Serum Concentrations of 11 Polyfluoroalkyl Compounds in the U.S. Population: Data from the National Health and Nutrition Examination Survey (NHANES) 1999-2000

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Abstract

We measured the concentrations of 11 polyfluoroalkyl compounds (PFCs), including perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorohexane sulfonic acid (PFHxS) in 1562 serum samples collected from a representative U.S. population 12 years of age and older in the 1999-2000 National Health and Nutrition Examination Survey. Participants represented both sexes, three race/ethnicities (non-Hispanic blacks, non-Hispanic whites, and Mexican Americans), and four age categories (12-19 years, 20-39 years, 40-59 years, and 60 years and older). PFCs were extracted from 100 µL of serum using on-line solid-phase extraction coupled to isotope dilution high performance liquid chromatography-tandem mass spectrometry; limits of detection ranged from 0.05 to 0.2 ng/mL. PFOS, PFOA, PFHxS, and perfluorooctane sulfonamide were detected in all samples analyzed; 2-(N-ethylperfluorooctane sulfonamido) acetic acid, 2-(N-methylperfluorooctane sulfonamido) acetic acid, and perfluorononanoic acid were detected in more than 90% of samples, which suggests prevalent exposures to several PFCs in the U.S. population. The concentrations of most PFCs were similar regardless of the participants' ages but were higher in males than in females. Mexican Americans had lower concentrations than non-Hispanic blacks and non-Hispanic whites, whose concentrations were similar. Higher education was associated with higher concentrations of PFOS and PFOA. These data will serve as a nationally representative baseline of the U.S. population's exposure to PFCs to which other populations can be compared, and will play an important role in public health by helping set research priorities, ranging from health effects studies to defining sources and pathways of exposure.

Introduction

Polyfluoroalkyl compounds (PFCs) have been used extensively in commercial applications including surfactants, lubricants, paper and textile coatings, polishes, food packaging, and fire-retarding foams. Some PFCs, including perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA), are persistent in humans and the environment, and they have been found worldwide in wildlife (*1*, and references therein) and in the general population (*2-7*).

Results of animal studies suggest potential adverse health effects including genotoxicity, reproductive and developmental toxicity, and carcinogenicity associated with exposures to PFOS and PFOA (*8-10*). By contrast, in a few occupational studies (*11-13*) and in one population exposed to PFOA through contaminated drinking water (*14*), no clear association has been established between exposure and adverse health effects.

The National Health and Nutrition Examination Survey (NHANES), conducted annually since 1999 by the Centers for Disease Control and Prevention (CDC), is designed to measure the health and nutritional status of the civilian noninstitutionalized U.S. population 2 months of age and older (*15*). The surveys include household interviews, collection of medical histories, standardized physical examinations, and collection of biological specimens. Some of these specimens can be used to assess exposure to environmental chemicals (*16*). Previously, we used 54 pooled serum samples collected from participants of the 2001-2002 NHANES to obtain estimates of mean concentrations of 11 PFCs in selected demographic groups (*17*).We now report the results of the analyses of 1562 individual serum samples collected from 1999-2000 NHANES participants. These data provide the first estimation of concentrations of these same 11 PFCs in a representative sample of the non-institutionalized U.S. population 12 years of age and older.

Materials and Methods

Survey Design. NHANES 1999-2000 was a complex, multistage probability survey conducted in 26 locations throughout the United States that included examinations of 9282 people. Informed written consent was obtained from all participants (*18*). Serum samples analyzed for PFCs were obtained by venipuncture from 1562 people, a random one third subsample of participants 12 years of age and older. Because the subsample was a random selection from the entire set, the representational aspect of the survey was maintained.

Laboratory Methods. Serum specimens were shipped on dry ice and stored at -70 °C. Using online solid-phase extraction coupled to high performance liquid chromatography-tandem mass spectrometry, described in detail elsewhere (*19*), we measured in 100 µL of serum 11 analytes, including PFOS, PFOA, perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctane sulfonamide (PFOSA), 2-(N-ethyl-perfluorooctane sulfonamido) acetic acid (Et-PFOSA-AcOH), and 2-(N-methyl-perfluorooctane sulfonamido) acetic acid (Me-PFOSA-AcOH) (Table S1). For quantification, we used $^{18}O_2$-PFOS and $^{18}O_2$-PFOSA (RTI International, Research Triangle Park, NC), and $^{13}C_2$-PFOA provided by Dupont Co. (Wilmington, DE). Low- and high-concentration quality control materials, prepared from a calf serum pool, were analyzed with the unknown samples to ensure data accuracy and reliability (*19*).

Statistical Analysis. Statistical analyses were performed using SAS (version 9.1) and SUDAAN (release 8.0 2001). SUDAAN calculates variance estimates after incorporating the sample population weights, which were designed for the one-third subset used and accounted for the unequal selection probabilities caused by the cluster design and planned oversampling of certain subgroups. Geometric means, calculated only for analytes detected in ≥60% of the samples, and percentiles for the PFCs concentrations (in ng/mL) were obtained using SUDAAN. For concentrations below the limit of detection (< LOD), a value equal to the LOD divided by the square root of 2 was used (*20*). Using a weighted regression model, we also determined the correlations among PFCs concentrations.

A variable based on self-reported data defined three race/ethnicity groups: non-Hispanic blacks, non-Hispanic whites, and Mexican Americans. Persons not defined by these groups were included only in the total population estimate. Age was reported in years at the last birthday. We used analysis of covariance to examine the influence of several variables, selected on the basis of statistical and biologic considerations, on the log-transformed serum concentrations of PFOS, PFOA, PFHxS, and PFNA. Concentrations of PFOS, PFOA and other PFCs differ by sex (*3, 7, 17, 21*) and race/ethnicity (*17*), while the influence of other variables (e.g., income, education, smoking status, body mass index [BMI]) is not known.

In this NHANES population, approximately 20% of the subjects were considered smokers based on their serum concentrations of cotinine (a marker of tobacco smoke exposure), and more than 50% of the nonsmokers and passive smokers had cotinine concentrations < LOD of 0.05 ng/mL (*16*). Had we used

serum cotinine as a continuous variable, the high percentage of nondetectable concentrations could have influenced the fitting of a regression line. Therefore, we categorized participants' smoking status as follows: nondetectable smoke exposure (if cotinine concentration was < LOD); passive smokers with exposure to environmental tobacco smoke (if cotinine concentration was ≥ LOD but ≤ 10 ng/mL); and smokers (if cotinine concentration was > 10 ng/mL).

Based on questionnaire responses, education was available as follows: less than high school diploma; high school diploma; and beyond high school. Similarly, two variables for annual household income were available: (1) < $20 000 and ≥ $20 000 and (2) amount in increments of $5000 (ranging from < $5000 to > $75 000). For the latter, to obtain comparable number of participants per income group, we categorized income as < $20 000, between $20 000 and $45 000, and > $45 000 (Table S2). The analyses were considered to be statistically significant when $p < 0.05$.

Results

The distributions of the seven most commonly detected PFCs in the 1562 NHANES 1999-2000 serum samples are presented in Tables 1-7. PFOS, PFOA, PFHxS, and PFOSA were detected in all of the samples analyzed; three other PFCs were frequently detected (Me-PFOSA-AcOH, 96%; PFNA, 95%; Et-PFOSA-AcOH, 91%). Four PFCs were detected less frequently (perfluorodecanoic acid [PFDeA], 25% (Table S3); perfluoroheptanoic acid, 10%; perfluoroundecanoic acid, 12%; perfluorododecanoic acid, < 1%), which suggests that human exposures are lower, or pharmacokinetic factors are different, and will not be discussed further.

Table 1. Geometric Mean and Selected Percentiles of Perfluorooctane Sulfonic Acid (PFOS) Concentrations in Serum (in ng/mL) for the U.S. population 12 years of age and older: Data from NHANES 1999–2000[a]

geometric mean		selected percentiles						N (%)[b]
		10th	25th	50th	75th	90th	95th	
total	30.4 (27.1-33.9)	15.1 (13.0-17.4)	21.9 (19.2-23.9)	30.2 (27.8-33.8)	43.5 (37.5-47.3)	57 (50.2-71.7)	75.6 (58.1-97.5)	1562
Age Group (Years)								
12-19	29.1 (26.2-32.4)	16.3 (12.0-18.4)	22.4 (18.5-25.3)	29.4 (26.8-34.2)	38.9 (35.9-45.0)	52.7 (45.6-56.2)	57.4 (52.7-66.5)	543
20-39	27.5 (24.9-30.2)	14.4 (11.9-17.6)	20.3 (18.8-22.3)	27.9 (24.8-29.7)	37.3 (33.9-42.3)	50.2 (45.5-55.9)	56.8 (51.4-71.7)	364
40-59	33.0 (28.0-38.8)	16.5 (14.3-17.9)	23.0 (18.7-27.8)	33.6 (28.0-38.7)	46.6 (37.9-57.0)	75.2 (47.1-98.4)	94.3 (58.0-131)	295
60+	33.3 (28.5-38.8)	15.0 (13.5-19.2)	23.6 (20.0-26.5)	33.7 (27.4-39.9)	46.1 (41.1-56.3)	67.0 (54.0-101)	95.6 (58.1-119)	360
Sex								
males	33.4 (29.6-37.6)	17.9 (14.3-20.2)	24.8 (21.1-28.4)	34.8 (31.1-37.9)	46.1 (41.0-50.2)	58.3 (50.2-78.3)	78.3 (58.0-108)	743
females	28.0 (24.6-31.8)	13.8 (11.4-16.6)	19.4 (17.3-22.3)	27.7 (24.5-30.2)	38.8 (32.7-46.0)	55.4 (46.3-70.2)	75.7 (56.1-98.4)	819
Race/Ethnicity[c]								
MA	22.7 (19.8-25.9)	11.9 (10.6-12.8)	16.0 (13.7-18.7)	23.7 (20.8-27.2)	32.9 (27.8-39.6)	41.7 (36.5-53.6)	53.6 (41.3-72.0)	584
NHB	33.0 (26.2-41.6)	14.9 (11.6-21.0)	21.9 (14.9-31.7)	32.0 (24.3-45.7)	50.6 (37.4-62.2)	68.8 (62.0-75.9)	82.8 (68.7-114)	309
NHW	32.0 (29.1-35.2)	16.8 (14.4-18.9)	23.7 (21.7-25.7)	32.4 (29.3-35.5)	44.8 (39.7-47.6)	56.2 (50.4-67.8)	75.7 (58.0-98.4)	529

[a] The 95% confidence intervals are shown in parentheses. [b] *N* (sample size). PFOS was detected in all samples. [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites).

Table 2. Geometric Mean and Selected Percentiles of Perfluorooctanoic Acid (PFOA) Concentrations in Serum (in ng/mL) for the U.S. Population 12 Years of Age and Older: Data from NHANES 1999–2000[a]

geometric mean		selected percentiles						*N* (%)[b]
		10th	25th	50th	75th	90th	95th	
total	5.2 (4.7-5.7)	2.8 (2.5-3.0)	3.8 (3.4-4.3)	5.1 (4.7-5.7)	6.8 (6.3-7.7)	9.4 (8.2-11.0)	11.9 (10.9-13.5)	1562
Age Group (Years)								
12-19	5.5 (5.0-6.0)	3.2 (2.9-3.8)	4.3 (3.9-4.6)	5.6 (4.8-6.1)	6.9 (6.2-7.5)	9.4 (7.7-11.0)	11.2 (10.2-12.5)	543
20-39	5.2 (4.7-5.7)	2.6 (2.3-3.0)	3.8 (3.2-4.5)	5.2 (4.7-6.2)	7.1 (6.4-7.8)	9.3 (7.8-11.0)	10.9 (8.4-14.0)	364
40-59	5.4 (4.7-6.2)	2.8 (2.4-3.4)	3.8 (3.4-4.4)	5.2 (4.5-5.9)	6.9 (6.0-8.7)	9.4 (7.7-14.1)	13.0 (10.0-17.7)	295
60+	4.8 (4.3-5.5)	2.6 (1.8-3.0)	3.4 (3.2-3.9)	4.8 (4.3-5.1)	6.4 (5.7-7.5)	8.8 (7.3-12.0)	11.5 (8.7-17.1)	360
Sex								
males	5.7 (5.2-6.3)	3.1 (2.8-3.5)	4.3 (3.8-4.9)	6.0 (5.4-6.4)	7.6 (6.8-8.4)	10.5 (9.0-11.8)	12.1 (11.0-13.1)	743
females	4.8 (4.3-5.3)	2.6 (2.3-2.8)	3.4 (3.0-3.9)	4.6 (4.2-5.0)	6.2 (5.6-7.0)	8.3 (7.5-9.9)	11.3 (9.2-14.4)	819
Race/Ethnicity[c]								
MA	3.9 (3.6-4.2)	1.9 (1.6-2.2)	2.8 (2.3-3.4)	4.2 (3.7-4.6)	5.8 (5.2-6.2)	7.6 (6.4-8.0)	8.0 (7.7-8.9)	584
NHB	4.8 (4.1-5.6)	2.5 (2.2-2.9)	3.3 (2.7-4.1)	4.8 (4.0-5.9)	6.5 (5.9-7.5)	8.8 (7.4-11.5)	11.1 (9.2-14.0)	309
NHW	5.6 (5.0-6.2)	3.2 (2.9-3.5)	4.1 (3.5-4.6)	5.5 (4.9-6.2)	7.3 (6.5-8.2)	10.0 (8.3-12.0)	12.9 (11.0-14.9)	529

[a] The 95% confidence intervals are shown in parentheses. [b] *N* (sample size). PFOA was detected in all samples. [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites).

Table 3. Geometric Mean and Selected Percentiles of Perfluorohexane Sulfonic Acid (PFHxS) Concentrations in Serum (in ng/mL) for the U.S. Population 12 Years of Age and Older: Data from NHANES 1999–2000[a]

	geometric mean	selected percentiles						*N* (%)[b]
		10th	25th	50th	75th	90th	95th	
total	2.1 (1.9-2.4)	0.8 (0.7-0.8)	1.2 (1.1-1.4)	2.1 (1.8-2.3)	3.3 (3.0-3.8)	5.7 (5.1-6.7)	8.7 (7.0-10.0)	1,562 (100)
Age Group (Years)								
12-19	2.7 (2.1-3.4)	0.8 (0.7-1.1)	1.4 (1.2-1.8)	2.4 (2.0-3.7)	5.0 (3.5-6.5)	7.9 (5.7-12.9)	12.9 (6.8-15.6)	543 (100)
20-39	2.0 (1.7-2.3)	0.6 (0.5-0.7)	1.0 (0.8-1.2)	1.8 (1.5-2.3)	3.3 (2.7-3.9)	5.7 (4.7-6.9)	8.4 (5.7-10.6)	364 (99)
40-59	2.1 (1.8-2.3)	0.7 (0.7-0.9)	1.2 (1.0-1.5)	2.0 (1.7-2.3)	3.2 (2.9-3.9)	5.0 (4.0-5.8)	6.7 (5.2-7.9)	295 (100)
60+	2.2 (1.9-2.5)	0.9 (0.6-1.0)	1.4 (1.2-1.5)	2.1 (1.9-2.4)	3.2 (2.6-4.0)	5.9 (4.4-8.8)	9.5 (5.2-10.6)	360 (99)
Sex								
males	2.6 (2.3-3.0)	0.9 (0.7-1.1)	1.5 (1.4-1.8)	2.5 (2.2-2.9)	4.0 (3.4-4.5)	6.6 (5.3-9.4)	10.1 (6.9-15.0)	743 (99)
females	1.8 (1.6-2.1)	0.7 (0.5-0.7)	1.0 (0.9-1.2)	1.7 (1.3-1.9)	2.7 (2.3-3.5)	5.1 (4.1-6.7)	8.0 (5.7-9.0)	819 (100)
Race/Ethnicity[c]								
MA	1.5 (1.1-1.9)	0.4 (0.4-0.6)	0.7 (0.6-1.0)	1.4 (1.0-2.0)	2.7 (1.8-3.8)	4.4 (3.3-6.9)	6.6 (4.6-9.5)	584 (99)
NHB	2.2 (1.6-2.9)	0.7 (0.5-1.1)	1.2 (0.7-1.9)	2.2 (1.3-3.0)	3.4 (2.7-4.7)	6.7 (4.3-10.7)	10.6 (7.2-14.3)	309 (100)
NHW	2.3 (2.0-2.5)	0.8 (0.8-1.0)	1.3 (1.1-1.5)	2.1 (1.8-2.5)	3.6 (3.2-4.1)	5.9 (5.2-6.7)	8.3 (7.0-9.6)	529 (100)

[a] The 95% confidence intervals are shown in parentheses. [b] *N* (%), Sample size (percentage of detection) [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites).

Table 4. Geometric Mean and Selected Percentiles of Perfluorononanoic Acid (PFNA) Concentrations in Serum (in ng/mL) for the U.S. Population 12 Years of Age and Older: Data from NHANES 1999–2000[a]

	geometric mean	selected percentiles						*N* (%)[b]
		10th	25th	50th	75th	90th	95th	
total	0.5 (0.5-0.7)	<LOD	0.4 (0.3-0.4)	0.6 (0.5-0.6)	0.9 (0.7-1.0)	1.2 (1.0-1.5)	1.7 (1.3-2.4)	1,562 (95)
Age Group (Years)								
12-19	0.5 (0.4-0.5)	<LOD	0.2 (0.2-0.3)	0.4 (0.4-0.5)	0.7 (0.5-0.8)	0.9 (0.8-0.9)	1.1 (0.9-1.4)	543 (96)
20-39	0.5 (0.4-0.6)	<LOD	0.3 (0.3-0.4)	0.4 (0.4-0.5)	0.7 (0.6-0.9)	1.1 (0.8-1.5)	1.5 (1.2-2.3)	364 (96)
40-59	0.6 (0.4-0.7)	<LOD	0.4 (0.3-0.4)	0.6 (0.5-0.7)	1.0 (0.7-1.2)	1.3 (1.0-2.2)	1.9 (1.3-2.4)	295 (91)
60+	0.6 (0.5-0.8)	<LOD	0.4 (0.2-0.4)	0.5 (0.5-0.7)	1.0 (0.8-1.2)	1.8 (1.2-2.2)	2.1 (1.8-3.6)	360 (97)
Sex								
males	0.6 (0.5-0.7)	0.2 (0.2-0.3)	0.3 (0.3-0.4)	0.6 (0.5-0.6)	0.8 (0.7-1.0)	1.3 (1.0-1.4)	1.7 (1.3-2.3)	743 (96)
females	0.5 (0.4-0.6)	<LOD	0.3 (0.2-0.3)	0.5 (0.4-0.5)	0.7 (0.6-0.9)	1.3 (0.9-1.9)	1.7 (1.2-2.4)	819 (93)
Race/Ethnicity[c]								
MA	0.3 (0.3-0.4)	<LOD	<LOD	0.4 (0.3-0.4)	0.4 (0.4-0.6)	0.6 (0.6-0.8)	0.9 (0.7-1.2)	584 (89)
NHB	0.8 (0.6-1.0)	0.3 (0.2-0.4)	0.5 (0.4-0.6)	0.6 (0.5-0.8)	1.2 (0.8-1.7)	1.8 (1.4-2.4)	2.3 (1.8-2.9)	309 (99)
NHW	0.6 (0.5-0.7)	<LOD	0.4 (0.3-0.4)	0.6 (0.5-0.6)	0.9 (0.7-1.1)	1.2 (1.0-1.7)	1.7 (1.3-2.3)	529 (96)

[a] The 95% confidence intervals are shown in parentheses. LOD (limit of detection) is 0.1 ng/mL. [b] *N* (%), Sample size (percentage of detection) [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites).

Table 5. Geometric Mean and Selected Percentiles of 2-(N-methyl-perfluorooctane Sulfonamido) Acetic Acid (Me-PFOSA-AcOH) Concentrations in Serum (in ng/mL) for the U.S. Population 12 Years of Age and Older: Data from NHANES 1999–2000[a]

	geometric mean	selected percentiles						*N* (%)[b]
		10th	25th	50th	75th	90th	95th	
total	1.0 (0.8-1.1)	0.4 (0.3-0.4)	0.5 (0.5-0.6)	0.9 (0.8-1.1)	1.6 (1.3-1.9)	2.5 (2.1-2.9)	3.2 (2.8-3.6)	1,562 (96)
Age Group (Years)								
12-19	1.3 (1.2-1.5)	0.6 (0.5-0.7)	0.8 (0.7-1.0)	1.4 (1.2-1.5)	2.0 (1.5-2.5)	3.0 (2.5-3.5)	3.7 (3.2-4.4)	543 (100)
20-39	1.0 (0.8-1.2)	0.4 (0.3-0.5)	0.5 (0.5-0.7)	0.9 (0.8-1.2)	1.7 (1.3-2.1)	2.5 (1.9-3.1)	3.1 (2.4-4.2)	364 (97)
40-59	0.9 (0.8-1.1)	0.4 (0.3-0.4)	0.4 (0.4-0.6)	0.8 (0.7-1.0)	1.3 (1.2-1.7)	2.2 (1.9-3.0)	3.0 (2.2-4.6)	295 (97)
60+	0.8 (0.6-0.9)	<LOD	0.5 (0.4-0.5)	0.7 (0.5-0.9)	1.3 (1.0-1.5)	1.8 (1.5-2.3)	2.6 (1.9-3.5)	360 (93)
Sex								
males	1.0 (0.9-1.2)	0.4 (0.3-0.5)	0.6 (0.5-0.7)	0.9 (0.8-1.1)	1.5 (1.3-1.9)	2.5 (2.3-3.2)	3.2 (2.5-3.6)	743 (97)
females	0.9 (0.8-1.1)	0.3 (0.3-0.4)	0.5 (0.5-0.6)	0.9 (0.7-1.0)	1.5 (1.2-1.7)	2.2 (2.0-2.6)	3.0 (2.6-3.5)	819 (96)
Race/Ethnicity[c]								
MA	0.8 (0.6-0.9)	<LOD	0.4 (0.4-0.6)	0.8 (0.6-0.9)	1.2 (1.0-1.5)	2.1 (1.5-2.5)	2.6 (1.9-3.8)	584 (93)
NHB	1.1 (1.0-1.3)	0.4 (0.3-0.5)	0.7 (0.5-0.8)	1.1 (0.9-1.4)	1.7 (1.5-2.0)	2.6 (2.2-3.0)	3.6 (2.5-4.8)	309 (99)
NHW	1.0 (0.9-1.2)	0.3 (0.3-0.4)	0.6 (0.5-0.7)	1.0 (0.8-1.1)	1.5 (1.3-1.9)	2.4 (2.1-3.0)	3.2 (2.6-3.5)	529 (97)

[a] The 95% confidence intervals are shown in parentheses. LOD (limit of detection) is 0.2 ng/mL. [b] *N* (%), Sample size (percentage of detection) [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites).

Table 6. Geometric Mean and Selected Percentiles of 2-(N-ethyl-perfluorooctane Sulfonamido) Acetic Acid (Et-PFOSA-AcOH) Concentrations in Serum (in ng/mL) for the U.S. Population 12 Years of Age and Older: Data from NHANES 1999–2000[a]

	geometric mean	selected percentiles						*N* (%)[b]
		10th	25th	50th	75th	90th	95th	
total	0.6 (0.6-0.7)	<LOD	0.4 (0.3-0.4)	0.5 (0.5-0.6)	1.1 (1.0-1.1)	1.6 (1.5-1.7)	2.2 (1.9-2.7)	1,562 (91)
Age Group (Years)								
12-19	0.8 (0.8-0.9)	0.4 (0.3-0.4)	0.4 (0.4-0.5)	0.7 (0.7-0.8)	1.2 (1.0-1.3)	1.6 (1.4-1.9)	2.4 (1.8-2.7)	543 (98)
20-39	0.6 (0.5-0.7)	<LOD	0.3 (0.3-0.4)	0.5 (0.5-0.7)	1.0 (0.8-1.0)	1.4 (1.2-1.6)	1.9 (1.6-2.4)	364 (91)
40-59	0.6 (0.6-0.7)	<LOD	0.3 (0.3-0.4)	0.5 (0.4-0.7)	1.1 (0.8-1.2)	1.6 (1.4-1.7)	2.1 (1.6-2.8)	295 (90)
60+	0.6 (0.5-0.6)	<LOD	<LOD	0.5 (0.4-0.5)	1.1 (0.8-1.3)	1.8 (1.4-2.5)	2.7 (1.9-3.4)	360 (86)
Sex								
males	0.6 (0.6-0.7)	<LOD	0.3 (0.3-0.4)	0.5 (0.5-0.6)	1.0 (0.9-1.1)	1.5 (1.3-1.6)	1.8 (1.6-2.3)	743 (90)
females	0.7 (0.6-0.7)	<LOD	0.3 (0.3-0.4)	0.7 (0.5-0.7)	1.0 (0.9-1.2)	1.7 (1.4-2.0)	2.4 (2.0-2.7)	819 (92)
Race/Ethnicity[c]								
MA	0.6 (0.5-0.7)	<LOD	<LOD	0.6 (0.4-0.7)	1.0 (0.8-1.1)	1.6 (1.3-2.0)	2.5 (1.8-2.7)	584 (85)
NHB	0.5 (0.5-0.6)	<LOD	<LOD	0.4 (0.4-0.5)	0.8 (0.7-1.0)	1.4 (1.2-1.6)	2.2 (1.4-3.1)	309 (87)
NHW	0.7 (0.6-0.7)	<LOD	0.4 (0.3-0.4)	0.6 (0.6-0.7)	1.1 (0.9-1.1)	1.7 (1.5-1.8)	2.4 (1.9-2.8)	529 (91)

[a] The 95% confidence intervals are shown in parentheses. LOD (limit of detection) is 0.2 ng/mL. [b] *N* (%), Sample size (percentage of detection) [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites).

Table 7. Geometric Mean and Selected Percentiles of Perfluorooctane Sulfonamide (PFOSA) Concentrations in Serum (in ng/mL) for the U.S. Population 12 Years of Age and Older: Data from NHANES 1999–2000[a]

	geometric mean	selected percentiles						*N* (%)[b]
		10th	25th	50th	75th	90th	95th	
total	0.4 (0.3-0.4)	*d*	0.2 (0.1-0.2)	0.3 (0.3-0.4)	0.7 (0.5-0.8)	1.0 (0.8-1.1)	1.4 (1.0-1.7)	1562
Age Group (Years)								
12-19	0.4 (0.4-0.5)	*d*	0.2 (0.1-0.2)	0.3 (0.3-0.4)	0.6 (0.6-0.7)	1.1 (0.9-1.3)	1.5 (1.1-2.9)	543
20-39	0.3 (0.3-0.4)	*d*	0.2 (0.1-0.2)	0.2 (0.2-0.3)	0.5 (0.4-0.7)	1.0 (0.7-1.3)	1.2 (0.9-1.6)	364
40-59	0.4 (0.3-0.5)	*d*	0.2 (0.1-0.3)	0.3 (0.3-0.5)	0.7 (0.5-0.8)	1.0 (0.8-1.4)	1.5 (1.1-2.3)	295
60+	0.3 (0.3-0.4)	*d*	0.2 (0.1-0.2)	0.2 (0.2-0.3)	0.6 (0.4-0.8)	0.9 (0.8-1.5)	1.4 (0.9-2.0)	360
Sex								
males	0.4 (0.3-0.4)	*d*	0.1 (0.1-0.2)	0.4 (0.3-0.4)	0.5 (0.4-0.7)	0.9 (0.7-1.0)	1.2 (0.9-1.6)	743
females	0.4 (0.3-0.4)	*d*	0.2 (0.1-0.2)	0.2 (0.2-0.3)	0.6 (0.5-0.8)	1.1 (0.9-1.4)	1.5 (1.2-2.0)	819
Race/Ethnicity[c]								
MA	0.3 (0.3-0.3)	*d*	0.1 (0.1-0.2)	0.3 (0.2-0.3)	0.4 (0.4-0.5)	0.7 (0.7-0.8)	1.1 (0.8-1.4)	584
NHB	0.4 (0.3-0.4)	*d*	0.2 (0.1-0.2)	0.2 (0.2-0.3)	0.5 (0.4-0.7)	1.0 (0.7-1.7)	1.5 (0.9-2.6)	309
NHW	0.4 (0.3-0.5)	*d*	0.2 (0.1-0.2)	0.4 (0.3-0.5)	0.7 (0.5-0.8)	1.1 (0.9-1.4)	1.5 (1.1-2.0)	529

[a] The 95% confidence intervals are shown in parentheses. LOD (limit of detection) is 0.05 ng/mL. [b] *N* , Sample size. PFOSA was detected in all samples. [c] MA (Mexican Americans), NHB (non-Hispanic blacks), NHW (non-Hispanic whites). [d] < 0.1 ng/mL.

Statistically significant correlations existed between the log-transformed concentrations of PFOS and PFOA (Pearson correlation coefficient $r = 0.64$, $p < 0.01$), PFHxS ($r = 0.60$, $p < 0.01$), and PFNA ($r = 0.52$, $p = 0.01$); and between the log-transformed concentrations of PFOA and PFHxS ($r = 0.51$, $p < 0.01$) and PFNA ($r = 0.44$, $p = 0.09$) (Table S4). The correlations of PFOS with the fluorooctanyl sulfonamides were weaker (PFOSA, $r = 0.38$, $p < 0.01$; Me-PFOSA-AcOH, $r = 0.35$, $p = 0.36$; Et-PFOSA-AcOH, $r = 0.37$, $p < 0.01$) than with the fluoroacids.

The initial models for PFOS, PFOA, PFHxS, and PFNA included sex, race-ethnicity, education, income, and smoking status as categorical variables, and BMI and age as continuous variables. We considered all possible 2-way interactions. We could not include all terms in one model because the degrees of freedom were limited by the study design. To arrive at the final models, a backward procedure in SUDAAN was used to eliminate the nonsignificant interactions one at a time until all remaining interactions were significant. Then, nonsignificant main effects were removed one at a time and the model re-run to determine whether the beta coefficients for significant main effects or interactions changed by more than 10%. If any did, the nonsignificant main effect was retained in the model as confounder. Once the backward procedure was completed, in a forward procedure, main effects and interactions were added back into the model one at a time to determine if any were significant. If any were, they were retained in the final model (Table S5).

The final models included sex, race, education ($p = 0.04$), age, sex-by-age interaction ($p < 0.01$), and race-by-age interaction ($p = 0.01$) for PFOS; sex, race ($p < 0.01$), education ($p = 0.04$), smoking status, BMI, age, sex-by-age interaction ($p < 0.01$), and smoking status-by-BMI interaction ($p = 0.04$) for PFOA; sex, race, age, education, and sex-by-race ($p = 0.01$), sex-by-education ($p < 0.01$), race-by-education ($p < 0.01$), and sex-by-age ($p < 0.01$) interactions for PFHxS; and sex, race, education, income ($p = 0.02$), age, and sex-by-race ($p < 0.01$), sex-by-education ($p < 0.01$), and race-by-age ($p < 0.01$) interactions for PFNA. Because of these interactions, concentrations were compared at the 25th (age = 26 years), 50th (age = 39 years), and 75th (age = 55 years) percentiles of age or at the 25th, 50th, and 75th percentiles of BMI (Tables S5-S8). Geometric mean PFOS and PFOA concentrations were higher in males than in females, but only statistically different at the 25th and 50th percentiles of age (Table S6). PFOS and PFOA concentrations were lowest in Mexican Americans; the concentrations in non-Hispanic whites and non-Hispanic blacks were not statistically different for PFOS, but significantly higher in non-Hispanic whites for PFOA. People with an education beyond high school had the highest PFOS and PFOA concentrations, but the differences were only statistically significant among those in the highest and lowest education categories (Tables S5-S7).

Discussion

PFOS, PFOA, PFHxS, and PFOSA were detected in all 1562 persons. As previously shown (*2*-*5*), PFOS demonstrated the highest serum concentrations followed by PFOA and PFHxS. PFNA, Et-PFOSA-AcOH, and Me-PFOSA-AcOH were detected in more than 90% of the samples examined. These findings confirm that exposures to PFOS, PFOA, PFHxS, and four other PFCs were widespread in the U.S. general population during 1999-2000. In 2002, the 3M Company—the sole manufacturer of PFOS in the United States—discontinued the production of PFOS and related perfluorooctanyl fluoride-based chemistries. Perfluoroalkyl carboxylates including PFOA, its salts, and PFOA precursors are still being manufactured by other companies.

The correlations between the log-transformed concentrations of PFOS and PFOA, PFHxS, and to a lesser extent, PFNA, and the correlations between the log-transformed concentrations of PFOA and both PFHxS and PFNA suggest a similar or common source(s) or pathway(s) of exposure for these four PFCs (Table S4).

Females had lower median concentrations of PFOS, PFOA, PFHxS, and PFNA than males (Tables 1-4). Previous data have suggested that sex differences may affect concentrations of these chemicals (*7*, *17*). Geometric mean concentrations of PFOS and PFOA were reported to be slightly higher in adult men than in women in the United States (*3*); similar trends were observed in adult populations in Japan (*21*). In this 1999-2000 NHANES population, males had higher PFOS and PFOA geometric mean concentrations than did females regardless of age. The differences were statistically significant both at 26 and 39 years of age but not at age 55 (Tables S5-S7), suggesting that sex differences are more pronounced in younger than in older people. Sex differences in exposure cannot be ruled out. Furthermore, the pharmacokinetics of PFCs may be such that differences occur according to sex. Mean serum concentrations of PFOA and PFOS were very similar regardless of age in 20 Japanese adult males, and the concentrations were comparable to those of 8 postmenopausal Japanese females; however, these men had greater mean PFOS and PFOA concentrations than did 20 females 20-50 years old (*22*). The authors hypothesized that menstrual bleeding may be an elimination route for PFCs.

Unlike lipophilic persistent pollutants that display increasing serum concentrations as people age (*16*), the concentrations of most PFCs, except PFHxS and Me-PFOSAAcOH, were similar among age groups (Tables 1-7), in agreement with previous reports (*3*-*5*), despite PFCs having been used since the 1950s and the relatively long human serum elimination half-lives of some PFCs (e.g., PFHxS, PFOS, PFOA). The lack of a general trend showing concentrations of PFOS and PFOA increasing as people age could be explained by in-utero transfer (*23*, *24*), exposure early in life to these PFCs, ongoing exposures being

much higher than earlier historical exposures, and poor urinary elimination due to the renal resorption of perfluoroalkyl acids by organic anion transporters (*25*), or a combination of these factors.

Previously, we found that the concentrations of most PFCs differed on the basis of race/ethnicity using pooled sera collected from participants of the 2001-2002 NHANES (*17*). The present study confirms the existence of racial differences. Specifically, Mexican Americans had the lowest geometric mean concentrations of most PFCs; non-Hispanic whites and non-Hispanic blacks had similar concentrations (Tables 1-7, S5-S8). For PFOS, these differences are more likely to be statistically significant as people age, although the difference between non-Hispanic whites and non-Hispanic blacks never reached statistical significance; for PFOA, all racial differences were statistically significant regardless of age (Tables S6-S7).

To evaluate whether socioeconomic factors may contribute to these differences, we examined the effect of household income and education in a multivariate analysis. All final models for PFOA, PFOS, PFHxS, and PFNA included education. Education and household income were strongly associated (chi-square significance 0.003). Most participants (52%) in the lowest education category had the lowest household income, and 56% of those with the highest income had an education beyond high school (Table S2). For PFOS and PFOA, we found that the geometric mean concentrations were highest for those who had an education beyond high school, although the differences were only statistically significant among those in the lowest and the highest education categories (Tables S5, S7). Because people younger than 18 years of age are unlikely to have obtained an education beyond high school, we performed the analysis including only adults older than 18 years of age. These analyses and those for the whole population produced comparable results (data not shown). These data suggest that education/income may be predictors of exposures that result in increased serum PFC concentrations. Although the sources and routes of human exposure to PFCs are not well understood, diet, lifestyle and prolonged use of PFCs for various applications, including protective coatings for fabrics, carpets, and paper may be important contributors.

In summary, these NHANES 1999-2000 PFCs data can be used to establish a nationally representative baseline of exposure, a baseline to which PFCs levels in future populations can be compared to identify exposure trends, and to evaluate the effectiveness of 3M's phasing-out its perfluorooctanyl fluoride-based chemistries, the impact of alternative technologies that gained market share as a result of this intervention, and the effect of proposed reductions in manufacturing emissions of PFOA, PFOA precursors, and related chemicals. The reported high prevalence of exposure to some PFCs and the differences among sex, race/ethnic groups, and socioeconomic status highlight the need for additional research to identify sources of human exposure to PFCs and to study the environmental distribution of these chemicals. Starting with 2003-2004 NHANES, we will obtain biannual distributions of selected PFCs in a one-third subset of samples collected from participants 12 years of age and older. We also plan to measure PFCs in pooled sera collected from NHANES participants between the ages of 3 and 11 years to obtain information on the prevalence of exposure to PFCs among young children.

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The use of trade names is for identification only and does not constitute endorsement by the U.S. Department of Health and Human Services or the CDC. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of CDC.

Supporting Information Available

A table including analyte name, abbreviation, CAS numbers, and LODs for the 11 PFCs studied; a table showing the distribution of participants by education and income; a table including geometric mean and selected percentiles of PFDeA concentrations; a table including the Pearson correlation analysis of PFCs concentrations; tables including model estimated geometric mean concentrations of PFOS, PFOA, PFHxS, and PFNA; and tables including the statistical significance differences between these PFOS, PFOA, PFNA and PFHxS concentrations for various demographic groups. This material is available free of charge via the Internet at http://pubs.acs.org.

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