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Per- and polyfluoroalkyl substances (PFAS) exposure in the U.S. population: NHANES 1999–March 2020

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Abstract

Per- and polyfluoroalkyl substances (PFAS), also known as “forever chemicals” because of their persistence in the environment, have been used in many commercial applications since the 1940s. Of late, the detection of PFAS in drinking water throughout the United States has raised public and scientific concerns. To understand PFAS exposure trends in the general U.S. population, we analyzed select PFAS serum concentration data from participants ≥ 12 years old of nine National Health and Nutrition Examination Survey (NHANES) cycles. Our goals were to a) evaluate concentration changes of four legacy PFAS—perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA) from 1999 to 2000 to 2017–March 2020, b) discuss serum concentrations and assess demographic predictors of two PFAS measured for the first time in 2017–2018, perfluoro-1-heptanesulfonic acid (PFHpS) and 9-chlorohexadecafluoro-3-oxanonane-1-sulfonic acid (9CLPF), and c) compare concentration profiles of legacy PFAS in NHANES to profiles in exposed communities. We report a decrease in geometric mean concentrations of the four legacy PFAS (16%–87%, depending on the PFAS) from 1999 to 2000, although in 2017–March 2020, more than 96% of people aged 12–19 years, some of whom were born after PFAS production changes started in the early 2000s, had measurable concentrations of these PFAS. An estimated 78% of the U.S. general population had detectable concentrations of PFHpS, and 8% had detectable concentrations of 9CLPF (>44% of whom self-identified as Asian). Comparing profiles in NHANES and people living in communities with PFAS contamination can help identify exposure sources and evaluate and monitor exposures in select areas or among specific population groups. Collectively, our findings highlight the usefulness of NHANES data to help researchers, public

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2025.120916>.

health officials, and policy makers prioritize investigations, monitor exposure changes, and evaluate effectiveness of efforts to limit exposures.

Keywords

Biomonitoring; NHANES; Serum; PFAS; PFOA; PFOS; PFHxS; PFNA; PFHpS; 9CLPF

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) include thousands of variable length alkyl-chain chemicals with a perfluoroalkyl portion (C_nF_{2n+1}) (Buck et al., 2011; Evich et al., 2022); manufacture of PFAS started in the 1940s (National Academies of Sciences Engineering Medicine, 2022). PFAS are used as surfactants or repellants in the manufacture of industrial and consumer products that include non-stick cookware, water-repellant clothing, stain resistant fabrics and carpets, paper coating and food wrapping, cosmetics, and aqueous film-forming foam (AFFF) (Gaines, 2023).

PFAS distribute widely in the environment (Kurwadkar et al., 2022), and can contaminate food, soil, air, and drinking water supplies (Evich et al., 2022; Ramírez Carnero et al., 2021). In April 2024, the U.S. Environmental Protection Agency (EPA) announced the final National Primary Drinking Water Regulation to monitor levels, implement plans to reduce levels, and set legally enforceable contamination levels for several PFAS, including four legacy PFAS: perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA) (USEPA, 2024a).

Some PFAS can accumulate in humans (ATSDR, 2021), and studies suggest associations between PFAS and harmful health effects in people (National Academies of Sciences Engineering Medicine, 2022; ATSDR, 2021; NTP, 2016; USEPA, 2016a). Exposure to certain PFAS can lead to increased cholesterol levels, changes in liver enzymes, increased risk of kidney or testicular cancer, decreased birth weight, increased risk of pre-eclampsia in pregnant women, and decreased vaccine response in children (Anderko et al., 2020; Schilleman et al., 2023; Haug, 2023; Dunder et al., 2022; Costello et al., 2022; Sen et al., 2022; Borghese et al., 2022; Shearer et al., 2020; Steenland et al., 2021; Marks et al., 2021; Bangma et al., 2020; Zhang et al., 2022; Crawford et al., 2023). In November 2023, the International Agency for Research on Cancer revisited their 2017 evaluation of PFOA and determined that PFOA is carcinogenic to humans (Group 1) and that PFOS is possibly carcinogenic to humans (Group 2 B) (Zahm et al., 2024). In April 2024, the U.S. EPA designated PFOA and PFOS as hazardous substances under the Comprehensive Environmental Response, Compensation, and Liability Act (USEPA, 2024b).

With concerns over potential adverse health effects, manufacturing of legacy long-alkyl chain PFAS, including PFOA and PFOS, changed in the United States starting in 2000–2002 (ATSDR, 2021; USEPA, 2016a; Brennan et al., 2021). Consequently, other PFAS providing similar performance (i.e., alternative PFAS) can also be used. Some of these PFAS have shorter alkyl-chains (e.g., perfluorohexanoic acid (PFHxA)) or different chemical functional groups (e.g., ammonium salt of 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-

propanoic acid (GenX)) as compared to legacy PFAS (Calafat et al., 2019). Even though these alternative PFAS are also environmentally persistent, many appear to be less bioaccumulative and have shorter elimination half-lives than legacy PFAS (ATSDR, 2021; Wallis et al., 2023; Wang et al., 2013).

As part of its National Biomonitoring Program, the U.S. Centers for Disease Control and Prevention (CDC) have measured 17 PFAS in blood serum collected from a random one-third subsample of participants 12 years of age and older from the National Health and Nutrition Examination Survey (NHANES) since 1999–2000 (Calafat et al., 2019; Kato et al., 2011a; Calafat et al., 2007a; Calafat et al., 2007b; National Center for Environmental Health, 2022). The number and type of PFAS quantified have changed depending on the NHANES cycle (Table S1). Some PFAS have been measured continuously since 1999–2000. By contrast, measurement of certain PFAS was phased out after several NHANES cycles, often when weighted detection frequencies were below 5% (e.g., perfluorobutane sulfonic acid). Some PFAS were incorporated in subsequent cycles as with the 2017–2018 NHANES cycle which included five additional PFAS measured for the first time in serum: GenX, ADONA (4,8-dioxo-3H-perfluorononanoic acid), 9CLPF (9 chlorohexadecafluoro-3-oxanonane-1-sulfonic acid), PFHxA, and PFHpS (perfluoro-1-heptanesulfonic acid).

Other noteworthy aspects of the NHANES PFAS biomonitoring program are the absence of PFAS data in the 2001–2002 cycle because the volume of individual sera was insufficient for analysis. Also, the 2019–2020 cycle was incomplete as NHANES had to suspend its field operations in March 2020 due to the coronavirus pandemic. As a result, data collected from 2019 to March 2020 were combined with those from 2017 to 2018 NHANES to create a nationally representative NHANES pre-pandemic dataset (referred therein as 2017–March 2020 NHANES) available for the first time in June 2024 (National Health and Nutrition Examination Survey, 2022). Furthermore, select additional NHANES specimens were analyzed for PFAS in 2013–2014 including sera from a random one-third subsample of participants 3–11 years of age (Ye et al., 2018), and urine from a random one-third subsample of persons six years of age and older (Calafat et al., 2019). The data for these two special projects addressed specific data gaps, namely the lack of nationally representative PFAS exposure information for pre-school aged children and to evaluate the usefulness of urine as a biomonitoring matrix for PFAS.

Concentrations of legacy PFAS in NHANES are comparable to those of other general populations around the world during similar time periods (Kato et al., 2011a; Calafat et al., 2007b; Sonnenberg et al., 2023; Lin et al., 2021; Jain, 2018; Zhang, 2024; Schultz et al., 2023; Richterová et al., 2023; Forthun et al., 2023; Runkel et al., 2023; Norén et al., 2021; Göckener et al., 2020; Duffek et al., 2020; Yu et al., 2020; Toms et al., 2019; Lee et al., 2017). Our goals here were to evaluate serum concentration changes of the four most commonly studied legacy PFAS, namely PFHxS, PFOS, PFOA and PFNA, in the general U.S. population of adolescents and adults over two decades from 1999 up to March 2020 as well as to discuss serum concentrations and assess demographic predictors of 9CLPF and PFHpS, two PFAS measured for the first time in NHANES in 2017–2018. We also compared NHANES serum concentration profiles of PFHxS, PFOS, PFOA and PFNA to

the profiles in select specific populations, including people in exposed communities, mainly from drinking contaminated water.

2. Materials and methods

2.1. NHANES design

NHANES is a continuous survey conducted in two-year cycles by CDC's National Center for Health Statistics (NCHS) to assess the health and nutrition status of the general U.S. population. NHANES participants are selected to represent the civilian noninstitutionalized population of the United States using a complex, multistage probability sampling design. NHANES includes direct household interviews with demographic, socioeconomic, dietary, and health-related questions, as well as collection of biological samples at the time of health examinations (NHANES Survey Methods and Analytic, 2024). Some of these samples are used to assess exposure to environmental chemicals including PFAS (Calafat et al., 2019). The NCHS Ethics Review Board reviewed and approved the NHANES protocol. To participate in NHANES, respondents 18 years and above gave informed written consent, parents or guardians provided written consent for participants younger than 18 years, and children 7–17 years old provided assent.

2.2. Quantification of PFAS in serum

Details on the collection and processing of NHANES sera are public and detailed on the NHANES website for each cycle (NHANES Survey Methods and Analytic, 2024). After collection, NHANES serum specimens were aliquoted and shipped overnight on dry ice to CDC's National Center for Environmental Health (NCEH) for storage at -70°C until analysis; analyses for PFAS occurred from 2005 to 2023. The analytical methods used to measure PFAS in NHANES samples over this time period—based on solid phase extraction, separation by reversed phase high-performance liquid chromatography, and detection by isotope dilution-electrospray ionization tandem mass spectrometry—have been published (Kato et al., 2011b, 2018; Kuklennyik et al., 2004, 2005). Also, the standard operating procedures used to analyze the NHANES samples for PFAS are public and posted on the NHANES website. Depending on the PFAS and NHANES cycle, limits of detection (LOD) ranged from 0.05 $\mu\text{g/L}$ to 1.0 $\mu\text{g/L}$. Method accuracy, determined from repeated measurements of serum spiked with various concentrations of the target PFAS, was $100\% \pm 10\%$; and precision, expressed as the relative standard deviation of multiple measurements of quality control (QC) materials in a two-month period, was generally below 15%. To ensure high-quality and integrity of data, calibration standards, reagent blanks, and NHANES samples were analyzed with serum-based high- and low-concentration QC materials that were evaluated using standard statistical probability rules (Caudill et al., 2008). Furthermore, multiple times per year, the CDC laboratory successfully participates in proficiency testing programs to continuously demonstrate accuracy and precision of the analytical methods. These practices are part of CDC's rigorous quality assurance programs and are based on compliance with the requirements set forth in the Clinical Laboratory Improvement Amendments (CLIA) of 1988. Efforts assure comparability of the NHANES data throughout time, even when obtained using different analytical methods have been published (Kato et al., 2011b, 2018; Kuklennyik et al., 2004, 2005).

2.3. Data analysis: We used SAS (version 9.4; SAS Institute Inc., Cary, North Carolina) and SUDAAN (version 11.0.3; RTI International, Research Triangle Park, North Carolina) for statistical analyses and to calculate variance estimates that accounted for the complex, clustered design of NHANES. As recommended by NCHS, we used subsample population weights to produce estimates that are representative of the U.S. population. We set statistical significance at $P < 0.05$.

For concentrations below the LOD, we used the imputed value of LOD divided by the square root of 2 (LOD/SQR2) for all statistical calculations (Hornung et al., 1990). We used the specific LOD for each PFAS and survey cycle. Beginning with 2013–2014 NHANES, we quantified separately linear and branched isomers of both PFOS and PFOA. We summed the concentrations of the respective linear and branched isomers to calculate the total concentrations of these two PFAS (referred therein as PFOS or PFOA) (CDC, 2022). When the concentration of any of the isomers was below the LOD, we used the imputed value of LOD/SQR2 before summing the concentrations of the respective isomers. The sum of isomers is comparable to the concentrations of these two PFAS reported from 1999 to 2000 NHANES up to 2011–2012 NHANES (National Health and Nutrition Examination Survey, 2022).

We calculated the weighted detection frequency for the various PFAS, including the four most detected PFAS (PFOA, PFOS, PFHxS, PFNA), for all samples using PROC SURVEYFREQ and the cycle specific LOD. We also estimated the proportion of the general population with detectable serum concentrations of four or more of the PFAS measured by NHANES cycle.

For descriptive statistics, and based on self-report, we stratified age at the last birthday in two groups (12–19 years, ≥ 20 years), and race/ethnicity in five main categories: non-Hispanic Black, non-Hispanic White, all Hispanic (which includes Mexican American and other Hispanic persons), Mexican American, and Asian. Age and race/ethnicity categories were selected in accordance with NHANES analytic guidelines to account for changes in sample design and oversampling over time. Starting with 2007–2008, all Hispanic persons were oversampled. Starting with 2011–2012, Asian persons were oversampled. Of note, until 2009–2010 NHANES, the main race/ethnicity categories used were non-Hispanic Black, non-Hispanic White, and Mexican American that were expanded to the five above starting with 2011–2012 NHANES. We calculated geometric mean PFAS concentrations—only when the estimated weighted detection frequency was $\geq 60\%$ —and select distribution percentiles for the total population and by sex, age group, and race/ethnicity.

For the PFAS only measured in 2017–2018 NHANES with a weighted detection frequency of at least 5% percent (i.e., PFHpS, 9CLPF), we conducted weighted logistic regressions to examine the likelihood of having concentrations above the 95th percentile (a value selected to reflect an unusually high concentration compared to the average concentration for the population) by sex, age (continuous), and race/ethnicity. All three predictors were included in the initial models, but only the statistically significant predictors remained in the final models.

For this specific analysis, we categorized race/ethnicity as non-Hispanic Black, non-Hispanic White, Hispanic (encompassing both Other Hispanic and Mexican American) and Asian. We report both Bonferroni adjusted and unadjusted P-values and 95% confidence intervals (95% CI) for the odds ratios (ORs) for pairwise comparisons.

Because 9CLPF was detected most frequently among persons of Asian ethnicity (Table S2), we used Rao-Scott Chi-Square tests for cross tabulation between race, categorized as Asian vs non-Asian, and the following factors: a) having been born in the United States (vs other countries), b) having been in the United States <10 years (vs ≥ 10 years), and c) having detectable concentrations of 9CLPF.

We also used SAS Proc Surveyfreq to produce stratified Odds ratio by race/ethnicity (Asian vs non-Asian) for the cross tabulation between having 9CLPF concentrations above the 95th percentile and having been born in the United States (vs other countries). Furthermore, we performed weighted logistic regressions with Asian as the independent variable adjusted by sex and age with separate dependent variable: a) 9CLPF concentration being detectable, b) having been born in the United States (vs other countries), c) having been in the United States <10 years (vs ≥ 10 years). For these analyses, we used the variables DMDYRSUS ("length of time the participant has been in the US") and DMDBORN4 ("In what country {were you/was SP} born?").

3. Results and discussion

3.1. Changes in PFAS serum concentrations: 1999–March 2020

Summary data tables containing geometric means and select percentiles (e.g., 50th, 75th, 90th, 95th) by sex, age, and race/ethnicity for PFAS measured from 1999 to 2000 up to 2017–2018 NHANES, including PFHxS, PFOS, PFOA, and PFNA, are available in CDC's National Report on Human Exposure to Environmental Chemicals (National Center for Environmental Health). The Report is cumulative (i.e., includes all data tables since 1999–2000) and is updated periodically as the concentrations of chemicals measured for NHANES, including PFAS, become available. The 2017–March 2020 PFAS tables, never published before, are given in the Supporting Information (Tables S3–S13).

In NHANES, the most detected PFAS are four legacy PFAS: PFOA, PFOS, PFHxS, and PFNA. Other PFAS, including more recently manufactured PFAS are detected not as frequently, if at all, and at considerably lower concentrations. The estimated percent of the U.S. general population with detectable concentrations of one of the following PFAS has been consistently at least 95% in every cycle since 1999–2000: PFHxS (96.86–99.77%), PFOS (98.97–100%), PFOA (98.94–99.99%), and PFNA (95.00–99.81%) (Table S14). These four PFAS are also the predominately detected PFAS in other studies, even studies that evaluated more PFAS than those included in NHANES (Göckener et al., 2020). Concentrations of legacy PFAS in NHANES are comparable to those of other general populations around the world during similar time periods (Kato et al., 2011a; Calafat et al., 2007b; Sonnenberg et al., 2023; Lin et al., 2021; Jain, 2018; Zhang, 2024; Schultz et al., 2023; Richterová et al., 2023; Forthun et al., 2023; Runkel et al., 2023; Norén et al., 2021; Göckener et al., 2020; Duffek et al., 2020; Yu et al., 2020; Toms et al., 2019; Lee

et al., 2017). Furthermore, analyses of NHANES PFAS data up to 2017–2018, done by us and others, have showed that legacy PFAS serum concentrations vary by demographic factors such as sex, race/ethnicity, and age; in general, males having higher concentrations of PFAS than females, and older people having higher concentrations than younger people (Kato et al., 2011a; Calafat et al., 2007b; Sonnenberg et al., 2023; Lin et al., 2021; Jain, 2018). Those same demographic determinants and others such as parity and breastfeeding were also identified in studies of populations around the world (Zhang, 2024; Schultz et al., 2023; Richterová et al., 2023; Forthun et al., 2023; Runkel et al., 2023; Norén et al., 2021; Göckener et al., 2020; Duffek et al., 2020; Yu et al., 2020; Toms et al., 2019; Lee et al., 2017).

The geometric mean concentrations of all PFAS examined in NHANES over the two decades between 1999 and 2000 and 2017–March 2020, including the four most studied PFAS to date, namely PFOS, PFOA, PFHxS, and PFNA, decreased ((National Center for Environmental Health) and Tables S3–S13). In particular, the geometric mean concentrations of PFOS, PFOA, and PFHxS declined 87%, 74%, and 52%, respectively (Table 1, Fig. S1). On the other hand, the geometric mean of PFNA increased 130% from 1999 to 2000 to 2009–2010 followed by a 63% decrease from 2009 to 2010 to 2017–March 2020, with an overall decline of 16% between 1999 and 2000 and 2017–March 2020 (Table 1, Fig. S1).

Interestingly, looking at all PFAS measured in each NHANES cycle, the estimated proportion of the U.S. general population (95% CI) having detectable concentrations of four or more PFAS together in 1999–2000 was 99.95% (99.87–100%) in persons ≥ 12 years old and 99.92% (99.73–100%) in those 12–19 years of age, minimally dropping to 97.11% (95% CI: 94.98–99.25%) and 96.49% (95% CI: 92.27–100%), respectively, during 2017–March 2020 (Table S15). Collectively, these results reflect widespread exposure to PFHxS, PFOS, PFOA, PFNA and several other PFAS among the U.S. general population for the last two decades. Moreover, these data suggest that despite downward trends, about 96% of U.S. adolescents, many of whom were born after the changes in manufacturing practices started in 2000–2002, still have detectable concentrations of four or more PFAS in their serum even during 2017–March 2020. Notably, the NHANES data presented here spans almost two decades; during this time period, the analytical method, and LOD for some PFAS, changed. The LODs for some PFAS were highest during the analysis of the 2003–2004 NHANES samples (Tables S14–15), which could explain the slight decrease in the weighted detection frequency observed during that cycle. Yet, the overall trend suggesting that the vast majority of the general population had been exposed is clear.

The decrease in concentrations over the last 20 years agree with previous reports (Kato et al., 2011a; Calafat et al., 2007a; Lin et al., 2021; Jain, 2018; Göckener et al., 2020; Yu et al., 2020; Nguyen et al., 2019; Dong et al., 2019; Pollock, 2021) and suggest that body burden of legacy PFAS continues to decline over time. The decrease likely reflects discontinued production of perfluorooctanesulfonyl fluoride-based PFAS and related compounds in the United States that started in 2000–2002 (Brennan et al., 2021). The decrease is also in line with efforts from U.S. industry and the U.S. EPA to reduce production and emissions of PFOA and related chemicals by 95% by 2010 and elimination by 2015 (USEPA, 2016a;

USEPA, 2016b; ITRC, 2022). The PFNA initial concentration increase may reflect a slower adoption of removal of this PFAS or degradation of volatile precursors such as fluorotelomer alcohols to PFNA (Ellis et al., 2004; Prevedouros et al., 2006). Besides manufacturing practice changes, the different rates of decline in concentrations for these PFAS depend on other factors including existence of current exposure source(s) as well as biological elimination half-life. For example, PFHxS, compared to PFOA or PFOS, has a longer estimated half-life (Table 1), which could explain the slower concentration decline compared to that of PFOA and PFOS (ATSDR, 2021; Li et al., 2018). Nevertheless, even with declining detection frequencies and concentrations, these PFAS are still detectable in the vast majority of the U.S. population, including people born after production or environmental emissions of several PFAS were curtailed or phased out.

3.2. PFAS serum concentrations reported for the first time: NHANES 2017–2018

With the changes in manufacturing of long-alkyl chain legacy PFAS, alternative PFAS, including short-alkyl chain PFAS and other PFAS, may be increasingly used (Calafat et al., 2019; Brendel et al., 2018). Of the five PFAS (PFHpS, PFHxA, GenX, ADONA, 9CLPF) whose serum concentrations were reported for the first time in 2017–2018 NHANES (National Center for Environmental Health), the weighted detection frequency was highest for PFHpS (78.2%) and below 8% for the others (7.98% [9CLPF], <0.4% [PFHxA, GenX, ADONA]) (Table 2). The relatively low detection frequency of PFHxA, GenX, and ADONA may relate, at least in part, to their much shorter biological elimination half-life compared to that of long-alkyl chain PFAS, days versus years (Wang et al., 2013). Collectively, NHANES data suggest that these PFAS do not accumulate in serum to the same degree as long-chain legacy PFAS.

For chemicals that are not biologically persistent, urine, not serum, is the preferred matrix for exposure assessment (Needham et al., 2007). However, even with half-lives of the order of days, 2013–2014 NHANES data showed that the estimated proportion of the U.S. general population 6 years of age and older with detectable concentrations (≥ 0.1 $\mu\text{g/L}$) of PFHxA, GenX and ADONA in urine was 22.7%, 1.2% and 0%, respectively (Calafat et al., 2019). In other studies, Borghese et al. detected PFHxA, GenX, ADONA, 9CLPF, and PFHpS in 35.6%, 47.1%, 15.9%, 15.9%, and 66.1%, respectively, in samples from the Maternal-Infant Research on Environmental Chemicals (MIREC) Canadian pregnancy cohort; 95th percentiles were 0.130 $\mu\text{g/L}$ (PFHxA), 0.028 $\mu\text{g/L}$ (GenX), 0.008 $\mu\text{g/L}$ (ADONA), 0.029 $\mu\text{g/L}$ (9CLPF); 0.076 $\mu\text{g/L}$ (PFHpS) (Sonnenberg et al., 2023). Similarly, Schultz et al. detected 9CLPF and PFHpS in 41.7% and 96.4%, respectively, of samples from the Survey of the Health of Wisconsin (SHOW) participants; geometric means were 0.168 $\mu\text{g/L}$ (PFHpS) and 0.071 $\mu\text{g/L}$ (9CLPF) (Schultz et al., 2023). The MIREC and SHOW samples were analyzed using methods with lower LODs than the method used to analyze the NHANES. While, as expected, detection frequencies differ between NHANES and these other studies because LOD are different, it is noteworthy that PFHpS concentrations were remarkably similar, and for the other PFAS, namely GenX, ADONA, PFHxA, and 9CLPF, concentrations were at or below 0.1 $\mu\text{g/L}$, the LOD of the method used for the NHANES samples. Collectively, NHANES data using current methods with LODs of 0.1 $\mu\text{g/L}$ for alternative PFAS, do not suggest widespread exposure to these PFAS in the U.S.

general population even though exposure in specific areas (e.g., nearby sources) can occur. Targeted studies in areas with suspected contamination with PFAS that include collection of environmental samples and dietary information, among other data, can increase our understanding of exposure to these other PFAS in specific populations.

PFHpS is a long-alkyl chain PFAS with a biological elimination half-life similar to legacy PFAS, lasting years (Table 2). Like with other long-alkyl chain PFAS, geometric mean (95% CI) concentrations of PFHpS were higher in males (0.277 (0.224–0.342) µg/L) than in females (0.178 (0.150–0.212) µg/L); adults also had higher geometric mean concentrations than adolescents (0.233 (0.197–0.275) µg/L vs. 0.152 (0.116–0.200) µg/L, respectively), but the 95% CI overlapped (National Center for Environmental Health).

The final weighted logistic regression model to determine the likelihood of having PFHpS serum concentrations above the 95th percentile was not associated with sex ($P = 0.38$), age ($P = 0.78$), or race/ethnicity ($P = 0.07$). By contrast, in the final model for 9CLPF (Table 3), race/ethnicity ($P < 0.01$) and age ($P < 0.01$) were significant variables, after excluding sex that was non-significant ($P = 0.98$). For every one-year increase in age, 9CLPF (odds ratio [OR] (95 % CI)) was 1.02 (1.01–1.03) times more likely to be above the 95th percentile. These results agree with previous reports suggesting that older people have higher serum/plasma concentrations of other PFAS with similarly long biological half-lives compared to younger people (Kato et al., 2011a; Calafat et al., 2007a; Sonnenberg et al., 2023; Jain, 2018; Schultz et al., 2023; Yu et al., 2020). Interestingly, Asian persons were 7.77 (2.5–24.14), 5.68 (2.19–14.71), and 24.34 (6.59–89.85) times more likely than Hispanic, non-Hispanic Black, and non-Hispanic White persons, respectively, to have 9CLPF concentrations higher than the 95th percentile (Table 3).

Race (Asian vs non-Asian) was significantly associated with having detectable concentrations of 9CLPF (Chisq P -Value < 0.01), country of birth (United States vs other) (Chisq P -Value < 0.01), and length of time (< 10 vs ≥ 10 years) lived in the United States (Chisq P -value < 0.01). Furthermore, Asian persons (adjusted OR (95%CI)) were 14.2 (6.73–29.97) times more likely than non-Asian persons to have detectable concentrations of 9CLPF, Asian persons (adjusted OR (95%CI)) were 25.83 (15.5–43.6) times more likely than non-Asian persons to have been born outside of the United States, and Asian persons were 1.98 (1.23–3.19) times more likely than non-Asian persons to have lived in the United States less than 10 years ($P < 0.01$).

Moreover, stratified cross tabulation analyses showed that for people having concentrations of 9CLPF above the 95th percentile, 93.97% (95%CI: 88.00–99.95%) of Asians had been born outside the United States, whereas for those whose concentrations were ≤ 95 th percentile, 71.27% (95%CI: 60.59–81.96%) of Asians had been born outside the United States. The analysis also showed that Asians and non-Asians who had been born outside of the United States (OR (95%CI)) were 6.28 (1.83–21.62) and 4.41 (2.44–7.97) times more likely, respectively, to have 9CLPF concentrations above the 95th percentile than those who were born in the United States.

While we recommend caution when interpreting the above 9CLPF findings (e.g., the variable related to the number of years a person lived in the United States had a relatively large number of missing observations with <20% participation), collectively these results suggest that some exposures to 9CLPF could have occurred outside the United States. The differences by race/ethnicity may relate to lifestyle habits and potential exposures prior to residency in the United States. 9CLPF is a PFOS alternative, also known as 6:2 Cl-PFESA or by its trade name F53-B, that has been used as a commercial mist suppressant by the Chinese electroplating industry since the 1970s (He et al., 2022). Because 9CLPF is used in production processes and not directly as part of specific products, exposure is potentially limited to locations where 9CLPF is used (Hamid et al., 2024). There is widespread detection of 9CLPF in environmental matrices such as surface water, seawater, sediment, sewage sludge, and wildlife, mostly in China (Hamid et al., 2024; Awad et al., 2020; He et al., 2022; Pan et al., 2018)). Documented use of 9CLPF outside of China is not known, but due to 9CLPF long half-life (15.3 years (Shi et al., 2016)) and potential to bioaccumulate, global contamination could be of concern thus highlighting the relevance of future studies to continue to monitor human exposure to 9CLPF.

3.3. Legacy PFAS serum concentration profiles

The relative serum concentrations of PFHxS, PFOS, PFOA, and PFNA in NHANES, presented in a pie graph, reflect the pattern of general population exposures to these four most commonly detected PFAS (Fig. 1, S2, S3). While concentrations of these four PFAS have decreased over the nine NHANES cycles, the relative concentration pattern has remained quite steady (Fig. S2). Of note, the profiles of these legacy PFAS, both at the geometric mean and higher concentrations (e.g., 95th percentile), consistently show PFOS with the highest proportion of the pie graph and PFNA with the lowest, irrelevant of concentration, suggesting similar exposure sources to these four PFAS nationally regardless of the magnitude of the exposures (e.g., median vs 95th concentration percentiles) (Kato et al., 2021). These NHANES PFAS profiles reflect exposures to these PFAS experienced by the general population from the many environmental sources of PFAS, but the profiles alone cannot identify the nature of the sources.

Interestingly, in the presence of dominant source(s) of PFAS, such as contamination of drinking water supplies from industrial pollution or AFFF use, the resulting profiles and the NHANES profiles for these four PFAS at similar time periods may differ considerably. For example, as shown in Fig. 1, NHANES profiles are quite different from those in a) a convenience sample of Mid-Ohio Valley, WV residents in 2005–2006 who had their water districts contaminated with PFOA from a nearby chemical plant (Gallo et al., 2013), b) a convenience sample of Paulsboro, NJ residents, recruited during 2016–2017, whose community water supply had been contaminated with PFNA and PFOA, likely from a nearby manufacturing facility that had used PFNA in its processes (Graber et al., 2019), and in c) residents of the City of Airway Heights, WA, in 2019, near Fairchild Air Force Base known to have PFAS in its drinking water from use of AFFF (ATSDR, 2022).

Noteworthy, even when exposure source(s) are similar, such in communities near current or former military bases with known presence of PFAS in their drinking water, profiles

for these four PFAS could be quite different because of differences in the magnitude and duration of the exposures, composition of the AFFF used, design of the drinking water systems, and use of water treatment systems, among other factors (Fig. S3). Similarly, 9CLPF is one of the top three detected PFAS in the Chinese population (He et al., 2022); as such, it is expected that PFAS profiles in China would differ from the NHANES profiles that have PFOS as the most abundant PFAS.

3.4. Strengths and limitations

Our analysis has important strengths as well as some limitations. NHANES has provided nationally representative serum concentrations for select PFAS over two decades. These data can be used to track trends of exposure to select PFAS, mainly legacy PFAS. This is because at the onset of the PFAS NHANES program, about 20 years ago, PFAS research was largely limited to long-alkyl chain PFAS. Although we have included PFAS only measured in recent NHANES cycles, additional data for these other PFAS are needed to understand exposure trends. Notably, the PFAS NHANES data for this manuscript were generated from 2005 to 2023. While we took meticulous care to ensure the integrity of the data, during this period, for some PFAS, method LODs changed, and we recommend care when comparing detection frequencies. It should be noted that the serum concentrations cannot distinguish between direct exposure to PFAS and indirect exposure from degradation of PFAS precursors. For instance, PFOA serum concentrations could reflect a combination of direct PFOA exposures and exposures to PFOA precursors (e.g., fluorotelomer alcohols) that can be transformed to PFOA in vivo. Nevertheless, the detection frequency for PFHxS, PFOS, PFOA and PFNA remained at or above 95% throughout the time period evaluated.

Also, because of NHANES study design, serum for measuring PFAS is only available for persons 12 years of age and older, and not for younger children. Furthermore, NHANES is not designed to provide information at the regional, state or local level. However, comparing PFAS concentration profiles for specific populations with those from NHANES, and used in combination with other data (e.g., levels of PFAS in environmental media, information on proximity to manufacturing sites or military facilities) can help identify exposure sources and, thus, inform public health efforts to reduce or stop exposures in potentially affected communities. Last, information gathered from the analysis of NHANES data reflects U.S. general population exposures but provides no information on sources. In addition, local exposures as well as occupational exposures, may be missed in such an assessment.

4. Conclusions

Two decades of NHANES data from 1999–March 2020 show an overall decline in the serum concentrations of several PFAS including PFHxS, PFOS, PFOA and PFNA. Nonetheless, the vast majority of the U. S. population still has measurable quantities of these legacy PFAS in their blood, including people born after the initial phase-out of production or environmental emissions of some PFAS. For five PFAS measured for the first time in serum in 2017–2018 NHANES, about three-quarters of the U.S. general population had measurable serum concentration of PFHpS, about 8% to 9CLPF (more than 44% of whom self-identified as Asian), and fewer than 0.4% to PFHxA, GenX, or ADONA. This NHANES nationally

representative information can also be an important tool to help identify PFAS exposures in specific segments of the population affected by accidental exposures or industrial pollution. Moreover, these NHANES data can provide the scientific basis to influence regulations and other actions to reduce exposures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC. Use of trade names is for identification only and does not imply endorsement by the CDC, the Public Health Service, or the US Department of Health and Human Services. The authors declare no competing financial interest.

Data availability

Data is part of NHANES which is publicly available data

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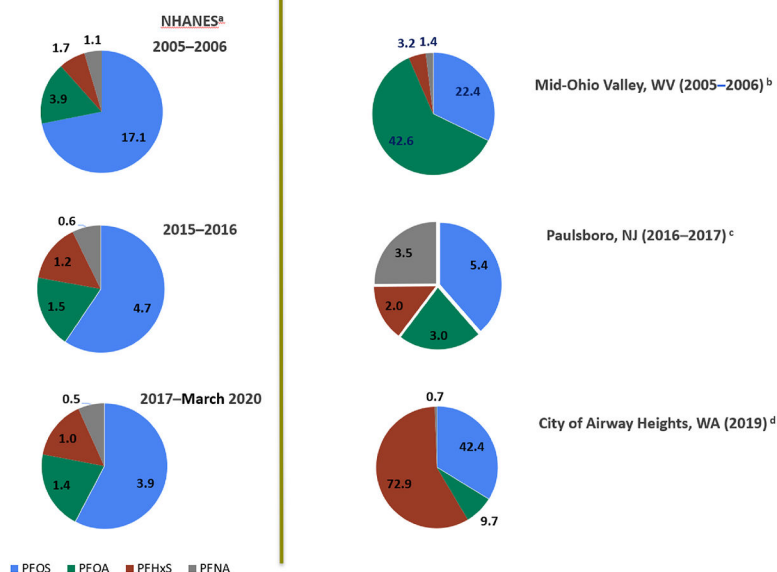


Fig. 1.

Profiles of PFOS, PFOA, PFHxS and PFNA based on their serum geometric mean concentrations (µg/L). These PFAS profiles differ based on dominant exposure source when compared to NHANES PFAS profile of the same time period.

^aData are from CDC's National Report on Human Exposure to Environmental Chemicals (National Center for Environmental Health).

^bConvenience sample of Mid-Ohio Valley, WV residents in 2005–2006 who had their water districts contaminated with PFOA from a nearby chemical plant (Gallo et al., 2013).

^cConvenience sample of Paulsboro, NJ residents, recruited during 2016–2017, whose community water supply had been contaminated with PFNA and PFOA, likely from a nearby manufacturing facility that had used PFNA in its processes (Graber et al., 2019).

^dResidents of the City of Airway Heights, WA, in 2019, near Fairchild Air Force Base known to have PFAS in its drinking water from use of AFFF (ATSDR, 2022).

Table 1

Biological half-life, geometric mean and 95% confidence interval (95% CI) for the four most abundant PFAS (PFOS, PFOA, PFHxS, PFNA), with the calculated percent change in serum concentrations among the U.S. general population 12 years of age and older, from 1999 to 2000 to 2017–March 2020.

	1999–2000	2017–March 2020	Percent Change	Biological half-life in humans (years)(ATSDR, 2021)
	Geometric Mean (95% CI) µg/L ^a			
PFOS	30.3 (27.1–33.9)	3.93 (3.68–4.21)	–87%	3.3 to 27
PFOA	5.22 (4.72–5.78)	1.38 (1.31–1.45)	–74%	2.1 to 10.1
PFHxS	2.15 (1.92–2.41)	1.04 (0.971–1.12)	–52%	4.7 to 35
PFNA	0.548 (0.456–0.663)	0.460 (0.412–0.514)	–16%	2.5 to 4.3

^aNHANES geometric mean and 95% confidence interval (95% CI) of PFAS serum concentrations are calculated from data available on the NHANES website (<https://wwwn.cdc.gov/nchs/nhanes/default.aspx>).

Table 2

Biological half-life in humans, weighted detection frequency, geometric mean and 95th percentile of serum PFAS concentrations for the U.S. population 12 years of age and older from 2017 to 2018 NHANES (N = 1672) for five PFAS measured NHANES cycles 17–18 for the first time.

	Biological half-life in humans	Weighted detection frequency %	Geometric mean ^a (95% CI) µg/L	95th Percentile ^b (95% CI) µg/L
GenX	1.74–168 days (Wallis et al., 2023)	0.03	NC	<LOD
ADONA	12–34 days (Wang et al., 2013)	0.00	NC	<LOD
9CLPF	10.1–56.4 years (Shi et al., 2016)	7.98	NC	0.100 (0.100–0.200)
PFHxA	13.7–327 days (Wallis et al., 2023)	0.38	NC	<LOD
PFHpS	0.9–8.6 years (Wallis et al., 2023)	78.2	0.221 (0.185–0.263)	1.00 (0.500–4.60)

^aNC (Not Calculated): proportion of concentrations below LOD was too high to provide valid results.

^bThe limit of detection (LOD) was 0.1 µg/L for all PFAS.

Table 3

Odds ratios and 95% confidence intervals for having serum 9CLPF concentrations above the 95th percentile from the logistic regression analysis with and without Bonferroni Adjustment for the U.S. population ≥12 years of age. Data from the National Health and Nutrition Examination Survey (NHANES) 2017–2018.

Effect	With Bonferroni Adjustment		Without Bonferroni Adjustment		
	OR (95% CI)	P-Values ^a	OR (95% CI)	P-Values ^a	
Race/Ethnicity ^b	Asian vs Hispanic	7.77 (2.50–24.14)	<0.01	7.77 (3.50–17.22)	<0.01
	Asian vs non-Hispanic Black	5.68 (2.19–14.71)	<0.01	5.68 (2.90–11.08)	<0.01
	Asian vs non-Hispanic White	24.34 (6.59–89.85)	<0.01	24.34 (9.73–60.90)	<0.01
	Hispanic vs non-Hispanic White	3.13 (1.35–7.25)	<0.01	3.13 (1.74–5.65)	<0.01
Age (years)	non-Hispanic Black vs non-Hispanic White	4.29 (1.50–12.24)	<0.01	4.29 (2.05–8.96)	<0.01
		1.02 (1.01–1.03)	<0.01	1.02 (1.01–1.03)	<0.01

^aConfidence intervals and P-values were adjusted for multiple comparisons.

^bHispanic persons encompass both Other Hispanic persons and Mexican American persons.