Time trends in Perfluoroalkyl and Polyfluoroalkyl substances (PFASs) in California women: declining serum levels, 2011-2015

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Introduction

Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are a large group of synthetic fluorinated chemicals widely used in industrial processes and consumer products since the 1950s.[1,2] Owing to their persistent and bioaccumulative properties, some of these compounds emerged during the 1990s as among the most pervasive global environmental contaminants.[1,2] In response to biomonitoring data that indicated widespread human exposures[3] and accumulating evidence of myriad toxic and potential adverse health effects, regulatory restrictions and voluntary phase-outs of many of these compounds were enacted shortly after the beginning of the 21st Century.[1,2] Representing a broad group of chemicals, the PFASs encompass a large number of compounds with a diversity of chemical properties that determine not only their toxicity, but their persistence.[4] Hence, restrictions have been targeted at what are believed to be the most worrisome chemicals within the family of PFASs, particularly the long-chained perfluoroalkyl acids (PFAAs) of which perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) are the most notable.[1,2]

Prior to 2002 when 3M, the primary global manufacturer of PFOS, voluntarily ceased its production, PFOS was the predominant PFAA in use. Shortly after the 3M phase-out of PFOS and other long-chain PFAAs, global production of PFOS dramatically dropped while global production of PFOA continued to increase.[5] Subsequently, in response to US EPA's PFOA Stewardship Program announced in 2006, eight of the largest users and producers of PFOA committed to reduce global emissions and use of PFOA, its precursors and other long chain PFAAs, by 95% by 2010 and completely eliminate them by 2015.[2] As concerns over potential human health effects associated with these compounds continue to mount, biomonitoring data offer a critical tool for evaluating the effectiveness of these regulatory and voluntary restrictions in mitigating human exposures. Published summaries of biomonitoring data suggest mixed success. While body burden levels of PFOS and PFOA appear to have declined since the early 2000s, [6-9,1,10,11,2] there is evidence that body burden measures of certain PFASs, particularly some of the other long-chain PFAAs, may be increasing.[6,8,9,1,10,12,11] The objective of the current analyses was to describe serum levels of PFASs in a large sample of middle-aged and older California women and to evaluate temporal trends in levels across the 4 years of sample collection from 2011 through 2015.

Materials and methods

Blood was collected in a 10 mL BD® tube (catalog#367985, Becton Dickinson) from 1,257 women, 40 to 94 years of age, who were participating as controls in a breast cancer case control study nested within the California Teachers Study, an on-going prospective cohort study of female California professional public school employees. Participants in the present analysis included those who had provided a blood sample between May 2011 and August 2015. Serum was separated using a portable centrifuge in the field, frozen and shipped to the laboratory where samples were stored at -20 ºC until analysis. Samples were analyzed for 12 PFASs, using an online SPE-HPLC- MS/MS method as

described in detail previously.[11] Briefly, 100 µL of serum was diluted in formic acid and spiked with isotopically labeled internal standards before injection into the online SPE-HPLC-MS/MS system (Symbiosis ™ Pharma, IChrom Solutions, Plainsboro, NJ, and AB Sciex 4000 QTrap mass spectrometer, AB Sciex, Redwood City, CA) for clean-up and analysis. Native and isotopically-labeled PFASs standards were purchased from Wellington Laboratories (Shawnee Mission, KS). Within each batch analysis of 20 samples, two in-house spiked calf serum samples and NIST 1958 Standard Reference Material were run in duplicate together with the samples for quality control.

Multivariable linear regression models were used to assess temporal trends in the serum PFASs concentrations. Two PFASs were excluded from statistical analyses due to low detection frequencies (DF): perfluorobutane sulfonic acid (DF=8.3%) and perfluorododecanoic acid (DF=9.6%). To symmetrize the skewed distributions, PFAS serum concentrations were $\log_{10}$-transformed and then regressed on blood sample collection date, adjusting for potential confounders, including sociodemographic, dietary and other behavioral and anthropomorphic factors. Only factors that were identified as significant ($p<0.05$) in backwards stepwise linear regression modelling or that changed the regression coefficient of sample collection date by 10% or more were retained in the final regression models. Time trend coefficients (β) obtained from regressing $\log_{10}$ concentration on date of sample collection were converted to annual percent change (APC) where $APC = 100*(10^{\beta*365.25} - 1)$.

Results and discussion

The distributions of serum PFAS concentrations are presented in Table 1. Most compounds were detected in over 90% of study participants. Median serum levels were highest for PFOS, followed by PFOA and PFHxS.

Table 1. Distributions of serum PFAS concentrations among 1,257 study participants, 2011-2015

			Serum concentration (ng/mL)				
Acronym	Name	DF[§]	LOD[#]	Mean	Median	Min.	Max.
PFOS	Perfluorooctanesulfonic acid	99.6	0.080	8.539	7.070	0.047	99.800
PFOA	Perfluorooctanoic acid	99.9	0.108	2.996	2.470	0.096	27.600
PFHxS	Perfluorohexane sulfonic acid	99.9	0.017	2.231	1.580	0.011	21.800
PFNA	Perfluorononanoic acid	98.5	0.036	1.070	0.909	0.017	10.400
PFDA	Perfluorodecanoic acid	90.1	0.048	0.279	0.221	0.022	3.910
PFUnDA	Perfluoroundecanoic acid	96.5	0.018	0.170	0.134	0.007	1.310
PFHpA	Perfluoroheptanoic acid	63.6	0.033	0.084	0.042	0.011	1.160
MePFOSA	2-(N-Methyl-perfluorooctane sulfonamido) acetic acid	96.4	0.017	0.378	0.195	0.006	9.200
EtPFOSA	2-(N-Ethyl-perfluorooctane sulfonamido) acetic acid	76.4	0.014	0.064	0.031	0.004	1.360
PFOSA	Perfluorooctane sulfonamide	69.6	0.017	0.075	0.039	0.001	1.240
PFBS	Perfluorobutane sulfonic acid	8.3	0.040	0.030	0.031	0.015	0.327
PFDoDA	Perfluorododeconic acid	9.6	0.090	0.071	0.080	0.025	1.570

[§] DF=detection frequency. [#] LOD=average level of detection.

The average annual percent change (APC) in serum PFAS levels, as estimated from multivariate linear models are presented in Table 2. Results from unadjusted models indicated that serum levels of all PFAS significantly declined over the period of the study. Adjustment for covariates did not substantially change the results, with the exception of

PFHxS, for which the decline was diminished and was no longer statistically significant. Average annual declines ranged from about 10 to 20 percent, with the most dramatic trends observed for PFHpA, followed by MePFOSA, PFOSA and EtPFOSA. Declines were more modest for PFOS and for PFOA. These results demonstrate the efficacy of current PFAS restrictions in reducing human exposures to some PFAS. However, as the longer chain PFASs have been phased-out, shorter chain PFASs are being introduced as substitutes and there remain thousands of PFASs still in use that are likely to have similar toxicological properties but remain poorly understood.[2] Continued and expanded biomonitoring of PFASs is warranted.

Table 2. Average annual percent change (APC) in serum PFASs levels (ng/mL), 2011-2015: results from unadjusted and multivariate adjusted linear models.

	Unadjusted			Adjusted		
compound	APC	95% CI	*p*-value	APC	95% CI	*p*-value
PFOS	-9.27	-12.37, -6.06	<.0001	-10.59	-14.49, -6.51	<.0001
PFOA	-7.73	-10.28, -5.10	<.0001	-9.28	-12.67, -5.77	<.0001
PFHxS	-5.02	-8.30, -1.63	0.0041	-2.33	-6.90, 2.46	0.3343
PFNA	-13.82	-16.37, -11.19	<.0001	-12.46	-15.99, -8.78	<.0001
PFDA	-14.46	-17.57, -11.23	<.0001	-11.06	-14.59, -7.39	<.0001
PFUndA	-11.59	-14.97, -8.07	<.0001	-10.19	-13.79, -6.45	<.0001
PFHpA	-15.07	-18.46, -11.54	<.0001	-19.38	-23.91, -14.57	<.0001
MePFOSA	-20.42	-24.22, -16.43	<.0001	-17.44	-22.52, -12.02	<.0001
EtPFOSA	-14.20	-17.99, -10.23	<.0001	-15.86	-20.72, -10.70	<.0001
PFOSA	-20.09	-24.29, -15.65	<.0001	-16.24	-20.98, -11.22	<.0001

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