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Biomonitoring of emerging contaminants, perfluoroalkyl and polyfluoroalkyl substances (PFAS), in New Jersey adults in 2016–2018

Chang Ho Yu[a], C. David Riker[a], Shou-en Lu[b], Zhihua (Tina) Fan[a,*]

[a] Environmental and Chemical Laboratory Services, Public Health & Environmental Laboratories, New Jersey Department of Health, Ewing, NJ, 08628, USA
[b] Environmental Epidemiology and Statistics, Environmental and Occupational Health Sciences Institute (EOHSI), School of Public Health, Rutgers University, Piscataway, NJ, 08854, USA

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ABSTRACT

New Jersey (NJ) residents in some areas may be exposed to perfluoroalkyl and polyfluoroalkyl substances (PFAS) due to PFAS contamination of public drinking water. This contamination stems from industrial discharges and the use of aqueous film-foaming foams at military bases and commercial airports for drills and locations where fires occurred. Exposure to PFAS has raised significant public health concerns due to its persistence both in the environment and human body. The potential toxicity of these chemicals may pose risks to human health. Statewide biomonitoring data is needed to establish a baseline of exposure and to identify the subpopulations at risk. The NJ Department of Health (NJDOH) conducted a statewide NJ Biomonitoring (NJBM) study for PFAS utilizing a cost-effective sampling approach, i.e. acquiring remnant sera from both clinical laboratories and blood banks across NJ. This convenience sampling approach was adopted as an alternative to a costly and labor-intensive probability-based population sampling. One thousand and thirty human sera were collected from NJ adults between 20 and 74 years of age from 2016 to 2018, with additional information of county, sex, and age. The serum collection was demographically and geographically dispersed across four seasons. Twelve PFAS analytes were measured for the specimens collected. The data were post-stratified by county, sex, and age groups (20–39, 40–59, and 60–74 years old). Stratified individual sample weights were developed and used to estimate population means, compare least-squared mean differences, and examine contributing variables. Geometric means (GMs) and percentiles with 95% confidence intervals (CIs) of the target analytes are presented, providing preliminary baselines of the statewide PFAS exposure for NJ adults. PFOA, PFNA, PFHxS, and PFOS were selected for in-depth analyses because their GMs were greater than 0.5 ng/mL and they were detected over 99% in study population. Subjects from this study had higher serum levels of PFOA, PFNA, and PFHxS compared to the general U.S. population reported by the latest National Health and Nutrition Examination Survey (NHANES in 2015–2016). However, the distributions of PFOA, PFNA, PFHxS, and PFOS across sex and age groups were consistent with the patterns found in NHANES, i.e. all differed by sex and age group. Further sex and age stratification showed significantly lower concentrations of the 4 analytes in younger females (20–59 years old) than in older females (60–74 years old) and males (20–74 years old). Future research is needed to identify PFAS exposure sources and to develop effective intervention strategies. Continuing PFAS biomonitoring using population sampling is recommended for tracking trends and better identifying subpopulations at risk.

1. Introduction

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are man-made chemicals. They have been extensively used for over 60 years in many applications. Some of these applications are water-proof fabrics, oil-repelling containers, aqueous film foaming foams (AFFFs), as well as emulsifiers and surfactants in industrial processes (Kissa, 2001). They have gained great attention recently because of their persistence and toxicity in the environment and in the human body (Lau, 2014). PFAS exposure sources are widespread (ATSDR, 2018). However, the most significant route of exposure to the general population is from consuming food and water contaminated with PFAS, specifically

* Corresponding author. Environmental and Chemical Laboratory Services (ECLS), Public Health & Environmental Laboratories (PHEL), New Jersey Department of Health, 3 Schwarzkopf Drive, Ewing, NJ, 08628, USA.
E-mail address: tina.fan@doh.nj.gov (Z.T. Fan).

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perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), (Trudel et al., 2008; Vestergren and Cousins, 2009; Gebbink et al., 2015). Elevated levels of PFAS were found in drinking water for the communities near the facilities which produced and/or use PFAS. Other contamination sources are leachate from landfill sites and effluents from wastewater treatment plants where PFAS-containing consumer products or wastes are processed (ITRC, 2018). Extended use of AFFFs in firefighting and/or training at military bases, commercial airports, and locations where fires occurred is also significant sources of PFAS contamination for drinking water (U.S. GAO, 2018; ITRC, 2018). For the general population, exposure to long-chain PFAS such as PFOA, perfluorononanoic acid (PFNA), perfluorohexanesulfonic acid (PFHxS), and PFOS at concentrations around 40 ng/L or even less than 40 ng/L in drinking water can be much more significant than the combined effects from food, consumer products, and house dust/soil found at prevalent levels. Exposure to PFAS through water consumption is more adverse for susceptible populations such as infants (Post et al., 2017). Exposures to PFAS are also found to be significant for those who come in direct contact with PFAS as part of their occupation. (ATSDR, 2018).

Increased PFAS exposure has been linked to various health effects. For example, higher PFOA and PFOS levels in serum were positively associated with lipid levels, especially for total cholesterol (Steenland et al., 2009; Frisbee et al., 2010; Nelson et al., 2010; Eriksen et al., 2013) and uric acid levels (Steenland et al., 2010; Shankar et al., 2011; Geiger et al., 2013). Potential negative health outcomes are low birth weight and reduction in immune responses observed in population studies (ATSDR, 2018). Health effects in hepatic, reproductive, cardiovascular, and endocrine systems have also been reported in epidemiological studies and animal tests (ATSDR, 2018). PFOA was classified as possibly carcinogenic to humans (Group 2B) by the International Agency for Research on Cancer (IARC) (IARC, 2016), and the Environmental Protection Agency (EPA) concluded that there is suggestive evidence for human carcinogenicity of PFOA and PFOS (EPA, 2016).

Biomonitoring is a useful tool that characterizes exposure levels in the study population and identifies disparities within the population (Tan et al., 2012). Biomonitoring data can assist in the intervention efforts to minimize body burdens in a highly exposed population. Demographic and location-stratified exposure data can be further utilized for developing effective risk management plans for the target subpopulation and specific areas. In addition, biomonitoring data can provide insights into plausible associations between increased PFAS exposures and potential health outcomes. To establish baseline exposure data for PFAS in the general U.S. population, the Centers for Disease Control and Prevention (CDC) has conducted nationwide PFAS biomonitoring since 1999 as a part of two-year cycle of the National Health and Nutrition Examination Survey (NHANES) (CDC, 2018). The NHANES PFAS data provides temporal trends nationally, however, NHANES PFAS data (n~2000) lacks the granularity to allow for stratification by the state or the county level. Therefore, further stratifications by different sex and age groups from each county within the state is impractical. To provide additional information and to fill in the data gaps, the New Jersey Department of Health (NJDOH) conducted a statewide biomonitoring program, NJ State Biomonitoring (NJBM), from 2014 to 2019. This program was supported by the CDC National Biomonitoring Program (CDC, 2019). NJBM is a study for exposures to various environmental contaminants, including emerging environmental contaminants PFAS. NJBM study used a cost-effective sampling approach by collecting remnant biospecimens from blood banks and clinical laboratories across NJ, and more than one thousand serum specimens (n = 1030) were collected from NJ adult (20–74 years old) between 2016 and 2018. This study was designed to collect data from a large, heterogeneous population, while minimizing cost and labor that are the primary limiting factors to implement such a large-scale human biomonitoring study.

This work presents a cross-sectional study of PFAS levels in more than one thousand of NJ adults, the first report of emerging PFAS body burdens in NJ. In-depth statistical analyses were employed to examine the differences between participating NJ adults and NHANES adults as well as the differences within six sex-age strata. Exploratory spatial analysis was further employed to identify specific locations with significantly clustered and higher PFAS levels than surrounding areas across NJ. In summary, this manuscript provides practical approaches to determine cross-sectional PFAS exposure levels at a state-scale and to identify subpopulations at increased risk, which can be applied to other state's biomonitoring studies.

2. Materials/subjects and methods

2.1. Study population

One thousand and thirty remnant serum specimens were acquired from two providers, one was a clinical laboratory serving the state with wellness visits and the other was a regional blood bank located in central NJ. Specimen collection was spanned over a three-year period (2016–2018) and throughout the four seasons to avoid the impact of any single event on the results. The target age range of 20–74 was selected for two reasons: this age range is the most probable range from blood donors and clinic patients and this age range is consistent with the main age groups represented in NHANES (Kato et al., 2011; Sjödin et al., 2014; Mortensen et al., 2014). The proposed sample size of 1000 sera was based on power calculation to detect differences between NJ adults and adults at the national level (e.g., NHANES) as well as within stratified groups such as sex, age, and residence location (i.e., NJ county). The de-identified remnant serum specimens were initially screened and randomly selected at each participating lab based on the study criteria (i.e., NJ residents between 20 and 74 years old). The serum specimens were checked again with each individual's demographic information such as sex, age, and ZIP code by the NJDOH-Environmental and Chemical Laboratory Services (ECLS) prior to analysis. Sample log-in, sample distribution, lab analysis, data upload, and result reporting were conducted and managed by the ELEMENT®, NJDOH-ECLS secure Laboratory Information Management System (LIMS).

2.2. Sample analysis

The samples were analyzed by ECLS laboratory using the optimized PFAS testing method, NJDOH PFAS method (Yu et al., 2017). This method was optimized from CDC Method (#6304.04) as a part of the NJBM project. The NJDOH method utilizes a high-throughput online solid phase extraction (SPE) (Spark Holland, Emmen, Netherlands) system and a highly sensitive tandem mass spectrometer (MS/MS) (Sciex QTrap 6500, Framingham, MA), which can detect 12 target PFAS analytes listed in Supplementary Table S1 as low as < 0.1 ng/mL within a 10-min run time. Detailed method development (Yu et al., 2017) and optimizations (Yu, 2017) were described, respectively. Since 2016, the ECLS analysis lab has participated in the CDC's bi-annual Biomonitoring Quality Assurance Support Program (BQASP) for PFAS in serum and passed all proficiency tests (PTs) with 100% score. According to NJDOH Quality Assurance/Quality Control (QA/QC) procedures, all analyzed samples and concentration data have been rigorously reviewed and audited. Prior to data reporting, all concentration data were validated against data quality control protocols.

2.3. Data analysis

2.3.1. Correction of sampling deviations & consideration of sampling design effects

Over-sampling or under-sampling for specific demographic/geographic strata (Lee and Forthofer, 2005) may occur, considering the sampling method employed by the NJBM. To adjust for sampling deviations, a population weight for individual samples was developed. Calculated sample weights for each strata and an example of calculation

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steps can be found in Supplementary Data (see Table S2 and Supplementary Material). The participants were divided into three age groups: 20–39, 40–59, and 60–74 years old, respectively. These groups represent young adults, middle-aged adults, and seniors. This method of age grouping was also utilized in previous PFAS studies (Kato et al., 2011; Olsen et al., 2017). Individual sample weight was determined by calculating a ratio of NJBM collection against reference NJ census data for each sex-age-county strata and multiplying it with a base NJBM weight and a correction factor. This post-stratification weighting is commonly used to correct biases in collected samples against a target population (Smith, 1991). Assigned individual sample weight was used for estimating population means and percentiles in descriptive statistics as well as comparing least-squared mean differences and estimating variances in regression analysis.

The NJBM serum acquisition was conducted by batch (usually n~50–70) at monthly or bi-monthly intervals. Samples collected from a sample provider during a specific time period are more correlated than the samples collected from the same provider at different time periods. Furthermore, samples collected from a specific sample provider are more clustered than the samples collected from different providers. These effects should be considered in analyzing data by defining the individual provider as *strata* and the sample acquisition time as *cluster* effects (Lewis, 2016). Utilizing the sample weights and adjusting for sampling design effects, data can better represent the population of NJ adults and be comparable to other studies.

2.4. Descriptive statistics

Biomonitoring data is generally skewed to the right, thus the logarithmic transformation was applied in the data analysis. Detection limit (DL), reporting limit (RL), measurement percentage detected above DL, and measurement percentage detected above RL for the 12 PFAS analytes are reported in Table S1. Among the 12 target analytes, four PFAS analytes (PFOA, PFNA, PFHxS, and PFOS) were specifically selected and further analyzed for this manuscript because these analytes were found in most samples at a rate of > 99% and had geometric means (GMs) higher than 0.5 ng/mL. The four PFAS analytes selected throughout this manuscript were also chosen to ensure that the statistical analyses used and presented in this study were relevant. If low-detected PFAS analytes (e.g., < 60% of detection) were included and used, the replacement of non-detected values with a single value would significantly affect estimated means and variances. Thus, only descriptive statistics for the rest of 8 analytes are separately presented in Supplementary Table S3. GMs were calculated and provided, only if the analytes were detected over 60% of the analyte's RL. Any missing or values less than DLs were replaced with DL/√2. These data handling procedures were consistent with the approaches used in NHANES biomonitoring studies (Kato et al., 2011; Sjödin et al., 2014; Mortensen et al., 2014). Statistical significance was determined by $p < 0.05$. All statistical analyses were conducted on the Statistical Analysis System (SAS) program ver. 9.4 (SAS Institute, Cary, NC). To fully utilize individual sample weights and consider sampling design effects (*strata* and *cluster*), SAS surveymeans procedure was used to calculate GMs and percentiles of 50%, 75%, 90%, and 95% with 95% confidence intervals (CIs).

2.5. Comparison between NJBM vs. NHANES

To test whether the measured PFAS levels of the participants in the NJBM study were higher than the national levels, the latest NHANES data surveyed in 2015–2016 was used for comparison (CDC, 2018). The subset of data with the same age range of 20–74 years old was used, which is comparable to the NJBM study. To ease the complexity in the sampling by factors such as sample weight and subset selection, a direct comparison was conducted on the un-weighted PFAS data from both NJBM and NHANES using non-parametric Wilcoxon test. To explore if high PFAS analyte concentration data was linkable to geographic patterns across NJ, the elevated PFAS in NJBM that were detected over the 95% threshold of the NHANES data were also identified (see Supplementary Table S4) and used for spatial analysis.

2.5.1. Correlations among PFAS and with serum lipids

NJBM measured serum lipid levels, including low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, total cholesterol (TC), triglyceride (TG), and total lipids (TL) in mg/dL, for each specimen. These serum lipid measurements were conducted by the Alere Cholestech LDX Analyzer (Abbott Laboratories, Chicago, IL) with a lipid profile cassette at the ECLS lab. Partial serum lipid data (n = 694 for LDL cholesterol, n = 747 for HDL cholesterol, and n = 978 for TC, TG, and TL) were available to investigate associations with serum PFAS data. Spearman correlation coefficients (r_s) and p-values were calculated to evaluate the strength of relationships between paired datasets. Correlations among the four PFAS data were also conducted and presented in the same correlation matrix.

2.5.2. Differences of PFAS in sex and age group

Previous studies have shown that PFAS levels could be influenced by demographic attributes (Kato et al., 2011; Olsen et al., 2017). A survey regression analysis was used to examine the impact of each variable on the measured PFAS data while controlling other covariates in the regression model. Prior to analyzing data in a survey regression model, fixed effects of sex (male vs. female), age (20–39, 40–59 and 60–74 years old), and an interaction of sex*age were initially tested in a generalized linear model. Significant effects were observed for sex ($p < 0.01$), age ($p < 0.01$), and an interaction of the two ($p < 0.01$) in all tested PFAS models. Thus, six sex-age strata (female*20–39, female*40–59, female*60–74, male*20–39, male*40–59, and male*60–74) were stratified and further examined in a survey regression model. The survey regression model also included serum lipid (TL; the most correlated among the lipid panel) to examine the factor while controlling sex and age variables in the same model.

The final survey regression model was established (equation (1)) with six strata of sex-age and individual TL data.

$$Ln(PFAS) = \beta_0 + \beta_{sa} \cdot Sex - Age + \beta_l \cdot TL + \varepsilon \quad (1)$$

where, Ln(PFAS) is a log-transformed (base of e) PFAS concentration (ng/mL);

β_0 is an intercept;
β_{sa} is an estimate of sex-age strata;
β_l is an estimate of TL; and
ε is an error term of the regression model.

SAS surveyreg procedure was specifically used for this regression analysis to account for the effect of sample provider (as *strata* in model), timing of sampling cycle (as *cluster* in model), and individual sample weight (as *weight* in model). Multiple comparisons were performed, if the regression model showed significant differences in any tested effects ($p < 0.05$).

2.5.3. Spatial analysis

To identify spatially clustered and significantly higher PFAS measurements in surrounding areas among collected NJBM datasets, a provisional analysis using a Geographical Information System (GIS) was developed and conducted. Specifically, all measured 1030 PFAS concentration data were averaged with discrete ZIP code (generating 317 datapoints), and the ZIP code-averaged PFAS data were geocoded using a GIS program. Exploratory spatial analysis was carried out by choosing a Getis-Ord Gi* approach with selecting a spatial relationship of "inverse distance" and a distance method of "Euclidean" in the ArcGIS program. The GIS program calculated Gi* statistics with z-scores (how much clustered) and p-values (how significant than surrounding areas)

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Table 1
Demographic attributes of serum specimens (n = 1030; 20–74 in age) collected for the NJBM study between 2016 and 2018 as well as the 2017 NJ Census data.

Characteristics	Classification	Number	NJBM in 2016–2018	NJ Census in 2017
Sex	Female	517	49.8%	49.0%
	Male	513	50.2%	51.0%
Age Group	20–39	315	30.6%	37.6%
	40–59	429	41.8%	40.4%
	60–74	286	27.7%	22.1%
NJ County	Atlantic	25	2.4%	3.1%
	Bergen	108	10.3%	10.5%
	Burlington	80	7.8%	5.1%
	Camden	30	2.9%	5.7%
	Cape May	3	0.3%	1.1%
	Cumberland	5	0.5%	1.8%
	Essex	66	6.4%	8.8%
	Gloucester	12	1.2%	3.3%
	Hudson	76	7.4%	8.0%
	Hunterdon	12	1.2%	1.4%
	Mercer	136	13.2%	4.2%
	Middlesex	86	8.4%	9.4%
	Monmouth	60	5.8%	7.0%
	Morris	41	4.0%	5.6%
	Ocean	46	4.5%	6.1%
	Passaic	127	12.3%	5.6%
	Salem	1	0.1%	0.7%
	Somerset	46	4.5%	3.7%
	Sussex	12	1.2%	1.7%
	Union	58	5.6%	6.1%
	Warren	2	0.2%	1.2%

for all imported 317 locations at confidence levels (CLs) of 95% (type I error; $\alpha = 0.05$) and 99% ($\alpha = 0.01$), respectively. Higher z-score and lower p-value indicated the identified location was spatially clustered and statistically higher than surrounding areas (i.e., hot spots). Identified those hot spots at 95% and 99% CLs were plotted in the NJ map to investigate how closely identified hot spots (from this biomonitoring data) were located across NJ. In addition, higher PFAS analyte concentration data (NJ adults that were detected over the 95% threshold of the NHANES data in 2015–2016) was also plotted on the same map to further investigate spatial relationships. All geographical analyses and mappings were conducted on the GIS program (ArcGIS Pro ver. 2.4; Esri, Redlands, CA).

3. Results and discussion

3.1. Statewide biomonitoring study

The demographic information of the serum specimens collected for this NJBM study are summarized in Table 1, with reference NJ Census data (in 2017) for comparison. Sex proportions in NJBM study were matched well with NJ reference data (goodness-of-fit test; $p = 0.60$), however three age groups were not ($p < 0.01$). A chi-squared test showed more subjects were sampled from old population (60–74 years old) and less-sampled from the young population (20–39 years old). This is probably due to the sources of the NJBM specimens collected from clinical patients that lean towards the older population. Geographic locations (represented by residents in NJ counties) were matched for most counties except for Mercer and Passaic counties. These two counties were over-sampled because the blood bank is located in Mercer County and the clinic laboratory is located in Passaic County, respectively. A regional blood bank, located in Mercer county, was assumed to serve more local blood donors than those who live far away. As shown in Table 1, the NJBM study acquired greater number of Mercer residents at 13.2% when compared to the reference population percentage of 4.2% in the same county. These sampling deviations were corrected by assigning a sample weight for each sample and utilizing it in data analyses.

3.2. PFAS means and percentiles in NJ adults

The summary statistics of the four selected PFAS analytes are

Table 2
Descriptive statistics (GM and percentiles [± 95% CIs]) for the selected four PFAS analytes stratified by sex and age group (n = 1030; 20–74 in age) between 2016 and 2018.

PFAS (ng/mL)	Statewide NJBM Study (2016–2018)				
	GM [95% CI]	50% [95% CI]	75% [95% CI]	90% [95% CI]	95% [95% CI]
PFOA	2.04 [1.81–2.30]	2.01 [1.80–2.25]	3.06 [2.70–3.46]	4.24 [3.55–5.07]	5.39 [4.50–6.44]
Male (n = 513)	2.31 [2.06–2.60]	2.37 [1.99–2.84]	3.41 [3.08–3.78]	4.57 [3.71–5.61]	5.29 [4.09–6.85]
Female (n = 517)	1.81 [1.57–2.09]	1.77 [1.57–2.00]	2.54 [2.10–3.08]	3.88 [2.97–5.07]	5.45 [4.28–6.94]
20-39 (n = 315)	1.87 [1.70–2.06]	1.89 [1.71–2.08]	2.74 [2.35–3.20]	3.64 [3.12–4.25]	4.71 [4.06–5.48]
40-59 (n = 429)	2.03 [1.73–2.38]	2.06 [1.73–2.45]	2.99 [2.48–3.60]	3.89 [2.76–5.49]	5.28 [3.40–8.20]
60-74 (n = 286)	2.44 [2.04–2.91]	2.50 [1.94–3.22]	3.99 [3.29–4.82]	5.75 [4.52–7.31]	7.66 [6.34–9.24]
PFNA	0.79 [0.69–0.89]	0.78 [0.69–0.89]	1.12 [0.99–1.27]	1.54 [1.31–1.81]	1.97 [1.61–2.42]
Male (n = 513)	0.88 [0.77–1.01]	0.93 [0.81–1.06]	1.26 [1.08–1.47]	1.59 [1.37–1.85]	1.97 [1.59–2.44]
Female (n = 517)	0.70 [0.62–0.80]	0.68 [0.60–0.78]	0.98 [0.88–1.09]	1.43 [1.19–1.71]	2.00 [1.49–2.68]
20-39 (n = 315)	0.71 [0.63–0.81]	0.71 [0.63–0.81]	1.02 [0.92–1.12]	1.39 [1.05–1.85]	1.49 [1.29–1.72]
40-59 (n = 429)	0.79 [0.67–0.93]	0.79 [0.66–0.95]	1.11 [0.99–1.25]	1.51 [1.21–1.87]	1.81 [1.15–2.85]
60-74 (n = 286)	0.93 [0.81–1.08]	0.98 [0.81–1.18]	1.43 [1.24–1.65]	2.05 [1.75–2.41]	2.57 [2.19–3.02]
PFHxS	1.10 [0.91–1.34]	1.22 [1.01–1.47]	1.92 [1.65–2.24]	3.28 [2.74–3.91]	4.29 [3.71–4.97]
Male (n = 513)	1.41 [1.21–1.65]	1.51 [1.32–1.72]	2.41 [2.14–2.72]	3.78 [3.21–4.45]	4.80 [3.96–5.81]
Female (n = 517)	0.87 [0.67–1.14]	0.89 [0.64–1.23]	1.48 [1.11–1.97]	2.43 [1.82–3.23]	3.64 [3.01–4.41]
20-39 (n = 315)	1.01 [0.83–1.23]	1.14 [0.93–1.39]	1.74 [1.42–2.15]	2.88 [2.23–3.73]	4.05 [2.86–5.75]
40-59 (n = 429)	1.06 [0.83–1.35]	1.18 [0.96–1.46]	1.87 [1.55–2.26]	2.87 [2.12–3.89]	3.70 [2.38–5.78]
60-74 (n = 286)	1.42 [1.11–1.83]	1.40 [1.06–1.86]	2.63 [2.03–3.41]	4.42 [3.66–5.34]	5.58 [4.66–6.67]
PFOS	2.94 [2.74–3.14]	3.04 [2.76–3.36]	4.80 [4.56–5.05]	7.51 [6.67–8.45]	9.95 [9.02–11.0]
Male (n = 513)	3.55 [3.24–3.89]	4.00 [3.60–4.44]	5.37 [4.91–5.86]	7.88 [7.18–8.66]	9.95 [8.34–11.9]
Female (n = 517)	2.45 [2.25–2.66]	2.38 [2.19–2.59]	3.91 [3.58–4.28]	6.41 [5.06–8.13]	9.83 [8.09–12.0]
20-39 (n = 315)	2.55 [2.33–2.78]	2.67 [2.46–2.89]	4.12 [3.70–4.58]	5.19 [4.79–5.62]	6.36 [5.43–7.44]
40-59 (n = 429)	2.97 [2.58–3.42]	2.98 [2.57–3.45]	4.81 [4.19–5.52]	7.69 [5.90–10.0]	9.76 [7.32–13.0]
60-74 (n = 286)	3.74 [3.18–4.38]	4.46 [3.98–4.98]	6.73 [6.12–7.40]	9.90 [8.96–10.9]	11.5 [9.62–13.7]

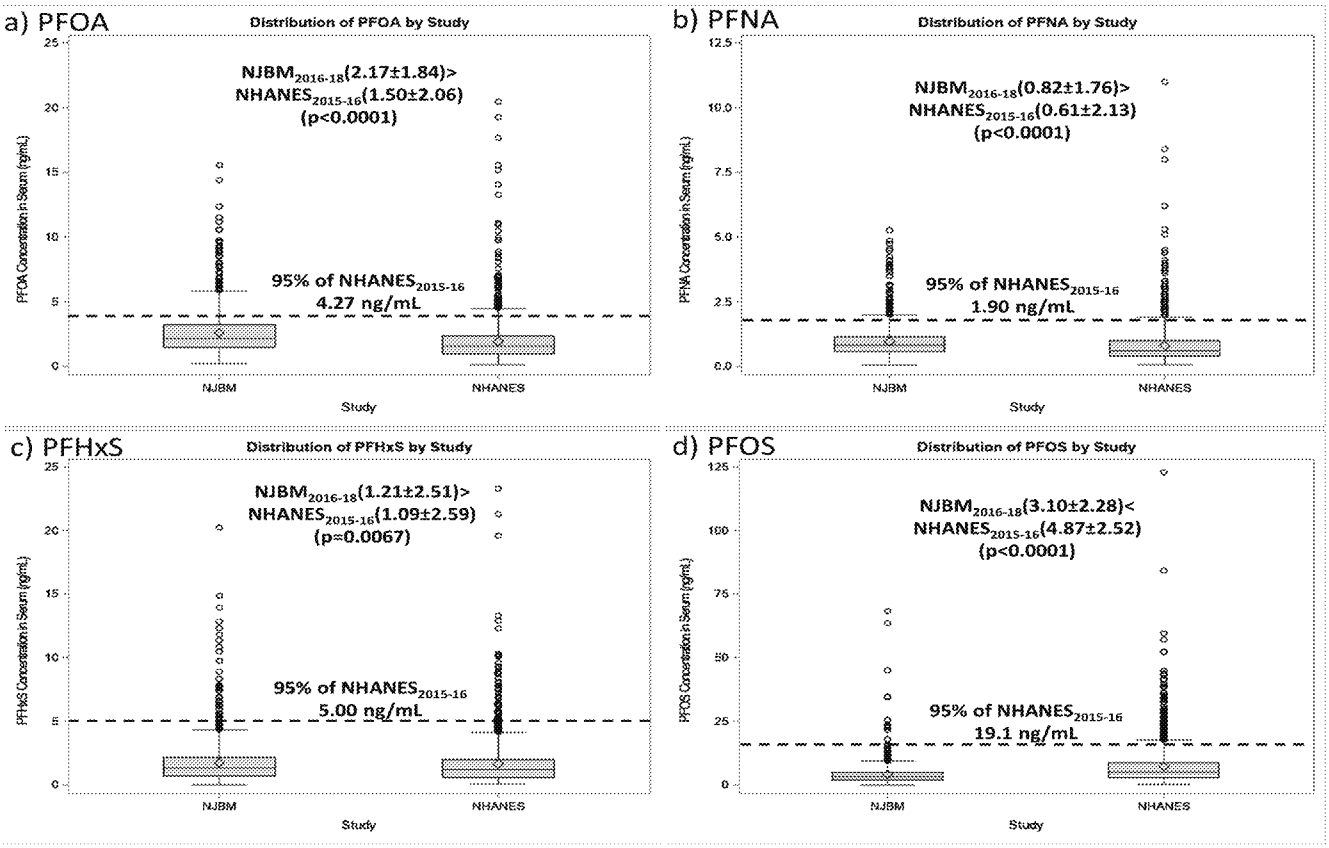

Fig. 1. Box plots for the four selected PFAS concentrations (GM ± GSD; ng/mL) measured in a statewide NJBM study (2016–2018; n = 1030; 20–74 years old) and the CDC nationwide US biomonitoring survey (2015–2016; n = 1473; 20–74 years old). Note: Mean differences were examined by a non-parametric Wilcoxon test ($\alpha = 0.05$).

provided in Table 2. Two sexes and three age groups are further stratified and presented in Table 2 as well. The remaining 8 PFAS analytes are summarized and provided in Table S3. Among the four selected PFAS analytes, the PFOS serum level is the highest (GM and [95% CIs] = 2.94 [2.74–3.14] ng/mL), followed by PFOA, PFHxS, and PFNA (2.04 [1.81–2.30], 1.10 [0.91–1.34], 0.79 [0.69–0.89] ng/mL), respectively. These levels are comparable to the concentrations reported for the U.S. general population (CDC, 2018). They are also comparable to other locations in the world, such as Germany (Yeung et al., 2013a, 2013b), Sweden (Gebbink et al., 2015), Spain (Bartolome et al., 2017), and Australia (Eriksson et al., 2017). Even though absolute concentrations could be different in geographic locations and populations studied, the rank of PFAS serum levels (i.e., PFOS > PFOA > PFHxS > PFNA) were consistent with the studies cited above.

3.3. Comparison with the NHANES data

PFAS serum levels found in this study (n = 1030; 2016–2018) were compared to the latest NHANES data (n = 1473; 2015–2016) (Fig. 1). The results showed that PFOA, PFNA, and PFHxS were higher in this study than in NHANES, but PFOS was lower in this study than in NHANES adults. A comparison between NJBM data vs. NHANES in 2017–2018 will be conducted to re-examine the findings when the NHANES data become available. The elevated data of PFOA, PFNA, and PFHxS suggest NJ may have additional sources or exposure routes for these compounds. However, PFOS levels in NJ adults were found to be lower during the 2016–2018 monitoring period compared to NHANES adults monitored in 2015–2016. This could partially be explained by the decreasing trend of PFOS over time in the general U.S. population (Kato et al., 2011) and the U.S. blood donors (Olsen et al., 2017), due to the voluntary phase out of PFOS production in U.S. since 2000.

Post et al. (2017) pointed out continuing exposure to long-chain PFAS, even at lower levels in drinking water, can substantially increases human body burdens, which remain elevated for many years after exposure ends. A NJDEP's statewide occurrence study detected PFOA (65%; ≥4 ng/L) and PFOS (30%; ≥4 ng/L) among 23 NJ PWS in 2006 (Post et al., 2009). In 2009–2010, NJDEP conducted the second statewide occurrence study by measuring 10 PFAS (detection limits ≥5 ng/L) among 30 NJ PWS (Post et al., 2013), and reported a similar percent of detection for PFOA (57%) and PFOS (30%) and additional detections of PFNA (30%) and PFHxS (13%). The Third Unregulated Contaminant Monitoring Rule (UCMR3) database (2013–2015) indicated that the NJ public drinking water system had a higher percent of detection than the national level, excluding NJ PWS, for PFOA (10.2% vs. 1.9%; ≥20 ng/L) and PFNA (2.3% vs. 0.2%; ≥20 ng/L), and similar detection percentages for PFHxS (1.1% vs. 1.1%; ≥30 ng/L) and PFOS (3.4% vs. 1.9%; ≥40 ng/L) (EPA, 2019). Some NJ PWS were linked to PFAS contamination via industrial activities or the use of AFFFs. For example, PFNA was detected in public water at high concentrations up to 150 ng/L in southwest NJ. This area is near a facility using PFNA as a processing aid in fluoropolymer manufacturing (Post et al., 2013). PFOA was detected in public water at high concentrations up to 100 ng/L in Ocean county, NJ (Post et al., 2013) from an industrial facility that used PFOA-containing materials (Procopio et al., 2017). Numerous PFAS (total PFAS concentration up to 174 ng/L) were detected at PWS in Atlantic county, NJ which was near a civil-military airport that uses AFFFs (Post et al., 2013). In general, specific areas are associated with community exposure to PFAS via drinking water. Such areas include contamination of groundwater and surface water near industrial facilities that produce/utilize PFAS (Landsteiner et al., 2014), landfill sites where PFAS-containing wastes are treated (Lindstrom et al., 2011), or military/civil airports from the use of AFFFs (Houtz et al., 2013). Besides PFAS-

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contaminated drinking water, other potential sources may also contribute to PFAS exposure, including food consumption, air inhalation in both indoor and outdoor environments, contact and ingestion of indoor and outdoor dust, soils, or consumer products. Dietary intake is the major PFAS exposure pathway for the general population, whereas drinking water exposure is dominant for populations whose drinking water source is contaminated (Vestergren and Cousins, 2009; Post et al., 2017; Bartell, 2017). PFAS has been detected in a variety of food including crops, fish, seafood as well as in food packaging (EPA, 2016).

The estimated half-lives of PFAS vary significantly by analyte, from 2.3 years to 15.5 years. The half-life of a chemical depends on its physicochemical properties, elimination mechanisms in human body (e.g., renal clearance), or exposure levels. Even for individual analyte, half-lives can be different by person and physiological conditions or excretion processes (e.g., menstrual blood loss or lactation) which differ by sex and age. For PFOA, previous studies reported PFOA half-life ranging from a median of 2.3 years (n = 200; Bartell et al., 2010) to a mean of 3.9 years (n = 39; Worley et al., 2017). However, the PFOA estimates varied from person-to-person (Olsen et al., 2007), ranging from 1.5 to 9.1 years in 26 retired fluorochemical production workers. For PFOS, the estimates were longer than PFOA in the same population studied. Li et al. (2018) reported the mean PFOS half-life of 3.4 years (vs. 2.7 years) and Olsen et al. (2007) reported the mean half-life of 5.8 years (vs. 3.8 years). On the other hand, a community exposure study reported a shorter PFOS half-life (3.3 years) compared to the PFOA half-life (3.9 years) (Worley et al., 2017). For PFHxS, the estimates were much longer than both PFOA and PFOS. The mean PFHxS estimated half-life ranging from 5.3 years (Li et al., 2018) to 15.5 years (Worley et al., 2017). In general, the estimated half-lives ranked (from shorter to longer) in the order of PFOA < PFOS < PFHxS. It is likely that the large variations in half-life are due to different exposure levels and study populations. Olsen et al. (2007) estimated half-lives based on very high levels for the retired workers (24 males and 2 females, 56–75 years old), with the mean of 1378 ng/mL for PFOA, 1976 ng/mL for PFOS, and 3109 ng/mL for PFHxS. Li et al. (2018) conducted a half-life study based on a community exposure case for a relatively younger population (20 males and 30 females, 15–50 years old). The exposure level of this study was much lower, with means of 21.1, 387, and 353 ng/mL for PFOA, PFOS, and PFHxS, respectively. Worley et al. (2017) carried out the community study for 153 subjects (≥12 years old), including 63 males and 90 females. The three target analytes were found at much lower levels, with GM of 16.3, 39.8, and 6.4 ng/mL, for PFOA, PFOS, and PFHxS, respectively.

3.4. Associations among PFAS and between PFAS and serum lipid levels

LDL cholesterol, HDL cholesterol, TC, TG, and TL contents were measured for each sample. Correlations of the measured PFAS concentrations with the five serum lipid levels as well as correlations among the four PFAS were examined. The results are presented in Table 3. The four selected PFAS were significant ($p < 0.01$) and strongly ($r_s \geq 0.5$) correlated with each other, indicating similar or common background source(s) or pathways(s) of exposure are present among the study population. Previous NHANES studies also reported distinct correlations ($p < 0.01$) among PFOA, PFNA, PFHxS, and PFOS in general population (≥12 years old; Calafat et al., 2007) and in younger populations (3–11 years old; Ye et al., 2018). Positive correlation coefficients and lower p-values indicated PFOA and PFOS were associated with four lipid levels (i.e., LDL cholesterol, TC, TG, and TL). Significantly positive associations remained the same for PFNA with the four lipid levels. PFHxS concentrations were assuredly associated with LDL cholesterol ($r_s = 0.08$), TG ($r_s = 0.10$), and TL ($r_s = 0.08$), but not for TC ($r_s = 0.05$). These relationships were observed in some of the previous studies, which showed positive associations between the increased serum PFOA/PFOS and TC levels (Nelson et al., 2010; Eriksen et al., 2013; Fisher et al., 2013; Geiger et al., 2014) as well as TG levels (Olsen et al., 2003; Steenland et al., 2009). A study showed positive associations between PFOA/PFNA/PFOS and TC, LDL, and TG levels in Taiwanese children (n = 225; age between 12 and 15 years old; Zeng et al., 2015). However, there were inconsistent findings in some of the other studies. The association between PFOA exposure and increased cholesterol levels was consistent, but it was inconsistent for LDL cholesterol and TG levels or almost not associated with HDL cholesterol levels (NJDEP, 2017). For PFOS, there was consistent evidence between PFOS exposure and increased cholesterol levels, but that association was somewhat less clear for LDL cholesterol levels or weak for HDL cholesterol or TG levels (NJDEP, 2018). One of those confounding variables may be related to dietary habits and/or lifestyle choices such as high fat diets, alcohol intake, smoking, and exercise. This study was designed to collect anonymous samples; therefore, personal information, including above variables and fasting conditions that may affect personal lipid levels, was not able to be obtained for further data analyses.

3.5. Differences in sex-age strata and total lipid data

Paired demographic and serum lipid data have been tested for the log-transformed PFOA, PFNA, PFHxS, and PFOS concentrations in the survey regression model, and the results are provided in Table 4. Multiple comparisons among the six sex-age strata were further conducted and the results are summarized in Fig. 2. The observed PFAS differences were driven by significant differences between lower PFAS levels in young (20–39 years old) and middle aged (40–59 years old) females compared to higher levels in males (20–74 years old) and senior females (60–74 years old). The pattern of the lower PFAS concentrations in younger females could be explained by greater excretion rate of this group, i.e., shorter half-lives in younger females are due to excretion through menstrual blood loss and lactation, in addition to the

Table 3
Spearman correlation coefficients, p-values and n for the selected four PFAS analytes (ng/mL; un-weighted) and five lipid levels (LDL cholesterol, HDL cholesterol, total cholesterol, triglyceride, and total lipid; mg/dL) measured in NJ adults for the NJBM study.

Correlation coefficient	PFOA (n = 1030)	PFNA (n = 1030)	PFHxS (n = 1030)	PFOS (n = 1030)	LDL cholesterol (n = 694)	HDL cholesterol (n = 747)	Total cholesterol (n = 978)	Triglyceride (n = 978)	Total lipids (n = 978)
PFOA	1.000	0.654**	0.702**	0.693**	0.088*	0.008	0.080*	0.078*	0.090**
PFNA		1.000	0.498**	0.680**	0.116**	−0.018	0.124**	0.109**	0.127**
PFHxS			1.000	0.613**	0.083*	−0.015	0.052	0.097**	0.077*
PFOS				1.000	0.120**	−0.034	0.085**	0.070*	0.088**
LDL cholesterol					1.000	0.305**	0.907**	0.258**	0.793**
HDL cholesterol						1.000	0.583**	0.066	0.460**
Total cholesterol							1.000	0.466**	0.945**
Triglyceride								1.000	0.699**
Total lipids									1.000

*$p < 0.05$; **$p < 0.01$.

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Table 4
Least-squared (LS) mean concentrations (ng/mL) from a survey regression analysis for log-transformed four PFAS measurements in NJ adults for NJBM study.

Model/Parameters	Estimate	Standardized Estimate	P-value	Model/Parameters	Estimate	Standardized Estimate	P-value
Ln(PFOA)				Ln(PFNA)			
Intercept	0.763	0.000	< .001	*Intercept*	−0.243	0.000	0.060
Sex-Age				*Sex-Age*			
Female, 20-39	−0.441	−0.286	< .001	Female, 20-39	−0.443	−0.305	< .001
Female, 40-59	−0.243	−0.163	0.028	Female, 40-59	−0.260	−0.186	0.011
Female, 60-74	0.133	0.069	0.171	Female, 60-74	0.054	0.030	0.575
Male, 20-39	0.034	0.022	0.665	Male, 20-39	−0.026	−0.018	0.795
Male, 40-59	−0.025	−0.016	0.778	Male, 40-59	−0.043	−0.029	0.630
Male, 60-74	0.000	0.000	–	Male, 60-74	0.000	0.000	–
Serum Lipid	0.000	0.032	0.448	*Serum Lipid*	0.000	0.077	0.024
Ln(PFHxS)				Ln(PFOS)			
Intercept	0.234	0.000	0.234	*Intercept*	1.088	0.000	< .001
Sex-Age				*Sex-Age*			
Female, 20-39	−0.714	−0.300	0.002	Female, 20-39	−0.636	−0.298	0.001
Female, 40-59	−0.541	−0.236	0.003	Female, 40-59	−0.435	−0.212	0.018
Female, 60-74	0.018	0.006	0.899	Female, 60-74	0.070	0.026	0.652
Male, 20-39	0.043	0.018	0.750	Male, 20-39	−0.069	−0.032	0.701
Male, 40-59	−0.083	−0.035	0.624	Male, 40-59	−0.006	−0.002	0.974
Male, 60-74	0.000	0.000	–	Male, 60-74	0.000	0.000	–
Serum Lipid	0.000	0.036	0.466	*Serum Lipid*	0.000	0.072	0.025

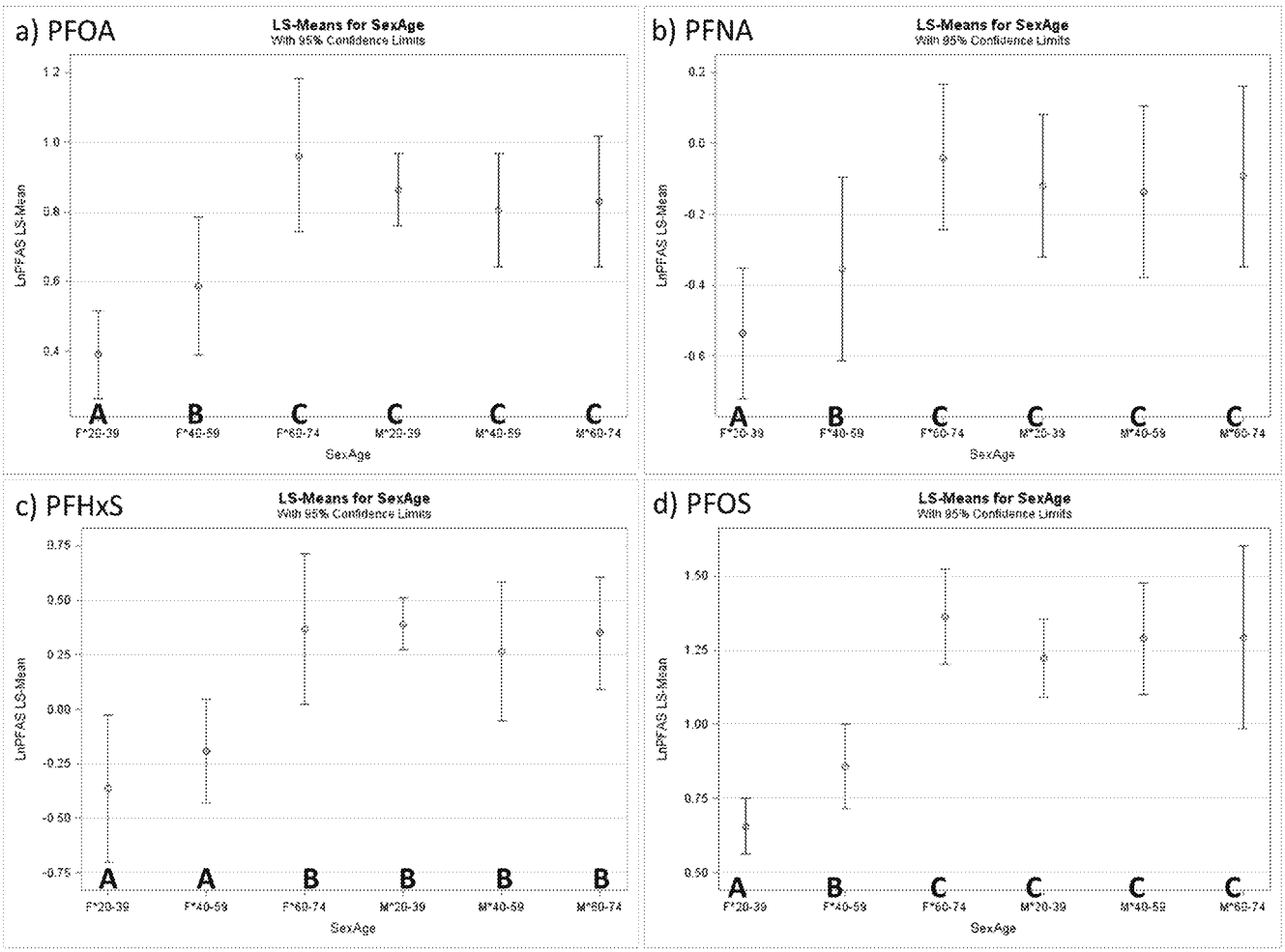

Fig. 2. Least-squared mean ± 95% CIs for the selected four PFAS, stratified by six sex-age strata and compared within the NJBM study. Note: Pairwise mean comparisons (significance level of $\alpha = 0.05$) were conducted for the six sex-age strata and summarized by ranking with letters, indicating A < B < C, in the figure.

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other excretion routes that occur in all age groups. PFAS half-lives for younger females is shorter than older females and males. Li et al. (2018) estimated half-lives of the three PFAS analytes for males and females between 15 and 50 years old. The authors reported shorter half-lives of PFOA (2.4 years), PFOS (3.1 years), and PFHxS (4.7 years) for females, and longer half-lives of 2.8 (PFOA), 4.6 (PFOS), and 7.4 (PFHxS) years for males in the same study population. The differences of half-lives between females and males were significant for PFHxS and PFOS ($p < 0.01$), but not significant for PFOA ($p = 0.29$). These sex and age differences were reported in previous studies. Kato et al. (2011) presented similar patterns of the four PFAS (PFOA, PFNA, PFHxS, and PFOS), i.e. higher in males vs. females and in older vs. younger counterparts in the general U.S. population. Olsen et al. (2017) reported similar sex and age differences for PFOA, PFHxS, and PFOS concentrations observed in adult blood donors across U.S. in the period of 2000–2015.

However, total lipid data were not consistently significant in all the four tested regression models. Specifically, PFNA and PFOS were significant ($p < 0.05$), but not for PFOA and PFHxS. As mentioned above in section 3.4, the increased serum lipid levels were generally associated with higher serum PFOA concentrations (NJDEP, 2017) and PFOS concentrations (NJDEP, 2018); but not consistently observed in all reviewed human studies. Thus, the observed patterns are somewhat similar to previous inconsistent findings above. In addition, standardized β estimates for serum TL (< 0.08; Table 4) were not stronger than the standardized estimates for sex-age strata (i.e., young and middle age females vs. the rest of the four sex-age strata (> 0.16)), which, in part, explains these insignificant serum lipid results for PFOA and PFHxS in the model, respectively.

3.6. Identification of hot spots and characterization of spatial patterns

As a part of NJBM study objectives, obtained NJBM PFAS data (i.e., PFOA, PFNA, PFHxS, and PFOS) were further applied to screen for disparities across the study population in NJ. An investigative spatial analysis to characterize spatial patterns among the monitored PFAS serum datasets was conducted and the results are presented in Fig. 3. Counts of individual high PFAS data and the number of collected samples, with corresponding ZIP codes, are provided in Table S4. A note was provided to specific ZIP codes if a ZIP code was also identified as a hot spot at 95% and 99% CLs. Based on visual inspections for finalized GIS maps (see Fig. 3), many locations with higher PFAS data (black circles) were situated in north and central NJ, specifically along the corridor between two highly-populated metropolitan areas such as New York and Philadelphia. According to EPA's UCMR3 database (EPA, 2019), multiple communities along or near the New York-Philadelphia corridor were identified as areas where PFAS-detected drinking water was observed in the past. In general, identified hot spot locations were substantially driven by higher PFAS measurements. For PFOA and PFNA, all identified hot spots at 95% (orange boxes) and 99% (red boxes) CLs were matched with the measured higher PFOA and PFNA concentration data (see Table S4 in detail). For PFHxS and PFOS, these spatial patterns were noticeable, but not as apparent as PFOA and PFNA cases. Some of the identified hot spots were from a single measurement in distinct zip code and the monitored PFAS serum data didn't cover all NJ locations. Therefore, our study findings are not definitive but suggestive for plausible spatial patterns for the four PFAS across NJ. Further quantitative spatial analysis combined with complete PFAS occurrence data and serving information for drinking water in NJ is recommended to confirm spatial patterns observed in this manuscript as well as to associate higher PFAS serum measurements with people living in areas served with PFAS-contaminated drinking water.

3.7. Study limitations

There are limitations associated with the NJBM study. First, remnant biospecimens from clinical laboratories and blood banks were used for the study. The estimated study means and percentiles were not truly obtained from population-based design, even though the justification was conducted to correct the sampling bias and the processed data showed that the results were comparable to the population data. Second, despite taking great efforts to obtain geographically distributed study subjects, some sex-age-county strata (Table S2) were missed. This would result in some uncertainties for the study-estimated data. Third, this study was limited to integrated cross-sectional PFAS levels in serum at a certain period of time, which is difficult to pin-point significant exposure route(s) or to track the trends of PFAS levels in study population. Lastly, this study design would not allow for collection of individual exposure information or dietary/lifestyle information, which limits the ability to identify potential exposure sources or routes. Given above limitations, cautions should be taken in interpreting data and comparing the results reported in this study with others.

4. Conclusions

Emerging contaminants of PFAS were not systematically monitored for NJ residents, although some residents may have been exposed to low levels of PFAS through contaminated drinking water. This study presented the first statewide biomonitoring data for emerging PFAS contaminants in selected NJ adult groups. The study results provide preliminary information to the State to assess PFAS exposure in NJ, design future general population study, classify subpopulations with PFAS risks, and identify potential PFAS hot spots in NJ.

By measuring PFAS in serum from 1030 NJ adults (20–74 years), the NJBM study showed PFOA, PFNA, and PFHxS were elevated in participating NJ adults compared to NHANES adults ($n = 1473$; in 2015–2016). Within the participating NJ adults, all 4 selected PFAS analytes were significantly elevated in males than in females as well as in older adults (60–74 years old) than younger counterparts (20–59 years old). Further stratification with sex and age strata revealed the differences were primarily derived from significantly lower PFAS levels in younger females vs. in older females and males of all ages.

Collective study findings may suggest NJ population was burdened by the emerging PFAS contamination, notably more influenced via PFAS-contaminated drinking water, besides daily exposures through food, consumer products and contacts with house dust or soil. Even though long-chain PFAS such as PFOA and PFOS are no longer manufactured in the U.S., these compounds persist in the environment and people can continue to be exposed to them. Therefore, statewide biomonitoring efforts toward collecting personal exposure and lifestyle information are recommended to 1) prospectively track the trends of PFAS in NJ population, 2) pinpoint hot spots in the State and 3) further differentiate contributing sources to PFAS data for the NJ population.

Disclaimer

The opinions expressed in this article are the author's own and do not necessarily reflect the view of the New Jersey Department of Health, or the New Jersey State Government. The authors declare that they have no conflict of interest.

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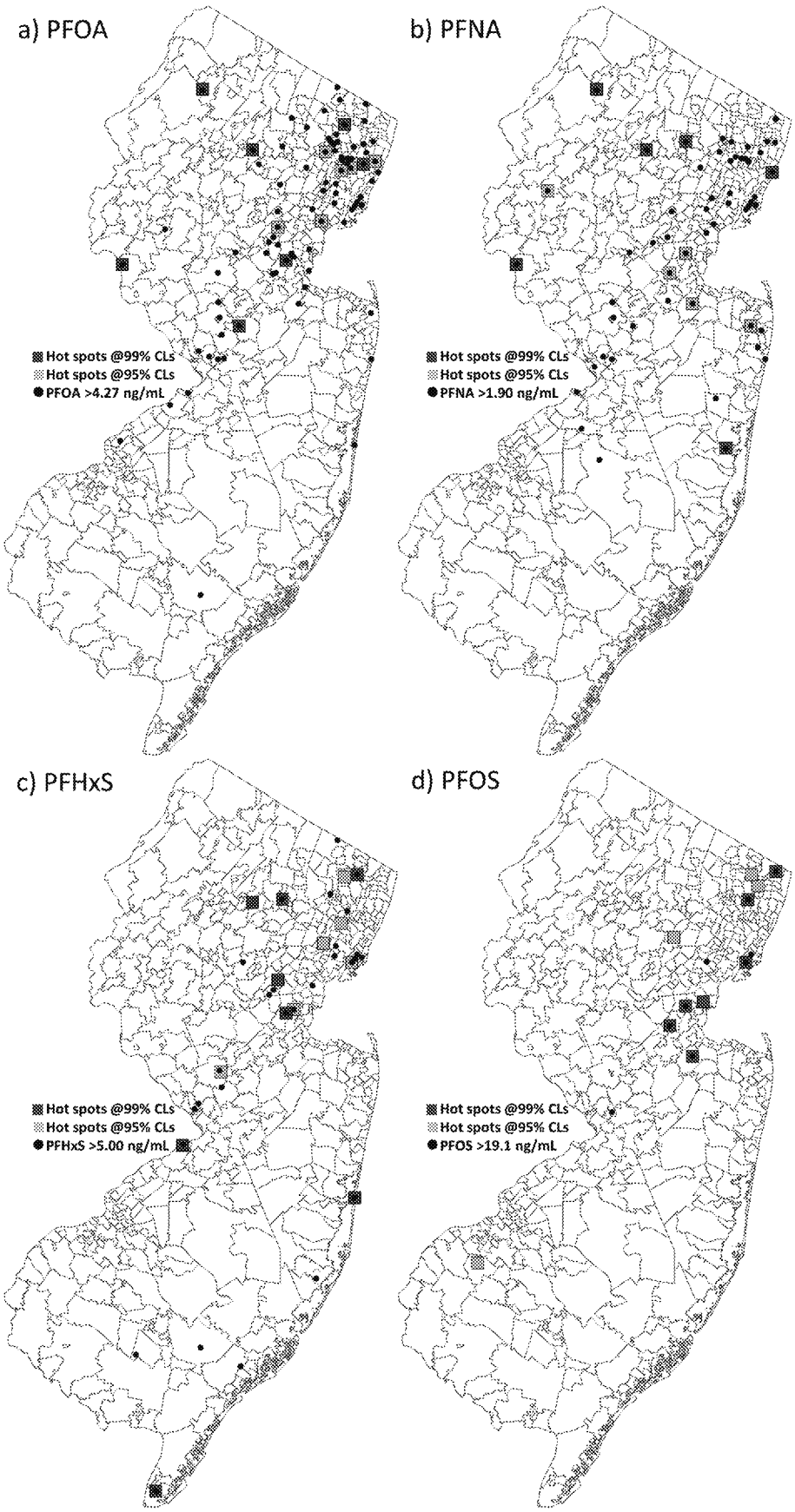

Fig. 3. Locations of subjects (black circles; detected over the 95% threshold NHANES in 2015–2016) and hot spots (orange and red boxes at 95% and 99% confidence levels (CLs), respectively) in NJBM study to show spatial patterns for a) PFOA, b) PFNA, c) PFHxS, and d) PFOS across NJ. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2019.10.008.

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