environ Sci Technol* 2017, 51, (8), 4482–4493. [PubMed: 28323424]
12. Wang Z; Cousins IT; Scheringer M; Buck RC; Hungerbuhler K, Global emission inventories for C4-C14 perfluoroalkyl carboxylic acid (PFCA) homologues from 1951 to 2030, Part I: production and emissions from quantifiable sources. *Environ Int* 2014, 70, 62–75. [PubMed: 24932785]
13. Zhang X; Zhang Y; Dassuncao C; Lohmann R; Sunderland EM, North Atlantic Deep Water formation inhibits high Arctic contamination by continental perfluorooctanesulfonate discharges. *Global Biogeochemical Cycles* 2017, 31, 1332–1343.
14. Bjerregaard-Olesen C; Bach CC; Long M; Ghisari M; Bossi R; Bech BH; Nohr EA; Henriksen TB; Olsen J; Bonefeld-Jorgensen EC, Time trends of perfluorinated alkyl acids in serum from Danish pregnant women 2008–2013. *Environ Int* 2016, 91, 14–21. [PubMed: 26891270]
15. Gebbink WA; Glynn A; Berger U, Temporal changes (1997–2012) of perfluoroalkyl acids and selected precursors (including isomers) in Swedish human serum. *Environ Pollut* 2015, 199, 166–73. [PubMed: 25660070]
16. Eriksson U; Mueller JF; Toms LL; Hobson P; Karrman A, Temporal trends of PFASs, PFCAs and selected precursors in Australian serum from 2002 to 2013. *Environ Pollut* 2017, 220, (Pt A), 168–177. [PubMed: 27726977]

17. Hurley S; Goldberg D; Wang M; Park JS; Petreas M; Bernstein L; Anton-Culver H; Nelson DO; Reynolds P, Time Trends in Per- and Polyfluoroalkyl Substances (PFASs) in California Women: Declining Serum Levels, 2011–2015. *Environ Sci Technol* 2018, 52, (1), 277–287. [PubMed: 29198103]
18. Weber AK; Barber LB; LeBlanc DR; Sunderland EM; Vecitis CD, Geochemical and Hydrologic Factors Controlling Subsurface Transport of Poly- and Perfluoroalkyl Substances, Cape Cod, Massachusetts. *Environ Sci Technol* 2017, 51, (8), 4269–4279. [PubMed: 28285525]
19. Okada E; Kashino I; Matsuura H; Sasaki S; Miyashita C; Yamamoto J; Ikeno T; Ito YM; Matsumura T; Tamakoshi A; Kishi R, Temporal trends of perfluoroalkyl acids in plasma samples of pregnant women in Hokkaido, Japan, 2003–2011. *Environ Int* 2013, 60, 89–96. [PubMed: 24013022]
20. Nost TH; Vestergren R; Berg V; Nieboer E; Odland JO; Sandanger TM, Repeated measurements of per- and polyfluoroalkyl substances (PFASs) from 1979 to 2007 in males from Northern Norway: assessing time trends, compound correlations and relations to age/birth cohort. *Environ Int* 2014, 67, 43–53. [PubMed: 24657493]
21. Weihe P; Debes Joensen H, Dietary recommendations regarding pilot whale meat and blubber in the Faroe Islands. *International Journal of Circumpolar Health* 2012, 71, (1), 18594. [PubMed: 22789518]
22. Weihe P; Kato K; Nielsen F; Wanigatunga AA; Needham LL; Grandjean P, Serum Concentrations of Polyfluoroalkyl Compounds in Faroese Whale Meat Consumers. *Environ Sci Technol* 2008, 42, 6291–6295. [PubMed: 18767701]
23. Grandjean P; Anderson EW; Budtz-Jorgensen E; Nielsen F; Molbak K; Weihe P; Heilmann C, Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. *Jama* 2012, 307, (4), 391–397. [PubMed: 22274686]
24. Dassuncao C; Hu XC; Zhang X; Bossi R; Dam M; Mikkelsen B; Sunderland EM, Temporal Shifts in Poly- and Perfluoroalkyl Substances (PFASs) in North Atlantic Pilot Whales Indicate Large Contribution of Atmospheric Precursors. *Environ Sci Technol* 2017, 51, (8), 4512–4521. [PubMed: 28350446]
25. Eriksson U; Karrman A; Rotander A; Mikkelsen B; Dam M, Perfluoroalkyl substances (PFASs) in food and water from Faroe Islands. *Environ Sci Pollut Res Int* 2013, 20, (11), 7940–8. [PubMed: 23589272]
26. Letcher RJ; Chu S; McKinney MA; Tomy GT; Sonne C; Dietz R, Comparative hepatic in vitro depletion and metabolite formation of major perfluorooctane sulfonate precursors in Arctic polar bear, beluga whale, and ringed seal. *Chemosphere* 2014, 112, 225–31. [PubMed: 25048910]
27. Galatius A; Bossi R; Sonne C; Riget FF; Kinze CC; Lockyer C; Teilmann J; Dietz R, PFAS profiles in three North Sea top predators: metabolic differences among species? *Environ Sci Pollut Res Int* 2013, 20, (11), 8013–20. [PubMed: 23532533]
28. Li M; von Stackelberg K; Rheinberger CM; Hammitt JK; Krabbenhoft DP; Yin R; Sunderland EM, Insights from mercury stable isotopes into factors affecting the internal body burden of methylmercury in frequent fish consumers. *Elementa: Science of the Anthropocene* 2016, 4, 000103.
29. Kirk LE; Jorgensen JS; Nielsen F; Grandjean P, Public health benefits of hair-mercury analysis and dietary advice in lowering methylmercury exposure in pregnant women. *Scandinavian Journal of Public Health* 2017, 45, 444–451. [PubMed: 28381203]
30. Sunderland EM, Mercury exposure from domestic and imported estuarine and marine fish in the U.S. seafood market. *Environ Health Perspect* 2007, 115, (2), 235–42. [PubMed: 17384771]
31. Mahaffey KR; Sunderland EM; Chan HM; Choi AL; Grandjean P; Marien K; Oken E; Sakamoto M; Schoeny R; Weihe P; Yan CH; Yasutake A, Balancing the benefits of n-3 polyunsaturated fatty acids and the risks of methylmercury exposure from fish consumption. *Nutr Rev* 2011, 69, (9), 493–508. [PubMed: 21884130]
32. Grandjean P; Heilmann C; Weihe P; Nielsen F; Mogensen UB; Budtz-Jorgensen E, Serum Vaccine Antibody Concentrations in Adolescents Exposed to Perfluorinated Compounds. *Environmental Health Perspectives* 2017, 125, (7).

33. Hu XC; Dassuncao C; Zhang X; Grandjean P; Weihe P; Webster GM; Nielsen F; Sunderland EM, Can profiles of poly- and Perfluoroalkyl substances (PFASs) in human serum provide information on major exposure sources? *Environ Health* 2018, 17, (1), 11. [PubMed: 29391068]
34. Revelle W psych: Procedures for Personality and Psychological Research, 1.7.3; Northwestern University, Evanston, Illionoid, USA, 2017.
35. Egeghy PP; Lorber M, 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* 2011, 21, (2), 150–68. [PubMed: 20145679]
36. Hansen S; Vestergren R; Herzke D; Melhus M; Evenset A; Hanssen L; Brustad M; Sandanger TM, 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* 2016, 94, 272–82. [PubMed: 27286038]
37. Olsen GW; Burris JM; Ehresman DJ; Froehlich JW; Seacat AM; Butenhoff JL; Zobel LR, Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. *Environ Health Perspect* 2007, 115, (9), 1298–305. [PubMed: 17805419]
38. Zhang Y; Beesoon S; Zhu L; Martin JW, Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. *Environ Sci Technol* 2013, 47, (18), 10619–27. [PubMed: 23980546]
39. Zhou Z; Shi Y; Vestergren R; Wang T; Liang Y; Cai Y, Highly elevated serum concentrations of perfluoroalkyl substances in fishery employees from Tangxun lake, china. *Environ Sci Technol* 2014, 48, (7), 3864–74. [PubMed: 24588690]
40. Trudel D; Horowitz L; Wormuth M; Scheringer M; Cousins IT; Hungerbuhler K, Estimating consumer exposure to PFOS and PFOA. *Risk Anal* 2008, 28, (2), 251–69. [PubMed: 18419647]
41. Vestergren R; Cousins IT; Trudel D; Wormuth M; Scheringer M, Estimating the contribution of precursor compounds in consumer exposure to PFOS and PFOA. *Chemosphere* 2008, 73, (10), 1617–24. [PubMed: 18834614]
42. Gebbink WA; Berger U; Cousins IT, Estimating human exposure to PFOS isomers and PFCA homologues: the relative importance of direct and indirect (precursor) exposure. *Environ Int* 2015, 74, 160–9. [PubMed: 25454233]
43. Martin JW; Asher BJ; Beesoon S; Benskin JP; Ross MS, PFOS or PreFOS? Are perfluorooctane sulfonate precursors (PreFOS) important determinants of human and environmental perfluorooctane sulfonate (PFOS) exposure? *J Environ Monit* 2010, 12, (11), 1979–2004. [PubMed: 20944836]
44. Rice DC; Schoeny R; Mahaffey K, Methods and Rationale for Derivation of a Reference Dose for Methylmercury by the U.S. EPA. *Risk Analysis* 2003, 23, (1), 107–115. [PubMed: 12635727]
45. Raes A; Van Aken S; Craen M; Donckerwolcke R; Vande Walle J, A reference frame for blood volume in children and adolescents. *BMC Pediatr* 2006, 6, 3. [PubMed: 16503982]
46. Nielsen ST; Mortensen R; Hoydal K; Erenbjerg SV; Dam M AMAP Faroe Islands Heavy Metals and POPs Core Programme 2009–2012; Environment Agency: Faroe Islands, 2014.
47. Ross MS; Wong CS; Martin JW, Isomer-specific biotransformation of perfluorooctane sulfonamide in Sprague-Dawley rats. *Environ Sci Technol* 2012, 46, (6), 3196–203. [PubMed: 22339592]
48. Benskin JP; Holt A; Martin JW, Isomer-Specific Biotransformation Rates of a Perfluorooctane Sulfonate (PFOS)-Precursor by Cytochrome P450 Isozymes and Human Liver Microsomes. *Environ Sci Technol* 2009, 43, 8566–8572. [PubMed: 20028053]
49. Harris MH; Rifas-Shiman SL; Calafat AM; Ye X; Mora AM; Webster TF; Oken E; Sagiv SK, Predictors of Per- and Polyfluoroalkyl Substance (PFAS) Plasma Concentrations in 6–10 Year Old American Children. *Environ Sci Technol* 2017, 51, (9), 5193–5204. [PubMed: 28325044]
50. Glynn A; Benskin J; Lignell S; Gyllenhammar I; Aune M; Cantillana T; Damerud PO; Sandblom O, Temporal trends of perfluoroalkyl substances in pooled serum samples from first-time mothers in Uppsala 1997–2014. Report to the Swedish EPA 2015.

51. Haug LS; Thomsen C; Becher GB, Time Trends and the Influence of Age and Gender on Serum Concentrations of Perfluorinated Compounds in Archived Human Samples. *Environ Sci Technol* 2009, 43, 2131–2136. [PubMed: 19368225]
52. Haug LS; Thomsen C; Brantsaeter AL; Kvale HE; Haugen M; Becher G; Alexander J; Meltzer HM; Knutsen HK, Diet and particularly seafood are major sources of perfluorinated compounds in humans. *Environ Int* 2010, 36, (7), 772–8. [PubMed: 20579735]
53. Harada KH; Hitomi T; Niisoe T; Takanaka K; Kamiyama S; Watanabe T; Moon CS; Yang HR; Hung NN; Koizumi A, Odd-numbered perfluorocarboxylates predominate over perfluorooctanoic acid in serum samples from Japan, Korea and Vietnam. *Environ Int* 2011, 37, (7), 1183–9. [PubMed: 21600654]
54. Benskin JP; Ikonomou MG; Gobas FA; Begley TH; Woudneh MB; Cosgrove JR, Biodegradation of N-ethyl perfluorooctane sulfonamido ethanol (EtFOSE) and EtFOSE-based phosphate diester (SAMPAP diester) in marine sediments. *Environ Sci Technol* 2013, 47, (3), 1381–9. [PubMed: 23305554]
55. Rhoads KR; Janssen EML; Luthy RG; Criddle CS, Aerobic Biotransformation and Fate of N-Ethyl Perfluorooctane Sulfonamidoethanol (N-EtFOSE) in Activated Sludge. *Environ Sci Technol* 2008, 42, 2873–2878. [PubMed: 18497137]
56. Makey CM; Webster TF; Martin JW; Shoeib M; Harner T; Dix-Cooper L; Webster GM, Airborne Precursors Predict Maternal Serum Perfluoroalkyl Acid Concentrations. *Environ Sci Technol* 2017, 51, (13), 7667–7675. [PubMed: 28535063]
57. Shoeib M; Harner T; Wilford BH; Jones KC; Zhu J, Perfluorinated Sulfonamides in Indoor and Outdoor Air and Indoor Dust: Occurrence, Partitioning, and Human Exposure. *Environ Sci Technol* 2005, 39, 6599–6606. [PubMed: 16190217]
58. Conder JM; Hoke RA; Wolf WD; Russell MH; Buck RC, Are PFCAs Bioaccumulative? A Critical Review and Comparison with Regulatory Criteria and Persistent Lipophilic Compounds. *Environ Sci Technol* 2008, 42, (4), 995–1003. [PubMed: 18351063]
59. Gomis MI; Vestergren R; MacLeod M; Mueller JF; Cousins IT, Historical human exposure to perfluoroalkyl acids in the United States and Australia reconstructed from biomonitoring data using population-based pharmacokinetic modelling. *Environ Int* 2017, 108, 92–102. [PubMed: 28818713]
60. Yeung LW; Miyake Y; Taniyasu S; Wang Y; Yu H; So MK; Jiang G; Wu Y; Li J; Giesy JP; Yamashita N; Lam PK, Perfluorinated Compounds and Total and Extractable Organic Fluorine in Human Blood Samples from China. *Environ Sci Technol* 2008, 42, (21), 8140–8145. [PubMed: 19031915]
61. Yeung LW; Miyake Y; Wang Y; Taniyasu S; Yamashita N; Lam PK, Total fluorine, extractable organic fluorine, perfluorooctane sulfonate and other related fluorochemicals in liver of Indo-Pacific humpback dolphins (*Sousa chinensis*) and finless porpoises (*Neophocaena phocaenoides*) from South China. *Environ Pollut* 2009, 157, (1), 17–23. [PubMed: 18805607]

Figure 1.

Schematic of measurements and data synthesized in this study. *POSF:

Perfluorooctanesulfonyl fluoride, the parent compound to PFOS and its precursors. PFOA: perfluorooctanoic acid.

Figure 2.

Panel (A) shows the average composition of 19 PFASs measured in Faroese children's serum over time. Panel (B) shows individual observations for each child as colored connected dots and population medians as black connected dots for nine select PFASs.

Figure 3.

Results from Principal Component Analysis (PCA) on measured PFASs in serum from Faroese children between 1993 and 2013. Panel (A) shows the loadings for each principal component with dominant loadings shaded. Panel (B) shows the first and third components of each data point plotted against each other and colored by year. The dominant compounds for each component are shown as vectors with magnitudes relative to a unit circle.

Figure 4.

Results from principal component analysis (PCA) on measured PFASs in serum from Faroese children between 1993 and 2013. Panel (A) shows the first and third components of each data point plotted against each other and colored by whether or not a child identified as eating pilot whale meat. The dominant compounds for each component are shown as vectors with magnitudes relative to a unit circle. Panel (B) shows the correlation coefficient, r , between hair Hg and PFUnDA in children who do and do not eat whale meat. The solid line represents the line of best fit and the shaded region represents the 95% confidence interval.

Figure 5.

Inputs and results of toxicokinetic modeling used to reconstruct seafood consumption magnitudes in Faroese children and PFOS and PFNA exposures. Panel (A) shows measured concentrations of mercury (Hg) in children's hair over time. Panel (B) shows modeled whale consumption rates calculated from toxicokinetic modeling for Hg. Panels (C) and (D) shows modeled serum PFOS and PFNA concentrations. Panels (E) and (F) show modeled contributions of pilot whale consumption to total PFOS and PFNA measured in serum.

Table 1.

Results of log-linear regression modeling for temporal trends in PFASs (year), adjusted for covariates.

Compound	Year ^a	<i>p</i>	Age ^b	<i>p</i>	Hair-Hg ^c	<i>p</i>	Weight ^d	<i>p</i>
PFHxS	-8.5%	<0.001	4.8%	0.46	2.8%	0.14	-3.3%	0.049
PFHpS	-4.4%	0.001	21%	0.20	27%	<0.001	-5.2%	0.22
PFOS	-14%	<0.001	15%	0.004	11%	<0.001	-3.4%	0.007
PFDS	-1.1%	0.14	-6.9%	0.31	0.1%	0.98	0.7%	0.66
PFHpA	-15%	<0.001	-5.0%	0.62	4.5%	0.25	-0.3%	0.91
PFOA	-13%	<0.001	9.3%	0.10	-1.3%	0.51	-4.9%	0.001
PFNA	-1.1%	0.019	-2.8%	0.59	12%	<0.001	-2.5%	0.10
PFDA	0.9%	0.046	7.7%	0.19	16%	<0.001	-3.2%	0.058
PFUnDA	-5.7%	<0.001	22%	0.021	26%	<0.001	-2.9%	0.23
MeFOSAA	-20%	<0.001	-30%	<0.001	-1.3%	0.62	-1.7%	0.34
EtFOSAA	-28%	<0.001	-7.1%	0.39	-2.0%	0.61	-0.7%	0.77

All covariates significant at the $p < 0.05$ level or greater are indicated in bold.

^aPercent change in children's serum PFAS concentrations between 2000–2013.

^bPercent change in children's serum PFAS concentrations per year of age.

^cPercent change in children's serum PFAS concentrations per doubling of hair Hg concentrations. Concentrations of Hg in hair are used as a proxy for seafood consumption magnitudes.

^dPercent change in children's serum PFAS concentrations per 10% increase in body weight.